949 | BEDSIDE
Prognostic value of excessive atrial ectopy in relation to atrial fibrillation and ischemic stroke in a large pooled scandinavian holter cohort
1Bispebjerg University Hospital, Copenhagen, Denmark; 2Skane University Hospital, Malmo, Sweden

Background: Increased atrial ectopy has in recent years shown to increase the risk of atrial fibrillation and possible through undetected paroxysmal atrial fibrillation also the risk of ischemic stroke.

Purpose: We aimed to estimate the prognostic value of increased atrial ectopy in relation to atrial fibrillation (AF) and ischemic stroke in a large pooled dataset of two population-based cohorts from Sweden and Denmark.

Methods: The Scandinavian Holter Cohort (n=1065) is a pooled cohort consisting of “Copenhagen Holter Study” (n=678) and “Men Born in 1914” (n=387). Both are previously known from published studies on increased atrial ectopy and the risk of atrial fibrillation or stroke and have a similar follow-up of 14 years. The combined cohort consists of a middle aged and elderly population between the age of 55 and 75 with cardiovascular risk factors but no previous incidence of stroke, myocardial infarction or atrial fibrillation. All subjects had up to 48-hours ambulatory ECG recording, blood sampling and a clinical examination.

According to previous studies excessive atrial ectopy was defined as >30 premature atrial contractions per hour/day.

Results: At baseline 114 subjects were classified as having increased atrial ectopy (10.7%). In the follow up 107 subjects (10.1%) were diagnosed with incident atrial fibrillation. 121 subjects (11.4%) suffered a first isometric stroke. AF and stroke occurred more frequently in subjects with excessive atrial ectopy than those without. (18.1 vs. 7.8/1000 person-years; P=0.001) and (20.3 vs. 8.9/1000 person-years; P=0.0002) respectively. In Cox regression models, excessive atrial ectopy remained associated with AF and stroke after adjustment for potential confounders. (HR, 2.25; 95% CI, 1.38–3.67; P=0.001) and (HR, 1.79; 95% CI, 1.13–2.84; P=0.014) respectively. The incidence of stroke in subjects with excessive atrial ectopy and a CHA2DS2VASC score of ≥2 was 2.5% per year which is comparable to the risk observed in atrial fibrillation.

Conclusions: Excessive atrial ectopy increases the risk of both incident atrial fibrillation and ischemic stroke in this large pooled population. The risk of stroke seems to be comparable with those reported in atrial fibrillation.

950 | BEDSIDE
Prognosis in patients with atrial fibrillation with a presumed temporary cause in a community based cohort study
L. Fauchier1, N. Clementy1, D. Angoulvant1, D. Babuty1, A. Bernard1, G.Y. H. Lip2.
1Laon University Hospital, Laon, France; 2Birmingham City Hospital, Birmingham, United Kingdom

Atrial fibrillation (AF) may be related to an acute, temporary cause, including alcohol use (eg, “holiday heart syndrome”), myocardial ischemia or infarction, myocardial/periocarditis, pulmonary embolism or other pulmonary diseases, hyperthyroidism, and other metabolic disorders. In such cases, successful treatment of the underlying condition may promote the resolution of AF. However, it remains unclear whether the risk of ischemic stroke is different in this setting, and if arrhythmic/antibiotic management should be different, particularly in patients with a low CHA2DS2-VASc score.

Our objective was to study the risk of stroke in AF patients with and without such precipitating cause.

Methods and results: All patients with AF seen in our institution between 2000 and 2010 were identified in a database. Adverse outcomes were investigated during follow-up. Among 8962 patients with AF, we focused the analysis on 5467 patients with non-permanent AF of whom 920 (17%) had at least one presumed “temporary cause” of AF, as defined above.

In AF patients with a “temporary cause”, CHA2DS2-VASc score was higher than in other patients (3.6±1.7 versus 3.0±1.7, p<0.0001) and treatment with oral anticoagulation was less frequent (37% versus 52%, p<0.0001). Over a mean follow-up of 2.5 years (maximum 10.0 years), 78 stroke/TE and 156 deaths were recorded in the 5467 patients. The rates of stroke/TE were similar in AF patients with a “temporary cause” compared to other AF patients (Crude hazard ratio 1.02, 95% CI 0.97–1.07, p=0.11; Adjusted HR 1.02, 95% CI 0.79–1.32, p=0.65, after adjustment for CHA2DS2-VASc and OAC use). Mortality was higher in patients with a “temporary cause” compared to other AF patients (Crude HR 1.82, 95% CI 1.52–2.16, p<0.0001; Adjusted HR 1.43, 95% CI 1.18–1.75, p=0.004 for CHA2DS2-VASc and OAC use).

The findings were similar in patients in the low, moderate- and high-risk groups for stroke according to CHA2DS2-VASc risk score. In patients with a “temporary cause” of AF, prescription of oral anticoagulation was independently associated with a better prognosis for death/stroke/thromboembolism (HR=0.55, 95% CI 0.38–0.71, p<0.0001 after adjustment for age and CHA2DS2-VASc score).

Conclusion: In a real life cohort study, AF patients with a presumed “temporary cause” had a similar risk of stroke/thromboembolism and a worse prognosis for all cause mortality compared to other AF patients. Use of oral anticoagulation was associated with a better prognosis in these patients.

951 | BEDSIDE
Incidence of atrial fibrillation in different types of cancer: a Danish nationwide cohort study
C. Jacobsen1, N. Carlson1, M. Lamberts2, M.L. Hansen1, C. Torp-Pedersen1, G.H. Gislason1, M. Schou1.
1Department of Cardiology, Gentofte Hospital, University of Copenhagen, Hellerup, Denmark; 2Department of Cardiology, Herlev Hospital, University of Copenhagen, Herlev, Denmark; 5Department of Cardiology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; 4Department of Health, Science and Technology, Aalborg University, Aalborg, Denmark; 3Department of Cardiology, Gentofte Hospital, University of Copenhagen, Herlev, Denmark

Background: The prevalence of both atrial fibrillation and malignancies are increasing in the elderly. Whether the two conditions are co-existing and whether malignancies are associated with future atrial fibrillation is, however, unknown.

Purpose: The aim of the present study was to examine the association between different types of cancer and future atrial fibrillation (AF).

Methods: Using national databases, the general Danish population was followed from 2000 until 2012. Patients <18 years of age and patients with diagnosed cancer or AF before 2000 were all excluded. Cancer types were identified, and incidence rate ratios (IRRs) of AF in sub types cancer patients compared to the general population were calculated in a Poisson regression model adjusted for risk factors, age and sex.

Results: A total of 5,539,824 individuals were included in the study. Cancer was diagnosed in 330,296 patients. The mean age of the cancer population was 66.5 years (66.5–66.5) and 47.4% were males. IRRs of AF in all cancer types were significantly increased and for overall cancer IRR was 1.50 (95% confidence interval (CI) 1.48–1.53). Stratified according to type of cancer, the strongest association was observed between AF and lung cancer (IRR of 3.59 (95% CI 3.43–3.76)). The other major types of cancer: colon cancer (IRR: 1.45 (95% CI 1.38–1.53)), renal cancer (IRR: 1.41 (95% CI 1.33–1.51)), breast cancer (IRR: 1.23 (95% CI 1.18–1.29)) prostate cancer (IRR: 1.22 (95% CI 1.18–1.27)) and the remaining other types of cancer were also associated with an increased (IRR: 1.61 (95% CI 1.53–1.70)) risk of AF (P<0.0001 for all cancer types).

Conclusion: In this nationwide cohort study we observed that different major cancer types were associated with an increased incidence of AF, particularly with regard to lung, colon and urinary tract cancers. More focus on management and research in atrial fibrillation in malignancy is warranted.

952 | BEDSIDE
Improving AF detection in patients with cryptogenic stroke. Insights from a prospective cohort with insertable cardiac monitor
B. Benito1, E. Valles2, E. Cuadrado3, S. Cabrera2, P. Ramos2, A. Ois2, A. Rodriguez-Campeo3, J. Roque1, J. Marti-Almort1, G. H. Lip1,2,3,4.
1Hospital del Mar Medical Research Institute (IMIM), Cardiology Research Program, Barcelona, Spain; 2Hospital del Mar, Cardiology Department, Barcelona, Spain; 3Hospital del Mar Medical Research Institute (IMIM), Neurology Research Program, Barcelona, Spain

Background: Up to 30% of ischemic strokes are of undetermined etiology or cryptogenic. Subjects with arrhythmogenic atrial fibrillation (AF) could be the underlying cause in some cases. Current guidelines are not specific about the best strategy for AF detection.

Aims: To assess the AF-detection rate and time-course in a population with cryptogenic stroke (CS) receiving an insertable cardiac monitor (ICM), in comparison to a standard outpatient strategy.

Methods: Between 2005–2014, 290 patients were diagnosed with CS at our center, and received one of these two strategies for post-admission AF-detection: 1) conventional strategy, i.e. ambulatory 24-h Holter; and, if negative, 7 day-Holter monitoring (historical cohort, 2005–2012); 2) ICM implant during initial hospital admission (prospective cohort, 2013–2014). AF episodes lasting >1 min were recorded during 1 year following CS.

Results: Of the 290 patients (59% women, mean age 78±7, 73% with hypertensive disease) 164 (56%) patients were selected to receive ICM implant during initial hospital admission. The AF-detection rate was significantly higher in the ICM group (41% vs. 3%, p<0.0001). The AF-detection time was significantly shorter in the ICM group (12±10 days vs. 90±80 days, p<0.001).

Conclusion: ICM implantation is of value in the acute hospital setting for the diagnosis and management of AF in patients with CS.
Conclusions: In patients with CS, continuous monitoring with ICM is superior to conventional strategies for AF-detection. The incidence of AF in patients with CS could be extremely high, especially within the first month following CS, which alerts about the need for early monitoring in these patients.

953 | BEDSIDE
Atrial high rate episodes and silent ischemic brain lesions in patients with cardiac implantable electronic devices: unmasking silent atrial fibrillation embolic risk


Background: Cardiac implantable electronic devices (CIED) monitoring reveal silent IBL on CT-scan. AHRE represent a kind of silent AF where manage-

AHRE is present. The incidence of AHRE was significantly related to the presence of silent IBL was significantly related to the presence of AHRE. Multivariable analyses demonstrated that the presence of AHRE was an independent predictor for silent IBL in patients without prior history of AF or stroke (OR 3.12 [1.06–9.20; p < 0.05]).

Table 1. Risk of ischemic brain lesions on CT-scan in patients with history of AF or Stroke/TIA

<table>
<thead>
<tr>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.04</td>
<td>0.97–1.11</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>2.19</td>
<td>0.73–6.61</td>
</tr>
<tr>
<td>CHADS score</td>
<td>1.63</td>
<td>0.94–2.91</td>
</tr>
<tr>
<td>CHA2DS2Vasc score</td>
<td>1.33</td>
<td>0.91–1.94</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>2.71</td>
<td>0.51–12.86</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.54</td>
<td>0.54–4.35</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>1.62</td>
<td>0.57–4.61</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>1.08</td>
<td>0.06–24.5</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>0.87</td>
<td>0.23–3.37</td>
</tr>
<tr>
<td>Small vessel disease</td>
<td>2.10</td>
<td>0.77–5.72</td>
</tr>
<tr>
<td>AHRE &gt; 5 min</td>
<td>3.28</td>
<td>1.18–9.08</td>
</tr>
</tbody>
</table>

955 | BEDSIDE
Is TEE mandatory in patients undergoing ablation of AF with uninterrupted NOACs? Results from a prospective multicenter registry

L. Di Biase 1, J.D. Burkhardt 1, C. Trivedi 1, S. Mohanty 1, P. Mohanty 1, D. Lakkireddy 1, J. Sanchez 1, J. Gallinghouse 1, S. Beheiry 3, A. Natale 1, D. Lakkireddy 2, J. Sanchez 1, J. Gallinghouse 1, S. Beheiry 3, A. Natale 1.

Cardiac Arrhythmia Institute at St David Medical Center, Un. of T exas and Medical Center, Kansas City, United States of America; 3 California Pacific Medical Center, San Francisco, United States of America

Introduction: Transesophageal Echocardiography (TEE) is suggested in patients undergoing atrial fibrillation ablation while on novel oral anticoagulants (NOACs). We sought to evaluate whether TEE is necessary before AF ablation in patients treated with NOACs.

Methods: We performed a prospective multicenter registry of AF patients undergoing radiofrequency catheter ablation on uninterrupted NOACs (apixaban and rivaroxaban).

All patients were on NOACs for at least four weeks before ablation. Heparin bolus was administered in all patients before trans-septal catheterization to maintain a target ACT above 300 seconds. A subset of 54 patients underwent brain dMRI to detect silent cerebral ischemia (SCI).

Results: A total of 970 patients [514 (53%) Apixaban patients and 456 (47%) rivaroxaban patients] were enrolled for this study. The mean age was 69.5±9.0 years with 82% (85%) patients having non-paroxysmal AF and 636 (65.6%) patients were male. The average CHADS2 VASc score was 3.01±1.3 and CHA2DS2 VASc score was 2±2 in 610 (62.8%) patients. Intracardiac echo showed no LAA thrombus in all patients and smoke in 407 (42%) of the cases. All the dMRI were negative for SCI. One (0.10%) thromboembolic event (TIA) with positive dMRI occurred in a patient on uninterrupted rivaroxaban with long standing persistent AF.

Conclusion: Our study shows that performing AF ablation while on uninterrupted apixaban and rivaroxaban without TEE is feasible and safe. This has important clinical and economical relevance.

956 | BEDSIDE
Successful approaches in reduction of fluorscopy time and radiation dose during catheter ablation for atrial fibrillation

B. Alldhoon, D. Wichterle, P. Peichl, R. Cihak, J. Kautzner. Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Introduction: Fluoroscopy is standard imaging technique for catheter ablation (CA) procedures. However, radiation can be harmful for both the patient and the operator and radiation dose reduction is highly desirable.

Purpose: We aimed to demonstrate our experience in reduction of fluoroscopy time and radiation dose during CA procedures.

Methods: We analysed prospectively collected data from our register for CA of AF performed consecutively from January 2013 to January 2015. 3D mapping system and intracardiac echocardiography were used in all procedures. CA done in 2013 were exposed as control group (group 1). Two approaches were sequentially im-

plemented in practice to decrease radiation dose while maintaining safety and adequate image quality. From January 2014 recommendations for decreasing radiation dose (collimation, minimizing oblique projections, and using the lowest possible x-ray frequency) were implemented (group 2). From November 2014 the low dose manufacturer’s setting including the lowest fluoroscopic dose rate (23 nan-
Ogy/pulse) was applied (group 3). The fluoroscopy time and the total radiation dose were compared between groups using ANOVA.

Results: A total of 922 CA procedures were analysed. The usage of described approaches led to a significant decrease of fluoroscopy time, radiation dose and dose per time (Table 1).

Table 1. Fluoroscopy time and radiation dose

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoroscopy time (min), mean ± SD</td>
<td>50.4±53.3</td>
<td>57.1±41.8</td>
<td>5.4±3.0</td>
</tr>
<tr>
<td>Radiation dose (μGy m²), mean ± SD</td>
<td>881.6±828.1</td>
<td>863.7±1112.3</td>
<td>252.0±279.4</td>
</tr>
<tr>
<td>Dose per time (μGy m²/min), mean ± SD</td>
<td>92.3±176.7</td>
<td>83.9±82.7</td>
<td>50.8±41.1</td>
</tr>
</tbody>
</table>

Conclusions: Radiation dose during CA for AF can be significantly reduced by general recommendations for radiation exposure reduction. Further significant dose reduction can be achieved by application of manufacturer’s low dose pro-

The overall radiation dose reduced by application of all recommendation reduced the overall radiation dose for CA procedures to one third.

957 | BEDSIDE
Long-term comparison of the number of supraventricular ectopic complexes after either radiofrequency ablation or anti-arrhythmic drug therapy in patients with atrial fibrillation (AF)

C. Althede 1, A. Johannesn 1, U. Diven 1, J.S. Jensen 2, P. Raatikainen 2, G. Hindricks 4, H. Wallentinsson 1, P.S. Hansen 1, J.C. Nielsen 1, C. Joens 1, on behalf of MANTRA AF investigators. 1 Gentofte University Hospital, Department of Cardiology, Gentofte, Denmark; 2 Hvidovre Hospital - Copenhagen University Hospital, Department of Cardiology, Hvidovre, Denmark; 3 Tampere University Hospital, Department of Cardiology, Tampere, Finland; 4 Leipzig University Hospital, Department of Cardiology, Leipzig, Germany; 5 Linköping University Hospital, Department of Cardiology, Linköping, Sweden; 6 Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark; 7 Rigshospitalet - Copenhagen University Hospital, Department of Cardiology, Copenhagen, Denmark

Introduction: The vast majority of supraventricular ectopic complexes (SVEC) that initiate atrial fibrillation (AF) originate in the pulmonary veins. Often, pa-

tients with frequent SVEC experience symptoms related to the ectopic activity. Pulmonary vein isolation has been shown to reduce recurrence of AF. The fre-
drometry of SVEC after anti-arrhythmic treatment was performed. The patients underwent TEE and dMRI to detect silent cerebral ischemia (SCI).

Results: A total of 970 patients [514 (53%) Apixaban patients and 456 (47%) rivaroxaban patients] were enrolled for this study. The mean age was 69.5±9.0
958 | BEDSIDE
A dual-phase cardiac CT protocol for complete delineation of left atrial appendage anatomy and thrombus exclusion prior to AF ablation or LAA device exclusion

E. Nicol1, C. Pavitt1, O. Lazoura2, A. Lindsay3, M. Sridharan3, M. Rubens1, S. Padley1, T. Wong3, Royal Brompton Hospital, London, United Kingdom; 1Royal Free Hospital, London, United Kingdom; 2King’s College Hospital, King’s College Hospital, London, United Kingdom

Background: Detection of left atrial appendage (LAA) thrombus and complete delineation of LAA anatomy is crucial prior to AF ablation and LAA device exclusion. Intervention is contra-indicated in the presence of LAA thrombus and appropriate device selection is dependent on complete visualisation of the LAA. Objectives: To assess the diagnostic accuracy of a limited, low-dose delayed contrast enhanced cardiac CT (CCT) of the LAA compared with the first-pass study for LAA morphological assessment and Transoesophageal Echocardiography (TOE) for the detection or exclusion of LAA thrombus in AF patients.

Methods: 128 consecutive patients undergoing CCT and TOE prior to LAA intervention were assessed. All had a two-phase CCT protocol (first-pass scan plus a limited, 60 second delayed scan of the LAA). Filling defects within the LAA on first-pass CCT were correlated with the delayed scan for assessment of LAA morphology; and LAA thrombus on TOE. Sensitivity, specificity, positive (PPV) and negative predictive value (NPV) were calculated.

Results: Filling defects were detected in 12/128 (9.4%) patients on the first-pass study. 9/12 (75%) were confirmed as pseudo-filling defects and did not allow full delineation of the LAA anatomy. The remaining three (25%, 2.3% of total co-

Conclusion: We found an increase in median SVEC in the early post-procedural period after RFA for AF followed by a continuous decrease during 24 months of follow-up. Throughout the follow-up period, the number of SVEC remained significantly higher in the RFA group compared to patients in the AAD group.

Acknowledgement/Funding: Biosense Webster, Aage & Gerda Henschi's Foundation, Hans & Nora Buchards Foundation, Jens Anker Andersen Foundation.

960 | BEDSIDE
Mechanisms of improvement in claudication after exercise training in peripheral arterial disease

J. Murrow1, J. Brizendine1, B. Djire1, H.J. Young2, K.R. Nilsson1, K.K. McCully2, 1Georgia Regents University - University of Georgia Medical Partnership, Athens, United States of America; 2University of Georgia, Kinesiology, Athens, United States of America

Background: The mechanism of clinical improvement from supervised exercise training for claudication in peripheral arterial disease (PAD) is not well understood. Near infrared spectroscopy (NIRS) allows for real-time assessment of skeletal muscle blood flow. NIRS-derived post-exercise recovery of muscle oxygen consumption to a mono-exponential curve yields both a time constant (Tc) that is an index of mitochondrial capacity (i.e., oxygen use) as well as ability to measure reperfusion (T1/2 max, reflecting oxygen delivery).

Methods: To test the hypothesis that improvements in muscle oxygen use (training) are mediated by increased mitochondrial activity rather than vascular oxygen delivery (microvascular effects) accounts for improvements in functional status after exercise training, we measured post-exercise NIRS-based assessment of mitochondrial capacity (Tc) and microcirculation (T1/2max) before and after a 12 week supervised exercise program in subjects with PAD. In addition, we tested whether ischemic calf pain vs. calf hypoxia measured by NIRS impacted training outcomes.

Results: Subjects with claudication from PAD trained thrice weekly for hour-long sessions over a 12 week period. Exercise intensity was determined by 15% reduction in resting skeletal muscle oxygenation by NIRS rather than by symptoms of pain. We randomly assigned subjects to NIRS-guided training (n=6, age 68.5±8.5, 33% female) versus traditional pain-guided training (n=7, age 71±21.9 years, 29% female). Training cohorts were similar in baseline ankle-brachial index (ABI, 0.8±0.2 vs. 0.8±0.3, p=NS) and baseline symptom-free walking time on a Gardner graded treadmill test (3.5±1.8 vs. 1.7±0.9 min, p=NS). At the conclusion of 36 training sessions, NIRS-trained subjects demonstrated similar improvements in symptom-free walking time (mean 7.3±3.3 vs 6.5±3.3 min at 12 week follow up, p<0.01 for change from baseline and p=NS between cohorts) as the traditional pain-based cohort. In both NIRS-guided and pain-guided cohorts, measurement of perfusion by ABI (p=0.3) and by T1/2 max for the entire cohort was unchanged (p=0.8). Meanwhile, mitochondrial oxidative capacity (Tc) improved in each PAD group (96±5.0 to 50.9±4.8 sec, 75±2±4.3 to 59±2.1 sec, respectively, p<0.01 compared to baseline). T1/2 max was significantly higher in the PAD cohort compared with age-matched controls without PAD (n=15; 90±5±5.2 vs. 17±9.8±3.3 sec, p<0.05).

Conclusions: Adaptations in mitochondrial oxidative capacity rather than improved tissue perfusion may account for improved walking times in subjects undergoing supervised exercise training in PAD.

Acknowledgement/Funding: American Heart Association
961 | BEDSIDE
Clinical impact of complete revascularization in elderly patients with multivessel coronary artery disease underwent percutaneous coronary intervention
M. Harada1, T. Miura1, H. Kobayashi2, T. Kobayashi2, M. Kobayashi3, H. Kimura3, H. Akamura3, S. Ebisawa4, Y. Miyashita5, U. Ikeda on behalf of The SHINANO Registry.1 Shinsyu University Hospital, Cardiology Department, Nagano, Japan; 2Shinshu Ueda Medical Center, Cardiology Department, Nagano, Japan; 3Nagano Redcross Hospital, Cardiology Department, Nagano, Japan; 4Matsumoto Kyoritsu Hospital, Cardiology Department, Nagano, Japan; 5Saku Central Hospital, Cardiology Department, Nagano, Japan; 6Iida Municipal Hospital, Cardiology Department, Nagano, Japan

Background: Prior report revealed that complete revascularization (CR) by percutaneous coronary intervention (PCI) decreased ischemic event. However, little is known about the efficacy of CR by PCI in elderly patients with multivessel coronary artery disease (CAD).

Purpose: We evaluated 1 year effectiveness of CR-PCI in elderly patients (>75 years old) with multivessel CAD.

Methods: The SHINANO Registry, a prospective, observational, multi-center, all comor cohort study enrolled 1923 patients. Seven hundred eighty eight patients (41%) had multivessel CAD. Among of them, 322 patients (41%) were elderly patients. The primary endpoint was major adverse cardiovascular events (MACE: all-cause mortality, myocardial infarction and stroke).

Results: In elderly patients with multivessel CAD, MACE occurred in 44 patients (13.7%). It was significantly lower in the CR group than in the incomplete revascularization (ICR) group (7.4% vs. 21.1%, P=0.001). In multivariate Cox proportional hazards analysis with age, sex, and left ventricular ejection fraction (LVEF), LVEF and CR were independent predictors of MACE (hazard ratio [HR], 0.95; 95% confidence interval [CI], 0.94–0.97; P<0.001). In patients without high comorbidity (log rank p<0.001), which was not the case in patients with high comorbidity (log rank p<0.10). In multivariate analysis, the only variables that were independently associated with prognosis were age, sex, and LVEF. MACE rate was significantly lower in the CR group than in the ICR group (6.6% vs. 18.1%, P<0.011).

Conclusions: Even in elderly patients over 75 years old, CR-PCI might suppress the short-term ischemic events.

962 | BEDSIDE
Comorbidity and intervention in octogenarians with severe symptomatic aortic stenosis

Background: Prior report revealed that complete revascularization (CR) by percutaneous coronary intervention (PCI) decreased ischemic event. However, little is known about the efficacy of CR by PCI in elderly patients with multivessel coronary artery disease (CAD).

Purpose: We evaluated 1 year effectiveness of CR-PCI in elderly patients (>75 years old) with multivessel CAD.

Methods: The SHINANO Registry, a prospective, observational, multi-center, all comor cohort study enrolled 1923 patients. Seven hundred eighty eight patients (41%) had multivessel CAD. Among of them, 322 patients (41%) were elderly patients. The primary endpoint was major adverse cardiovascular events (MACE: all-cause mortality, myocardial infarction and stroke).

Results: In elderly patients with multivessel CAD, MACE occurred in 44 patients (13.7%). It was significantly lower in the CR group than in the incomplete revascularization (ICR) group (7.4% vs. 21.1%, P=0.001). In multivariate Cox proportional hazards analysis with age, sex, and left ventricular ejection fraction (LVEF), LVEF and CR were independent predictors of MACE (hazard ratio [HR], 0.95; 95% confidence interval [CI], 0.94–0.97; P<0.001). In patients without high comorbidity (log rank p<0.001), which was not the case in patients with high comorbidity (log rank p<0.10). In multivariate analysis, the only variables that were independently associated with prognosis were age, sex, and LVEF. MACE rate was significantly lower in the CR group than in the ICR group (6.6% vs. 18.1%, P<0.011).

Conclusions: Even in elderly patients over 75 years old, CR-PCI might suppress the short-term ischemic events.

963 | BEDSIDE
Integration of frailty related blood biomarkers with standard frailty items to predict outcome after acute coronary syndrome

Background: No biomarkers have been considered among the instruments for frailty evaluation. Our aim was to investigate those biomarkers potentially involved in frailty and to integrate them into a frailty index, in elderly patients after acute coronary syndrome (ACS).

Methods: A total of 342 patients older than 65 years, survivors after ACS, were included. At discharge, frailty was measured using the Fried (5 items) and Green (4 items) scales. The following biomarkers were determined: inflammation (C-reactive protein, procalcitonin), coagulation (fibrinogen, D-dimer), hormonal dysregulation (vitamin D, dehydroepiandrosterone, insulin, glycaedhaemoglobin), nutrition (hemoglobin, albumin, prealbumin, ferritin, zinc), renal (creatinine-Cr) and liver dysfunction (nt-proBNP). The main outcome was mortality at 30-month median follow-up.

Results: In the multivariable analysis, hemoglobin, ferritin, D-dimer, vitamin D, nt-proBNP and cystatin-C levels were related to the Fried score (5 items) scales. The following biomarkers were determined: inflammation (C-reactive protein, procalcitonin), coagulation (fibrinogen, D-dimer), hormonal dysregulation (vitamin D, dehydroepiandrosterone, insulin, glycaedhaemoglobin), nutrition (hemoglobin, albumin, prealbumin, ferritin, zinc), renal (creatinine-Cr) and liver dysfunction (nt-proBNP). The main outcome was mortality at 30-month median follow-up.

Conclusions: A simple frailty index using walk time and nt-proBNP provide more prognostic information than the complex frailty scores after ACS.

964 | BEDSIDE
Depressive symptoms at repeated study visits, non-fatal vascular events, and risk of death over 10 years in older adults. The Three-City Study
R. Pequignot1, C. Dutouil2, C. Pruggger3, K. Peres2, S. Artero1, C. Tzourio2, J.P. Empana3 on behalf of The Three-City Study.1 National Institute of Health and Medical Research (INSERM), Paris, France; 2Inserm U897, University Victor Segalen, Bordeaux 2, Bordeaux, France; 3Inserm U970 - Paris Cardiovascular Research Center (PRCC), Cardiovascular Epidemiology-Sudden Death, Paris, France; 4Inserm U1061, Montpellier, France

Background: Whether or not the well-established association between depression and all cause mortality is mediated by the onset of vascular events is poorly known.

Purpose: We aimed to prospectively quantify the respective association of the course of depressive symptoms (DS) over time, the occurrence of non-fatal vascular events with all-cause mortality in older adults.

Methods and results: The Three City Study is a multisite population-based study in which older adults aged ≥65 years between 1999–2001 were examined at baseline and thereafter after 2, 4 and 7 years of follow-up. A score ≥16 on the 20-item Center for Epidemiologic Studies Depression Scale defined the presence of DS at baseline and during follow-up visits. The numbers of study visits with DS together with the occurrence of coronary heart disease (CHD) or stroke were used as time dependent variables in Cox proportional hazard model. The study population includes 8729 participants (61.0% females) aged 74.1 years (SD 5.5) who had a complete follow-up regarding vascular events and all-cause mortality.

DS were present in respectively 23.6%, 20.8%, 21.0% and 22.6% of the participants at baseline, 2, 4 and 7 years of follow-up. After a median follow-up of 8.6
years (SD 2.0 years), 944 subjects had suffered a first CHD or stroke events, respectively 260, 218, 249 and 217 at 2, 4, 7 and 10 years of follow-up, and 1700 had died. After adjustment for socio-demographic variables, vascular risk factors, impairment in daily life activities and antidepressant use, the presence of DS was associated with a significant 31% increased risk of mortality (HR=1.31, 95% CI: 1.15–1.51), while occurrence of a vascular event was related to a three-fold increased risk (HR=2.97, 95% CI: 2.56–3.44). There was no interaction between the presence of DS at study visits and occurrence of vascular event for the risk of mortality (p=0.50).

Conclusions: In older participants, the relative increased risk of all cause mortality associated with the presence of DS is independent of the occurrence of incident vascular events.

Acknowledgement/Funding: INSERM Bordeaux II University Sanofi-Aventis FRM DGS CNMTS MGEN et al.

965 | BEDSIDE Temporal trends in the treatment and outcomes of septuagenarian and nonagenarian with acute coronary syndrome

D. Radovanovic1, A.W. Schoenenberger2, S. Windedecker1, J.F. Iglesias4, G. Pedrazzini5, A.E. Stuck2, P. Erne5, UZH - Institute of Social and Preventive Medicine, AMIS Plus Data Center, Epidemiology, Biostatistics and Prevention Institute, Zurich; 2 Bern University Hospital, Department of Geriatrics, Bern; 3 Innsbruck Medical University, Department of Cardiology, Innsbruck; 4 University Hospital Centre Vaudois (CHUV), Service de Cardiologie, Lausanne; 5 Cardiocentro Ticino, Division of Cardiology, Lugano; 6 Klinik St Anna Hirslanden, Division of Cardiology, Luzern, Switzerland

Background: Old patients with acute coronary syndrome (ACS) are a growing demographic with higher risk of worse outcomes than younger patients.

Purpose: To determine whether treatment and outcomes of old ACS patients changed over time.

Methods: We analyzed 13,662 ACS patients ≥70 years enrolled in the Acute Myocardial Infarction in Switzerland (AMIS) cohort between 2001 and 2012. Use of guideline-recommended therapies and in-hospital outcomes were analyzed according to three 4-year periods (2001-2004, 2005-2008, 2009-2012). To determine associations between use of percutaneous coronary interventions (PCI) and in-hospital mortality, logistic regression modeling was used, odds ratios (ORs) and 95% confidence intervals (CIs) were used.

Results: Between first and last 4-year period, PCI use increased from 43.8% to 69.6% of older ACS patients (P<0.001). The highest relative increase was found for primary PCI use among nonagenarians with ST-elevation myocardial infarction (3.6-fold increase between first and last 4-year period, P<0.001). Use of guideline-recommended drugs as well increased. At the same time, in-hospital mortality of the overall population decreased from 11.6% in the first to 10.0% in the last 4-year period (P=0.020), and in-hospital major adverse cardiac and cerebrovascular events from 14.4% to 11.3% (P<0.001). The highest relative decrease of in-hospital mortality (22.7%) between first and last 4-year period was observed among octogenarians (P=0.005). In the overall population, PCI use was associated with lower odds of in-hospital mortality and ORs did not markedly change between first and last 4-year period (adjusted OR for PCI use vs. no PCI use 0.29, 95% CI 0.23–0.35, in 2001–2004; and, adjusted OR for PCI use vs. no PCI use 0.26, 95% CI 0.20–0.35, in 2009–2012).

Conclusions: Use of guideline-recommended therapies for ACS increased and in-hospital outcomes improved over the observed 12-year period. PCI use was associated with lower in-hospital mortality in similar ORs between first and last 4-year period. This study suggests that better guideline adherence improves in-hospital outcomes of older ACS patients.

966 | BEDSIDE Do risk factors explain the sex/gender gap in mortality from coronary heart disease?

J. Fritz1, M. Edlinger1, C.C. Kelleher2, S. Strohmair2, G. Nagel4, H. Concin5, M. Hochleitner1, E. Ruttmann1, H. Umer1, 1 Innsbruck Medical University, Innbruck, Austria; 2 University College Dublin, Dublin, Ireland; 3 University of Oslo, Oslo, Norway; 4 University of Ulm, Ulm, Germany; 5 Agency for Preventive and Social Medicine, Bregenz, Austria

Background: In Europe, per year, approximately 253,000 men, but only 77,000 women die prematurely from coronary heart disease (CHD) before the age of 65, while, when considering all ages, slightly more women do so than men. CHD rates increase with age, however to a varying extent between men and women.

Methods: One hundred and forty-two subjects (mean age 51±10.8 years, 94 men, 61 hypertensives) with no established cardiovascular disease were investigated in two examinations over a 2-year period (mean follow-up visit 1.84 years). Subjects were categorized in current smokers, non-smokers and ex-smokers. Smokers were further categorized according to the time elapsed since smoking cessation (5–15 years, >15 years). Subjects had at the beginning and end of the study determinations of carotid-femoral pulse wave velocity (PWV). Based on these measurements the annual absolute changes were calculated.

Results: Smoking at baseline was not associated with statistically significant differences in PWV. However, the annual change was statistically different between the groups of smokers, non-smokers and the 3 groups of ex-smokers (p=0.041) after adjustment for relevant confounders. Specifically, smokers had 0.23ms/year (95% CI: 0.10 to 0.35), non-smokers 0.17ms/year (95% CI: 0.08 to 0.25), quitters (>5 years) had 0.28ms/year (95% CI: 0.07 to 0.49), quitters (5–15 years) had 0.35ms/year (95% CI: 0.11 to 0.59) and quitters (>15 years) -0.07ms/year (95% CI: -0.26 to 0.13).

Conclusions: Quitting smoke seems to slow down progression of vascular aging over many years probably in an effort to compensate for former deleterious changes of smoking.

967 | BEDSIDE Quitting smoke ‘hits a late break’ in acceleration of vascular aging

D. Terentes-Preintzios, C. Vlachopoulos, P. Xipaniteris, N. Ioakeimidis, P. Pietri, D. Tousoulis, Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Purpose: Vascular aging, as assessed by structural and functional properties of the arterial walls, is an independent predictor of cardiovascular risk. Smoking has a detrimental effect on arterial properties. We sought to investigate the effect of quitting smoke on the progression of vascular aging.

Methods: One hundred and forty-two subjects (mean age 51±10.8 years, 94 men, 61 hypertensives) with no established cardiovascular disease were investigated in two examinations over a 2-year period (mean follow-up visit 1.84 years). Subjects were categorized in current smokers, non-smokers and ex-smokers. Ex-smokers were further categorized according to the time elapsed since smoking cessation (5–15 years, >15 years). Subjects had at the beginning and end of the study determinations of carotid-femoral pulse wave velocity (PWV). Based on these measurements the annual absolute changes were calculated.

Results: Smoking at baseline was not associated with statistically significant differences in PWV. However, the annual change was statistically different between the groups of smokers, non-smokers and the 3 groups of ex-smokers (p=0.041) after adjustment for relevant confounders. Specifically, smokers had 0.23ms/year (95% CI: 0.10 to 0.35), non-smokers 0.17ms/year (95% CI: 0.08 to 0.25), quitters (>5 years) had 0.28ms/year (95% CI: 0.07 to 0.49), quitters (5–15 years) had 0.35ms/year (95% CI: 0.11 to 0.59) and quitters (>15 years) -0.07ms/year (95% CI: -0.26 to 0.13).

Conclusions: Quitting smoke seems to slow down progression of vascular aging over many years probably in an effort to compensate for former deleterious changes of smoking.

968 | BEDSIDE Beta-blocker therapy optimization in elderly patients with left ventricular systolic dysfunction

M. Cortes Garcia1, A.M. Romero1, J.A. Franco1, J.A. Paffy1, A. Garcia1, M.L. Martin1, M. Lopez1, P. Avila1, E. De La Cruz2, J. Farre1, 1 Foundation Jimenez Diaz, Madrid, Spain; 2 University Hospital Principe de Asturias, Alcala de Henares, Spain

Introduction: The elderly population with left ventricular systolic dysfunction (LVSD) has been underrepresented in clinical trials of beta-blockers (BB) and maybe this is the reason why these drugs are used less commonly and in lower doses in this group of population. The objective of this study is to evaluate the importance of the optimization of the medical treatment with BB in elderly population with LVSD.

Methods: We included all patients (pts) ≥75 years old, with LVVEF <35%, studied in our center between January 2008 and April 2012. Clinical variables of interest were collected and clinical follow-up was performed. In each pt was collected information about treatment with BB and the dose reached. With this data we created a new variable between that determined the percent dose of BB (BB%) compared to the target level established in clinical guidelines (50 mg/d for carvedilol and 10 mg/d for bisoprolol). To analyze the effect of BB% on mortality and cardiovascular events (death, hospitalization for heart failure or ventricular arrhythmia), we used a Cox model adjusting for con founding and interaction with relevant clinical variables. In addition, to show the survival curves, the variable %BB was categorized into 3 groups (not BB, doses <50% and ≥50% of doses) and analyzed with log rank test.

Results: 566 pts were included. The mean age was 81.9 years, mean LVVEF was 25.9%. Smoking rate was 44% of patients, 25.7% did not take BB. 248 (48.2%) took low doses BB and 145 (26.1%) achieved high doses. During follow 223 pts died (40.2%), 92 in the untreated group, 97 in the low dose and 34 at the high dose. After adjusting the Cox model with confounding and interaction variables, we found
an HR estimated of mortality (for each 10% increase over the target dose) of 0.84 (95% CI 0.79–0.90). The final model included variables BB*, age, renal failure, previous heart failure, diuretics and LVEF. Finally, another Cox model for major events, showed a HR of 0.93 (95% CI 0.89–0.97) per every 10% increase in the BB dose.

**Conclusion:** The elderly population with LVSD clearly benefits from optimization BB treatment. In this study we estimates that for every 10% increase in BB dose to the target dose (ie, per 5 mg/d of carvedilol or every 1 mg/d of bisoprolol) the probability of death is reduced by 10 to 21% and the probability of death or hospitalization for heart failure or ventricular arrhythmia between 3 and 11%.

**NOVEL STRATEGIES FOR CARDIOPROTECTION**

**1080 | BENCH**

The cardioprotection of miRNA-221 is due to direct targeting on DD14/mTORC1/p-4EBP1 pathway

P.P. Wang 1, C.Y. Chen 1, M. Richards 1, National University of Singapore, Singapore; 2 Huashan Hospital, Shanghai, China, People’s Republic of

**Purpose:** DNA damage-inducible transcript 4 (DD14) is rapidly upregulated under multiple stresses including ischemia/reperfusion (I/R) and facilitates increased autophagy. DD14/miRNA-221 is a potential target of miR-221. Whether miR-221 could be a potential therapeutic target in cardioprotection is unknown. We hypothesized that miRNA-221 directly targets DD14 thus inhibiting I/R-induced autophagy.

**Methods:** Myoblast H9c2 cells and neonatal rat ventricular myocyte (NRVM) underwent 16 or 6 hours 0.2% O2 hypoxia, respectively followed by 2 hours reoxygenation (HR). The mTORC1 inhibitor, Rapamycin (200nm), was administered to further enhance autophagy. Both cells were transfected with miRNA-221 mimic (25 nmol) and scrambled mimic control (miR-146a and MC). Cell count/viability, WST assay, cell injury-induced LDH release, and GFP-LC3 labeled autophagosomes were measured. Finally, both H9c2 and NRVM were collected for RT-qPCR and WB analyses. Predicted miR-221 targeting of DD14 was assessed by Luciferase-reporter assay.

**Results:** miRNA-221 significantly reduced I/R injury as indicated by higher cell count/viability and WST activity, and reduced LDH (miR-221 vs. MC p<0.05). pQPCR confirmed that (1) miR-221 expression was reduced in HR; (2) RISC-loading of miR-221 was reduced. The above observations were corroborated by the converse responses induced by miR-221 inhibitor transfection. miRNA-221 directly targets DD14 and activates the mTORC1/p-4EBP1 pathway reducing autophagy. miRNA-221 is a promising therapeutic target in the treatment of I/R injury.

**Acknowledgement/Funding:** CVR Start-up grant (NUS, Singapore) and NMRIC grant (Ministry of Health, Singapore)

**1081 | BENCH**

Exosomes from human cardiac progenitor cells, but not those from patient-matched bone marrow-derived mesenchymal stem cells, improve cardiac function after myocardial infarction in vivo

L. Barile 1, E. Cerviio 1, M. Matteucci 1, T. Torre1, T. Moccetti1, V. Lionetti2, G. Vassalli1.

**Background:** Both human cardiac progenitor cells (CPC) and bone marrow-derived mesenchymal stem cells (MSC) have been tested in clinical trials of cell transplantation in patients with myocardial infarction. (MI). We have recently shown that Exosomes (secreted nanovesicles, Exo) from CPC account for cardioprotective and angiogenic activities of these cells both in vitro and in vivo. This study aimed to compare Exo-CPC and Exo-MSC in terms of cardioprotective effects and functional improvement after MI. The role of microRNA (miRNA) and ischemic preconditioning (IPC) were assessed.

**Materials and methods:** Exosomes were derived from right atrial appendage and bone aspirate from patients undergoing heart valve surgery. Samples from both tissues were obtained for a patient-matched comparison of Exo from the two cell lines. Exo were isolated by differential ultracentrifugation of conditioned media from CPC or MSC. Anti-apoptotic and cardioprotective effects of Exo-CPC and Exo-MSC were assessed in vitro and compared with Exo from human dermal fibroblast cell line (Exo-F). IPC was performed by subjecting CPC or MSC to two short rounds of hypoxia and glucose deprivation. miRNA profiles of Exo were assessed by real-time qPCR. Exo-CPC and Exo-MSC from 8 patients were injected intramyocardially in 8 rats each after permanent ligation of the left anterior descending coronary artery. Left ventricular ejection fraction (LVEF) was measured by echocardiography 1 and 4 weeks after MI.

**Results:** Although both Exo-CPC and Exo-MSC inhibited cardiomyocyte (CM) apoptosis after serum starvation in vitro if compared with Exo-F, Exo-CPC showed higher efficacy (21%±4 Exo-CPC; 28%±5 Exo-MSC; 40±5% Exo-F). IPC of Exo-producing cells further reduced numbers of apoptotic CM (17±1% Exo-CPC; 23±3% Exo-MSC). Exo-CPC, but not Exo-F, were proangiogenic in HUVEC. CM transfected with Exo-CPC and miR-146a among the most highly enriched in Exo-CPC. CM transfected with miR-20B or miR-132 mimics showed increased tolerance to apoptosis, whereas siRNA specific for these miRNA had opposite effects. In vivo, LVEF was significantly improved in hearts injected with Exo-CPC compared to those injected with patient-matched Exo-MSC both 1 week (87±0.9% vs 61±1.119; p<0.05) and 4 weeks after MI (75.4±8.9% vs 58.7±18.4%; p<0.05).

**Conclusion:** These results from patient-matched analyses show, for the first time, that Exo-CPC is superior to Exo-MSC at inhibiting CM apoptosis and improving cardiac function after MI in vivo. As a cell-free approach, Exo could streamline clinical translation of regenerative heart therapy.

**Acknowledgement/Funding:** Swiss Foundation for Cardiology

**1082 | BENCH**

Bnip3 drives mitochondrial damage in the early phase of myocardial ischemia/reperfusion injury

S. Ecken, U. Hengdener-Cotta, M. Kelm, T. Rassaf. University Hospital Dusseldorf, Department of Internal Medicine, Division of Cardiology, Pulmonology and Vascular Medicine, Dusseldorf, Germany

**Purpose:** A high percentage of the damage in myocardial infarction results from the reperfusion of the ischemic myocardium. Mitochondria are central players in cell death during the early phase of reperfusion. The permeabilization of the mitochondrial outer membrane (MOM) is a major determinant of apoptosis and necroptosis in cardiac cells. We have studied the role of Bnip3 in the formation of the MOM pore (MOMP) which leads to loss of apoptogens, caspase activation and cell death. The underlying mechanism is still unidentified. The Bcl-2 family member Bnip3 also seems to be involved in this process. Bnip3 is located in cytoplasmic fractions in the mouse model that the inhibition of Bnip3 leads to a significant reduction of the infarct size by 51%. In cell culture studies, the overexpression of Bnip3 leads to Bax/Bak activation and apoptotic cell death. In Bax/Bak double knockout cells Bnip3 shows no effects. This suggests that Bnip3 acts via activation of MOM formation. In our study we are focused on the role of Bnip3 during early phase of ischemia/reperfusion (IR) injury in vivo.

**Methods and results:** In the early phase of reperfusion we found a time-dependent increase of depolarized mitochondria in an in vivo mouse model. After 10 min of reperfusion 21% of whole heart mitochondria showed a depolarization (basal 5.5±1.5% vs. 10 min reperfusion=20.6±3.4%, n=5, p=0.001). The inhibition of Bnip3 using a TAT-Fusionprotein, TAT-Bnip3.TM (transmembrane deletion mutant of Bnip3, acting as a dominant negative blocker) significantly reduced the depolarized mitochondria level by 67% after 10 min of reperfusion (10 min reperfusion + Bnip3 inhibition = 6.7±3.2%, n=5, p=0.001). This is associated with a time-dependently increasing Bnip3 protein concentration by 70% in MOM in reperfusion (basal 100% vs. 30 min reperfusion=170±113%, n=3, p=0.0001). Inhibition of Bnip3 prevented the incorporation of Bnip3 into MOM (10 min reperfusion + Bnip3 inhibition = 94±21%, n=3, p=0.0057) as well as a significant increase of Bax concentration in MOM during reperfusion (basal 100% vs. 10 min reperfusion = 456±354%, n=10, p<0.05). The Bax translocation into MOM was reduced by 240% (10 min reperfusion + Bnip3 inhibition = 216±12%, n=10, p<0.05). Remarkably, during early phase of reperfusion no increase of cytochromeC level in cytoplasm was observed in vivo.

**Conclusion:** Bnip3 initiates mitochondrial damage and cell death in the early phase of reperfusion following ischemia by regulating Bax-concentration and depolarization of MOM in a cytochromeC independent process.

**1083 | BENCH**

Transvascular total left ventricular unloading in the acute phase of myocardial infarction markedly reduces infarct size and prevents heart failure in the long term

K. Saku, T. Kakino, T. Arimura, T. Akashi, K. Sunagawa, Kyushu University, Graduate School of Medical Sciences, Department of Cardiovascular Medicine, Fukuoka, Japan

**Background:** Infarction takes place when myocardial oxygen demand (MVO2) exceeds myocardial oxygen supply. Decreased myocardial infarction (MI) remains a major cause of chronic heart failure (CHF). Left ventricular assist device (LVAD) mechanically unloads the left ventricle (LV) and reduces MVO2. Theoretical analysis using the pressure-volume area (PVA), an index of MVO2, and pressure work (PW) indices of MO2. Although LVAD reduces preload and afterload, and thus does not effectively decrease PVA and MVO2. In contrast, the total LVAD unloading (t-LVAD) where LV no longer ejects, markedly decreases LV volume and pressure, and reduces PW and MVO2. We hypothesized that LVAD during the acute phase of MI could reduce the infarct size and prevent heart failure in the long term.

**Methods:** We used a transvascular LVAD for LV mechanical unloading. In anesthetized dogs, we ligated the left anterior descending coronary artery for 180 min
and then reperfused. We initiated LVAD at 80 min after the onset of ischemia until 90 min after reperfusion. We allocated 16 dogs into 3 groups, no support (Sham, n=5), p-LVAD (n=5) and t-LVAD (n=6). Four weeks after MI, we assessed the infarct size and LV function.

**Results:** t-LVAD markedly reduced the infarct size by more than 80% relative to Sham. t-LVAD significantly increased LV ejection fraction, and end-systolic elastance (Ees) and decreased LV end-diastolic pressure (LVEDP), indicating that t-LVAD preserved LV function. NT-proBNP as a biomarker of CHF also reduced in t-LVAD (Sham 3409±690 vs. t-LVAD 1781±177 pg/ml, p <0.05).

**Conclusion:** Total LVAD unloading in the acute phase of MI markedly reduces infarct size, preserves LV function and prevents heart failure in the long term.

1084 | BENCH
---

**The interplay of neutrophils and interferon gamma is critical for post-infarction survival in a murine model of myocardial infarction**

M. Kno11, S. Finger1, S. Karbach1, S. Koßmann1, M. Brandt1, T. Muenzel1, P. Wenzel1.

1 University Medical Center, Department of Medicine 2, Mainz, Germany

**Background:** Myelomonocytic cells are involved in both the initial injury phase as well as the later clearing phase of the healing process of myocardial infarction (MI). A differential spatial and temporal targeting of these cells would allow to investigate their role in this process and open up novel windows of therapy. However, the precise interplay of myelomonocytic cells and inflammatory cytokines like interferon gamma (INF-g) is not known.

**Methods and results:** MI was induced in 8 to 12 week old male mice on C57BL/6 background by ligation of the left anterior descending (LAD) coronary artery. Compared to sham operated LysMCre controls, LysM+ cells (within the Ly6G+ Ly6C− population) had been depleted of LysM+ cells for 3d prior MI by low-dose diphtheria toxin injection, revealed a decreased influx of Ly6G+ cells 1d post MI in the infarction zone and a attenuated cardiac mRNA expression of INF-g 1d and 7d post MI. Sequential repression of cardiac mRNA of MCP-1 and CCR2 ad d1 post MI as well as fractalkine and CX3CR1 at d7 post MI was paralleled by reduced influx of Ly6Chigh and Ly6Clo cells in anti-Gr1 treated mice. Compared to sham, administration of anti-Gr-1 antibody and detected a significant decreased influx of CD45.2+/CD3-/CD11b+/Gr-1high neutrophils into infarcted myocardium 1d post MI and a reduction of cardiac INF-g and tumor necrosis factor alpha mRNA expression 7d post MI. To assess more specifically the role of neutrophils, we depleted C57BL/6 mice with a monoclonal anti-Gr-1 antibody and detected a significant decreased influx of Ly6G+ cells 1d post MI in the infarction zone and a attenuated cardiac mRNA expression of INF-g 1d and 7d post MI. Reduced repression of cardiac mRNA of MCP-1 and CCR2 ad d1 post MI as well as fractalkine and CX3CR1 at d7 post MI was paralleled by reduced influx of Ly6Chigh and Ly6Clo monocytes in anti-Gr-1 treated mice. Sequential repression of cardiac mRNA of MCP-1 and CCR2 ad d1 post MI as well as fractalkine and CX3CR1 at d7 post MI was paralleled by reduced influx of Ly6Chigh and Ly6Clo monocytes in anti-Gr-1 treated mice.

**Conclusion:** Our results suggest an essential role of neutrophils and IFN-g for survival and remodeling following myocardial infarction, probably through their permissive function for monocyte chemotaxis. We conclude that strategies to combat the inflammatory injury in MI must consider a potentially beneficial effect of early neutrophil influx into infarcted myocardium.

1085 | BENCH
---

**Cardioprotective properties of matrix metalloproteinase inhibition: attenuation of nuclear protease activity, reduced DNA fragmentation and preserved OGG1**

R.M. Bell1, X. Rossello1, R. Breckenridge2, D.M. Yellon1.

1 University College Hospital, Hatter Cardiovascular Institute, London, United Kingdom
2 University College Hospital, Metabolism & Experiment Therapeutics, Div of Medicine, London, United Kingdom

**Background:** Matrix metalloproteinases (MMP) are integral to myocardial remodeling following injurious ischaemia/reperfusion, but intracellular activity increases cell death. The mechanisms of MMP-mediated injury remain elusive, but DNA repair enzymes, PARP, XRCC1 and OGG1 are known targets for MMP-mediated proteolysis, potentially degrading the cell's capacity to repair oxidative DNA injury and exacerbate cell death in response to lethal ischaemia/reperfusion injury (IRI).

**Purpose:** To determine whether pharmacological MMP inhibition attenuates necleic MMP activity, prevents protease degradation of DNA repair enzymes, preserves DNA integrity and thus ameliorates myocardial injury.

**Methods:** C57B16 mouse hearts were Langendorff perfused and subjected to 30 min global ischaemia before the onset of 10 min reperfusion prior to tissue harvesting in three groups: vehicle control (DMSO 0.05% v/v); MMP inhibitor, ilomastat (200nmol/l) and ischaemic postconditioning (6 cycles 10sec reperfusion, 10sec ischaemia). Contemporaneous experiments in the same groups were undertaken to 30 min reperfusion to determine the cardioprotective efficacy of the interventions by triphenyltetrazolium staining of viable tissue and planimetric assessment of infarct size. Cellular MMP activity was determined by in-situ zymography, intracellular visualisation by transmission electron-microscopy (TEM), and quantification of DNA base-excision repair enzyme, OGG1, by Western blot and immunofluorescent staining.

**Results:** Both ischaemic postconditioning and MMP inhibition with ilomastat significantly attenuated infarct size compared to control. Tissue zymography revealed MMP activity was significantly greater in the nucleus of cardiomyocytes following IRI in control hearts – a pattern not modified by ischaemic postconditioning. Conversely, MMP activity in the nucleus was abrogated by pharmacological inhibition of MMP with ilomastat. These data correlated with the histological preservation of nucleic DNA on TEM by ilomastat compared to control and postconditioned hearts, and with the post-ischaemic preservation of myocardial OGG1.

**Conclusions:** We present first evidence of a novel mechanism of MMP-mediated intracellular IRI that promotes DNA degradation and attenuates cellular viability. Acute targeting and inhibition of MMPs during IRI presents a cardioprotective strategy independent of current paradigms of cell death mediated through mitochondrial permeability transition pore opening, and thus offers the potential for disparate pharmacological targeting of multiple death pathways in the management of the coronary synapses for myocardial infarction.

**Acknowledgement/Funding:** Supported by the NIHR Biomedical Research Centre at University College London Hospitals NHS Foundation Trust and University College London

1087 | BENCH
---

**Different pathways and additive effects of exendin-4, glucose-insulin-potassium, and remote ischemic conditioning on infarct size in pigs**


1 Instituto de Recerca Hospital Vall d’Hebron, Lab. Cardiologia Experimental, Barcelona, Spain

**Background:** Remote ischemic conditioning (RIC) has been shown to reduce myocardial infarct size in patients.
Novel strategies for cardioprotection / Complications in devices

P1091 | BEDSIDE

Distinct mechanisms of cardioprotection by different H2S donors


Hydrogen sulfide has been shown to exert a variety of actions in the cardiovascular system; it promotes vasorelaxation and angiogenesis, reduces athrosclerosis and ameliorates heart failure. We and others have previously shown that H2S protects the heart from ischemia/reperfusion (I/R) injury. In the majority of studies evaluating cardioprotection, ultra fast H2S-releasing salts have been used. Here we investigated the ability of slow releasing and mitochondria-targeted H2S donors to reduce infarct size and compare them to the inorganic salt Na2S. Anesthetized male mice were subjected to 30 min regional myocardial ischemia by LAD ligation, followed by 2hr of reperfusion. Animals were randomized into 5 groups as follows: 1) control, no further intervention, 2) Na2S (4.2μmol/kg), 3) thiouila (4μmol/kg), 4) GYY4137 (26.6μmol/kg) and 5) AP39 (250nmol/kg). All drugs were administered as i.v. bolus at the 20th min of reperfusion. None of the treatments affected blood pressure and all of the groups had similar risk/all areas. After the end of the experiments the infarct size (I) and the area at risk (R) were estimated as % I/R; the necrotic area was evaluated by triphenyl tetrazolium staining. In a second series of experiments animals were subjected to the above interventions up to 10th min of reperfusion, when tissue samples were collected for measurement of eNOS and VASP phosphorylation.

Infarct to risk area (I/R) for the control group was 52.7±9.5% Na2S and GYY4137 (an ultra slow releasing HS2 donor) reduced infarct size to a similar extent (17.5±3.9% and 16.6±2.2 for Na2S and GYY4137, respectively). Similarly, we observed that thiolazidine reduced infarct size to 14.0±3.9% and AP39, the mitochondrial H2S donor reduced IR to 21.1±4.3%. Na2S and GYY4137 enhanced eNOS phosphorylation in the ischemic area; this was not observed with AP39 treatment. The infarct size-reducing effects of Na2S and GYY4137 were reversed by administration of the cGMP-dependent protein kinase-1 (PKG-1) inhibitor DT2 (2μmol/kg administered 10 min before reperfusion), with no change of the previously observed ischemia. In contrast, the beneficial effect of AP39 was not reversed by PKG-1 inhibition, suggesting that AP39 affords cardioprotection in a NO/cGMP-independent manner. This observation is in agreement with the finding that AP39 fails to increase cGMP levels and VASP phosphorylation.

We conclude that while both fast and slow H2S donors limit infarct size through a cGMP/PKG pathway, the mitochondrial targeted H2S donor AP39 exhibits cardioprotection following I/R injury via a NO-independent pathway.

Complications in Devices

P1092 | BEDSIDE

Transvenous removal of pacing and ICD leads: single referral center experience


Introduction: Device related complications are rising the need of Transvenous Lead Removal (TLR). Transvenous extraction of Pacing (PL) and Defibrillating Leads (DL) is a highly effective technique. Aim of this report is to analyse the long term outcome performed in a single Italian Referral Center.

Methods: Since January 1997 to December 2014, we managed 2250 consecutive patients (1718 men, mean age 63.5 years) with 4114 leads (mean pacing period 71.8 months, range 1–576). PL were 3328 (1582 ventricular, 1391 atrial, 355 coronary sinus leads), DL were 786 (765 ventricular, 6 atrial, 15 superior vena cava leads). Indications to TLR were infection in 83% (systemic 28%, local 55%), inappropriate rhythm, 11% (upsimulator, 15% atrial fibrillation, 15% atrial flutter), 9% (atrial tachycardia, 35% atrial tachycardia and ICD leads 84 (14.1%), 303 (32.5%); Full procedural success 561 (94.4%) vs 888 (94.9%) NS; Major complications 15 (2.5%) vs 7 (0.7%), p=0.006; Minor complications 18 (3.0%) vs 6 (0.8%), p<0.001; Procedure related death 3 (0.5%) vs 4 (0.2%), p=0.31; Long-term mortality 32 (25.2%) vs 173 (19%), p<0.001.

Results: Transvenous lead removal was attempted in 4105 leads because the technique was not applicable in 9 PL. Among these, 4019 leads were completely removed (97.9%), 44 (1.1%) partially removed, 42 (1.0%) not removed. Among 4020 exposed leads, 625 were removed by manual traction (15.5%), 2998 by mechanical dilatation using the venous entry site (74.6%), 32 by femoral approach (FA) (6.4%) and 279 by JA (7.0%). All the free-floating leads were completely removed, 25.8% by FA and 74.2% by JA. Major complications occurred in 13 cases (0.6%): cardiac tamponade (12 cases, 2 deaths), heomotrax (1 death).

Conclusions: Our experience shows that in centers with wide experience, TLR using single sheath mechanical dilatation has a high success rate and a very low incidence of serious complications. TLR through the Internal Jugular Vein (JA) was performed in case of free-floating leads or failure of the standard approach.

P1093 | BEDSIDE

Managing peri-procedural antiocoagulation therapy in patients undergoing cardiac electronic device surgery: survey in Austria, Germany and Switzerland

F. Blaschke, P. Lacour, L.H. Boldt, A. Wutzler, A. Parwani, M. Huemer, P. Attanasio, W. Haverkamp. Cardiology Operative Unit 2, Pisa, Italy

Introduction: Managing peri-procedural anticoagulation in patients undergoing cardiac electronic device surgery is a challenging field. Physicians must balance the thrombembolic and bleeding risks related to complications of such surgery. We performed an online survey in 2017 to assess current practice regarding anticoagulation in Austria, Germany and Switzerland.

Methods: A questionnaire was sent to a selection of cardiology societies in Austria, Germany (41/43) and Switzerland (28/40). Results: 71 members (13/14/25% from Austria, Germany, Switzerland respectively) responded.

Results: Most centers in Austria (92%) and in Germany (88%) use transvenous leads extraction and adjunction of GIK for prophylaxis of TLR (92% vs 67%). In 83% (88% vs 77%) of centers, GIK treatment is started before the intervention and in 81% (84% vs 74%) continued for 48 hours after the intervention in Austria and Germany respectively.

Conclusions: Our survey shows that in Europe the majority of centers perform device surgery with the aim of reducing the risk of complications and improving the efficacy of the procedure.
Methods: We conducted a web-based survey across centres in Austria, Germany and German-speaking Switzerland using the tool SurveyMonkey. The questionnaire included 17 questions and was sent to 202 Austrian centres, 101 German and 45 Swiss centres. The survey was completed by 252 of the 1392 centres (18.10% response rate). In managing patients on NOACs common practice was to stop NOACs in 95.83% (Austria), 89.52% (Germany) and 87.50% (Switzerland). NOACs were stopped in 88.18% (Austria), 51.40% (Germany) and 93.85% (Switzerland) one day before device implantation and usu-
ally restarted on the following day after device implantation. In the centres where NOACs were stopped for implantation, bridging with heparin was performed in patients with atrial fibrillation in 45.45% in Austria, in 41.90% in Germany, and only in 23.08% in Switzerland. In patients with a history of thrombosis/pulmonary embolism the percentage of bridging was higher. Most centres use low molecu-
lar weight heparin in therapeutic dosage. Management of patients on phenpro-
coumon varied significantly between each country. Anticoagulation was stopped in 66.67% of the centres in Austria, 46.00% of the centres in Germany, and 13.64% in Switzerland. Among patients with prosthetic valves, most centres discontinued oral anticoagulation and bridged with heparin.

Conclusions: Implantation of cardiac devices in patients on oral anticoagulation is increasingly common in clinical practice. Our data demonstrate that timing of NOACs cessation in NOACs users is heterogeneous. Among patients with heparin, a restarting of oral anticoagulation vary a lot among all centres. Our findings emphasize the need for further randomized controlled studies to determine the optimal strategy for managing anticoagulation in patients undergoing device surgery.

Methods and results: Between 2003 and 2014, 777 leads were removed from 366 patients (mean age 75±11.8); among these, 185 patients (50.5%; mean age = 69.7±13.2) had an implanted cardiac defibrillator or a cardiac resynchro-
nization device with or without ICD (CRT-D or CRT-P); 45 patients had CRT-P. 85 patients had CRT-D and 55 patients had a ICD; among these 185 patients, 265 leads were removed: 121 CS leads from 121 patients (mean age 72±15.8 years) and 141 ICD leads from 137 patients (mean age, years 68±13.4); device infection was the main indication to extraction (82.5% of cases); the mean implant time was 49.8±32.5 months (range 12–168) for CS leads and 55.7±47.5 months (range 12–240) for ICD leads (P < NS). To remove the leads, when simple man-
ual traction was ineffective, we performed dilatation technique using exclusively mechanical sheaths.

All ICD leads were extracted with 100% complete procedural success (removal of all targeted leads and all lead material from the vascular space); there has not been any major complication.

Conversely, we observed two adverse events among CS lead extraction pro-
dure: one procedure failed and required thoracotomy for remove the lead from coronary sinus (implant time = 105 months); one cardiac tamponade, requiring surgical repair, occurred during extraction of an active fixation coronary sinus lead (Attain StarFix lead, implant time = 41 months).

Conclusion: Despite the ICD coil account for unfavorable condition to transve-
nous lead extraction, all the 141 ICD leads were successfully removed (procedure-
r al and clinical success in 100%) without any major complication; while CS leads extraction procedure was more complex because of one fail procedure and one major complication.

Methods: Patients with IA indication for ICD system extraction according to guidelines were randomized to use either purely mechanical extraction including femoral approach or a combination of mechanical extraction and eximer laser technique. The primary endpoint was the efficiency and safety of the extraction procedure. Univariate logistic regression analysis was performed to identify pre-
dictors of complications associated with ICD therapy.

Results: 579 patients (391 men, 188 women, mean age 67±28 years) were re-
ferred to the complete ICD extraction with sepsis and evidence of bacterial en-
docarditis. The average time from the first implant of the electrodes was 72±37 months (range 121 months), the average number of electrodes in one per-
son was 2.7. The group included 637 ICD electrodes (477 dual coil), 121 atrial and 137 LV leads. Average procedure time was 172±37 minutes. In 292 patients we used the combination of an eximer laser (SLS II Spectranetics Corporation, USA) and mechanical extraction (Evolution®, Cook Medical, USA) in 287 patients we performed only mechanical extraction (in 29 cases transfemoral approach).

Results: Complete extraction was achieved in 96% of procedures, early mortality (24 hours) was 0.3%, 30-days mortality rate was 1.2%. Complications occurred in 6.47% of patients. The most common complication were sepsis, pulmonary ab-
scesses, hematoma indicated for a revision, and perforation of the right ventricle.

Predictors complications were: 1. Positive inflammatory markers at the time of implant (HR 2.71) 2. Multiple revisions of the ICD system (HR 1.78), 3. Impla-
ntation by electrophysiologist with experience < 50 procedures (HR 1.45), 4. LMWH use for anticoagulation (HR 2.59) 5. Low volume centre (HR 1.33) 6 Dual coil ICD lead (HR 1.39) 7. Medal puncture for lead implant (HR 1.27) 8. Advanced heart failure (NYHA III, IV) (HR 2.11), 9. Renal insufficiency with GF < 30 ml/min (HR 2.97), 10. Diabetes mellitus (HR 1.93), 11. COPD (HR 1.51).

Methods: From January 2002 to January 2015, we reviewed data from consecu-
tive patients (pts) referred to our institution for transvenous lead extraction with a special focus on OCT.

Clinical characteristics, procedural features, and per procedural major and minor complications were compared between OCT and younger pts.

All procedures were done in an operative theatre under general anesthesia with a cardiac surgical stand-by and a trans oesophageal echography during proce-
dure. Strategy consists in trying manual traction first, then locking stylet extraction, then laser assisted extraction and in case of failure (or impossible upper access) conversion into a femoral approach.

Results: Of 428 pts undergoing lead extraction during the study period, 108 (25.2%) were OCT (mean age 64,0.7 years; range 80–98, 73% males). A signif-
icantly higher percentage of OCT presented heart disease (37.96% in OCT vs 25,2%) were OCT (mean age 84,0.7 years; range 80–98; 73% males). A signif-
icant difference was observed in age demographics, the in-
creased use of implantable devices, the prevalence and rise of complications,
and the lack of literature about this specific group, we decided to analyze the clinical outcomes after laser-assisted extraction in the octogenarian (OCT) pop-
ulation. We report the safety and effectiveness of transvenous lead extraction in OCT.

Methods: From January 2002 to January 2015, we reviewed data from consecu-
tive patients (pts) referred to our institution for transvenous lead extraction with a special focus on OCT.

Clinical characteristics, procedural features, and per procedural major and minor complications were compared between OCT and younger pts.

All procedures were done in an operative theatre under general anesthesia with a cardiac surgical stand-by and a trans oesophageal echography during proce-
dure. Strategy consists in trying manual traction first, then locking stylet extraction, then laser assisted extraction and in case of failure (or impossible upper access) conversion into a femoral approach.

Results: Of 428 pts undergoing lead extraction during the study period, 108 (25.2%) were OCT (mean age 64,0.7 years; range 80–98, 73% males). A signif-
icantly higher percentage of OCT presented heart disease (37.96% in OCT vs 15.2% in pts <80 years; P=0.03) chronic renal failure (38.8% in OCT vs 13.68% in pts <80 years; P=0.03).

Infection (all types) was a more common indication for extraction in OCT than in younger pts (79.62% in OCT vs 51.56% in pts <80 years; P < 0.001), but malfunc-
tion was more prominent in younger pts than OCT (41.56% in OCT vs 17.59% in pts <80 years; P < 0.001).

Complete lead extraction efficacy were similar between both groups (97.22% in OCT vs 94% in pts <80 years; P=0.15). Laser assistance for extraction was re-
quired in 77 elderly pts (71%).

Femoral approach was required in 16 elderly pts (14.8%) and 22 younger adults (6.8%) (p=0.013).

No deaths occurred in the OCT group. No differences in terms of other peri pro-
cedural major and minor complications were found between the 2 groups.

Conclusion: The OCT group was a sicker population, as reflected by their high risk factors of complications, their advanced degree of heart failure and their high rate of device infection. The present findings demonstrate that laser lead extraction is a safe and effective method of treatment in octogenarian patients with multiple comorbidities.
KNOWING MORE ABOUT STEMI AND NON-STEMI

P1097 | BEDSIDE
Direct comparison of the safety and efficacy of two rule-out strategies for acute myocardial infarction: 1h-algorithm versus combination of 1h-algorithm and undetectable levels at presentation

Purpose: Addressing the increasingly recognized, yet unmet clinical need for rapid rule-out of acute myocardial infarction (AMI), several novel strategies have been developed. Due to the lack of direct comparisons in the same dataset, selection of the best strategy for clinical practice is challenging. We therefore aimed to directly compare the safety and efficacy of two previously defined strategies (1h-algorithm based on high-sensitivity cardiac troponin (hs-cTn) at presentation and its change within 1h versus the combination of the 1h-algorithm with undetectable levels of hs-cTn at presentation (1h-algorithm+LOD)).

Methods: In a prospective international multicentre diagnostic study enrolling 2213 patients presenting with suspected AMI to the ED, the final diagnosis of AMI was adjudicated by two independent cardiologists using all available clinical information including serial hs-cTnT concentrations. Safety was quantified as the negative predictive value for AMI in the rule-out zone of the respective rule-out strategies. Efficacy was quantified as the percentage of the overall cohort assigned to the rule-out zone by the respective strategy. Both strategies were applied using the two best-validated hs-cTn assays (hs-cTnT Roche: 1h-algorithm 0h–1h-3ng/l; 1h-algorithm+LOD 0h–5ng/l OR (0h–1ng/l and Δ0–1h-3ng/l); and hs-cTn Abbott: 1h-algorithm 0h –5ng/l and Δ0–1h-2ng/l; 1h-algorithm+LOD 0h–2ng/l OR (0h–5ng/l and Δ0–1h-2ng/l)) to ensure that findings are independent from the hs-cTn assay used. Patients presenting with STEMI were excluded.

Results: AMI was the final diagnosis in 17% of patients. Using hs-cTnT, the safety was very high and comparable with both algorithms (1h-algorithm: NPV 99.9%, 95% CI 99.6–100% versus 1h-algorithm+LOD: NPV 99.9%, 95% CI 99.5–100%, p=ns). Regarding efficacy, 1h-algorithm allowed rule-out in 59% of patients after 1h versus 59% with the 1h-algorithm+LOD (41% at presentation and 59% after 1h). Using hs-cTnT, the safety was very high and comparable with both algorithms (1h-algorithm: NPV 99.2%, 95% CI 98.4–99.6% versus 1h-algorithm+LOD: NPV 99.5%, 95% CI 98.9–99.6%, p=ns). The 1h-algorithm allowed the rule-out in 53% of patients after 1h versus 53% with the 1h-algorithm+LOD (31% at presentation and 69% after 1h).

Conclusion: Both investigated rule-out strategies allow a safe and comparable rule-out of AMI, irrespective of the underlying hs-cTn assay. While the 1h-algorithm requires retesting of hs-cTnT after 1h in all patients, the 1h-algorithm+LOD allows the safe rule-out of AMI in about every fifth patient already at presentation.

P1098 | BEDSIDE
CRUSADE Risk Score for Predicting Major Bleeding based on BARC Standardized Definition in Patients with Acute Coronary Syndromes
P.J. Flores-Blanco1, A.A. Lopez-Cuenca2, M. Gomez-Molina1, M. Sanchez-Mejias1, M.J. Sanchez-Galian1, E. Guererro-Perez1, A. Garcia-Narbon1, F. Cambronero-Sanchez2, M. Valdes1, S. Manzano Fernandez1,1 University Hospital Virgen De La Arrixaca, Murcia, Spain; 2 de la Vega Lorenzo Guirao Hospital, Cieza, Spain; 3 University Hospital Morales Meseguer, Murcia, Spain; 4 University of Murcia, School of Medicine, Department of Cardiology, Murcia, Spain.

Purpose: The CRUSADE bleeding risk score (CRBS) accurately predicts major bleeding in acute coronary syndromes. However, little information exists about its application for predicting major bleeding based on the recently proposed Bleeding Academic Research Consortium (BARC) standardized bleeding definition. We aimed to assess the ability of CRBS to predict in-hospital major bleeding based on the BARC criteria in acute coronary syndrome setting.

Methods: From January 2012 to August 2014, we prospectively included consecutive patients with acute coronary syndromes. Major bleeding was defined according to BARC criteria as bleeding types 3 to 5. Predictive ability of the CRBS was assessed under the ROC criteria in acute coronary syndrome setting.

Results: We included 1234 patients (mean age 68±13 years, 32% ST-segment elevation myocardial infarction and 64% radial access). Mean CRBS value was 31±16 points. Based on CRUSADE bleeding risk categories, 394 (32%) patients had CRBS <10, 324 (26%) had CRBS between 10 and 24, 244 (20%) had low risk, 257 (21%) had moderate risk, 186 (15%) had high risk and 153 (12%) were very high risk. A total of 29 (2.4%) patients had in-hospital major bleeding: 13 (45%) type 3a, 9 (31%) type 3b, 4 (14%) type 4 and 3 (10%) type 5b. The rates of in-hospital major bleeding across the CRUSADE risk categories were: 1% (very low risk), 0.8% (low risk), 2.7% (moderate risk), 5.4% (high risk), and 3.9% (very high risk); p=0.001. In the overall study population, AUC was 0.68 (95% CI 0.59–0.77), whereas in patients with and without ST-segment elevation acute coronary syndromes were 0.76 (95% CI 0.70–0.82) and 0.49 (95% CI 0.37–0.64), respectively. There were no differences in AUCs according to vascular access site (Radial: 0.66, 95% CI 0.51–0.80 and Femoral: 0.65, 95% CI 0.52–0.77).

Conclusions: CRBS shows a modest accuracy for predicting in-hospital major bleeding based on BARC criteria, especially in those subjects with non ST-segment elevation acute coronary syndromes. Further studies are needed to confirm these findings, and to explore alternative scores that predict more accurately in-hospital BARC major bleeding.

P1099 | BEDSIDE
Direct comparison of the safety and efficacy of 2 rule-out strategies for AMI: undetectable levels at presentation versus combination of 1h-algorithm and undetectable levels at presentation

Purpose: Addressing the increasingly recognized, yet unmet clinical need for rapid rule-out of acute myocardial infarction (AMI), several novel strategies have been developed. Due to the lack of direct comparisons in the same dataset, selection of the best strategy for clinical practice is challenging. We therefore aimed to directly compare the safety and efficacy of two previously defined strategies: LOD (Undetectable levels of high-sensitivity cardiac troponin (hs-cTn) at presentation) versus the combination of hs-cTn 1h-algorithm and LOD.

Methods: In a prospective international multicentre diagnostic study enrolling 2213 patients presenting with suspected AMI to the emergency department, the final diagnosis of AMI was adjudicated by two independent cardiologists using all available clinical information including serial hs-cTnT concentrations. Safety was quantified as the negative predictive value (NPV) for AMI in the rule-out zone of the respective rule-out strategies. Efficacy was quantified as the percentage of the overall cohort assigned to the rule-out zone by the respective strategy. Both strategies were applied using the two best-validated hs-cTn assays (hs-cTnT Roche: LOD <5ng/l; 1h-algorithm 0h –12ng/l and Δ0–1h-3ng/l; and hs-cTn Abbott: LOD <2ng/l; 1h-algorithm 0h –5ng/l and Δ0–1h-2ng/l) to ensure that findings are independent from the hs-cTn assay used. As both strategies should only be applied once ST-elevation MI (STEMI) has been excluded using the initial ECG, STEMI patients were excluded from the analysis.

Results: Acute myocardial infarction was the final diagnosis in 17% of patients. Using hs-cTnT, the safety was very high and comparable with both algorithms (LOD: NPV 99.8%, 95% CI 99.0–100% versus LOD+1h-algorithm: NPV 99.9%, 95% CI 99.5–100%, p=ns). Regarding efficacy, LOD allowed rule-out in 24% of patients versus 59% with 1h-algorithm+LOD (p<0.001). Using hs-cTnT, the safety was very high and comparable with both algorithms (LOD: NPV 100%, 95% CI 99.8–100% versus LOD+1h-algorithm: NPV 99.2% (95% CI 98.4–99.6, p=ns). Regarding efficacy, LOD allowed rule-out in 16% of patients versus 53% with the 1h-algorithm (p<0.001).

Conclusion: Both investigated rule-out strategies allow a safe rule-out of AMI, irrespective of the underlying hs-cTn assay. While LOD has the obvious advantage of allowing rule-out already with the measurement at presentation, the combination of LOD and 1h-algorithm is much more effective and more than doubles the number of patients eligible for rule-out.

P1100 | BEDSIDE
Direct Comparison of the Safety and Efficacy of 2 Rule-Out Strategies for Acute Myocardial Infarction: Undetectable Levels of hs-Troponin versus Copeptin in Combination with troponin

Purpose: Addressing the increasingly recognized, yet unmet clinical need for rapid rule-out of acute myocardial infarction (AMI), several novel strategies have been developed. Due to the lack of direct comparisons in the same dataset, selection of the best strategy for clinical practice is challenging. We therefore aimed to directly compare the safety and efficacy of two previously defined strategies: LOD (Undetectable levels of high-sensitivity cardiac troponin (hs-cTn) at presentation) versus the combination of copeptin and troponin.

Results: Acute myocardial infarction was the final diagnosis in 18.5% of patients. Using hs-cTnT, the safety was very high and comparable with both algorithms (99.8%, 95% CI 99.6–100% versus copeptin and troponin; 99.8%, 95% CI 97.9–99.4%, p=0.2). Using hs-cTnT, the safety was very high and comparable with both
algorithms (LOD: NPV 100%, 95% CI 98.7–100% versus copeptin and hs-cTnT: NPV 96.4% 95% CI 95.0–97.5, p=0.002) but slightly better for LOD. Regarding efficacy, LOD allowed the rule-out in 14.7% of patients versus 53.9% with dual marker strategy (p<0.001).

Conclusion: While both investigated rule-out strategies allow a safe rule-out of AMI, irrespective of the underlying hs-cTnT assay, the combination of hs-cTnT and copeptin is much more effective and more than doubles the number of patients eligible for rule-out.

P1101 | BEDSIDE
Comparison of 10-Year follow-up mortality rates in a randomized trial comparing routine invasive versus selective invasive management in patients with non ST-segment elevation acute coronary syndrome

D.N. Kalkman, P. Woudstra, P. Dammam, A. Hirsch, F. Windhausen, J.G. Tijsse, R.J. De Winter, Academic Medical Center of Amsterdam, Cardiology, Amsterdam, Netherlands

Background: Long-term outcomes after invasive versus conservative treatment in unstable coronary syndromes have been described up to 5 year follow-up.

Purpose: To determine if there is a difference in 10 year mortality between an early invasive versus a selective invasive treatment strategy in low, medium and high risk patients presenting with non-ST-segment elevation acute coronary syndromes (NSTEMI-AUC).

Methods: 1200 patients have previously randomly been assigned to an early invasive or selective invasive strategy. Risk stratification was performed on baseline characteristics: age, presence of diabetes, hypertension, ST-segment depression and body mass index was done according to the FFR (FRISC-ICTUS-RITA-3) risk score. At ten year follow-up vital status and time of death were obtained for all patients from the national population registry (Dutch Central Bureau of Statistics). Adjudicated MI event rates will be available at the time of presentation. Cumulative event rates were estimated by a Kaplan-Meier model.

Results: Mortality rates at 10 year follow-up were 26.9% in early invasive and 23.5% in selective invasive management, hazard ratio [HR]: 0.86, 95% confidence interval [CI]: 0.68 to 1.08, p=0.19. After risk stratification, HR in low risk: 1.00 (95% CI: 0.66–1.52), p=1.00, HR medium risk: 1.24 (95% CI: 0.86–1.78), p=1.26 and HR high risk: 1.06 (95% CI: 0.66–1.70), p=0.80.

Conclusion: Our study demonstrates no significant difference in death rates at 10 year follow-up in patients presenting with NSTE-ACS and elevated troponin T, treated with an early invasive strategy or selective invasive management and no significant differences after risk stratification.

P1102 | BEDSIDE
Guideline recommended care and excess mortality for NSTEMI: a national cohort study

T.B. Dondo1, M. Van Laar1, O.A. Alabas1, M.S. Gilthorpe1, P.D. Batin2, A.D. Timmis1, J.E. Dearfield1, H. Hemingway3, C.P. Gale1. 1University of Leeds, Division of Epidemiology and Biostatistics, LIACMM, Leeds, United Kingdom; 2Pinderfields General Hospital, Department of Cardiology, Wakefield, United Kingdom; 3Barts Health NHS Trust, The National Institute for Health Biomedical Research Unit, London, United Kingdom; 4University College London, National Institute for Cardiovascular Outcomes Research, London, United Kingdom; 5University College London, The Farr Institute, London, United Kingdom

Introduction: Adherence to guideline care for NSTEMI is associated with improved outcomes. However, the excess risk of death from non-adherence to guideline recommended care across a national health system is unknown.

Methods: Nationwide population-based cohort study (247 hospitals, 93516 NSTEMI in England and Wales, 2003–10) using data from the Myocardial Ischaemia National Audit Project (MINAP). Adherence to care was measured against ESC guidelines for the management of NSTEMI. Adjusted time ratios (TRs) were obtained from hierarchical accelerated failure time models to determine impact using guideline recommended care on all-cause mortality.

Results: Overall, 76% of patients did not receive ≥1 care opportunity for which they were eligible. There was a significant difference in unadjusted survival between those who received all care opportunities and those who did not (Figure 1).

After adjustment, survival times for those who missed ≥1 care opportunity were significantly shortened (TR=0.51, 95% CI 0.48–0.55) compared to patients who received optimal care. If all patients during the 8 year study period received all eligible care opportunities, then 11,650 (95% CI 11,337–11,884) deaths could have been postponed for at least 1 year.

WHAT’S NEW IN IMAGING FOR VALVULAR HEART DISEASE?

P1104 | BEDSIDE
Novel method for determination of mitral regurgitation severity before and after percutaneous edge-to-edge mitral valve repair by contrast echocardiography

M. Huntgeburth, H. Ten Freyhaus, C. Sunderkamp, S. Baldus, V. Rudolph. Cologne University Hospital - Heart Center, Clinic III for Internal Medicine, Cologne, Germany

Background: There is no validated method for determination of residual mitral regurgitation (MR) following percutaneous edge-to-edge mitral valve repair. Existing
methods have either been demonstrated to overestimate MR severity or are derived from a multitude of echocardiographic parameters and are therefore prone to measurement errors. We herein propose a novel, simple method for determination of MR severity based on contrast echocardiography, which is not affected by the double orifice morphology following percutaneous edge-to-edge mitral valve repair.

Methods and results: Apical 4-chamber, low mechanical index contrast echocardiographic images using a 1.5 ml of a sulphur hexafluoride contrast agent at steady state conditions were recorded in 21 patients before and after percutaneous mitral valve repair. Echocardiographic backscatter in the left ventricle (LV) and atrium (LA) was determined using QLab quantification software. As compared to before the procedure a significant approximation of LV and LA backscatter was observed with reduction of MR after the procedure (enddiastolic difference between LA and LV backscatter: 2.7±3.3 dB vs. 3.3±2.6 dB; p <0.001). This decrease was mainly driven by a significant increase in LV backscatter after MitraClip implantation (enddiastolic LV backscatter: 25.5±3.9 dB vs. 23.5±4.7 dB; p <0.01), possibly explained by a higher degree of resonance of microbubbles remaining in the ultrasound field for several heart cycles as they travel forth and back between LA and LV in mitral regurgitation. In accordance with the above described observation, healthy individuals exhibited a significantly lower difference between LA and LV backscatter compared to individuals with severe MR (3.7±1.0 dB vs. 7.2±3.3 dB; p <0.01).

Conclusions: Our data suggest that MR can be assessed by contrast echocardiography. As this novel method does not underlie the limitations of color Doppler imaging and is readily quantifiable it might evolve as valuable tool for quantification of MR especially in the setting of complex flow patterns as encountered at percutaneous edge-to-edge mitral valve therapy.

P1108 | BEDSIDE
Predictive factors for echocardiographic overestimation of aortic valve area by continuity equation in patients with severe aortic stenosis

H. Inoue, H. Abe, K. Yasumura, H. Nishida, K. Shinouchi, H. Miura, M. Koide, M. Date, Y. Koresutine, H. Kusuoka. Osaka National Hospital, Cardiovascular Division, Osaka, Japan

Background: Echocardiographic evaluation of aortic valve area (AVA) is a non-invasive method to assess the severity of aortic stenosis (AS). Left ventricular outflow tract (LVOT) acceleration flow is well known as a potential risk factor for overestimating echocardiographic AVA by continuity equation (EAVA), eventually leading to underestimation of AS severity. However, cut-off values for acceleration flow velocity and predictive factors for overestimation of EAVA have yet to be clarified.

Purpose: To clarify predictive factors for overestimation of EAVA compared with AVA by cardiac catheterization using Gorlin’s method (CAVA) in patients with severe AS.

Methods: We performed a retrospective analysis of 32 consecutive patients with severe AS who underwent both echocardiography and cardiac catheterization in our hospital before aortic valve replacement from January 2012 to December 2014.

Results: AVA and trans-aortic valve mean pressure gradient by echocardiography and cardiac catheterization were 0.72±0.23 vs. 0.67±0.23 cm H2O, and 53±18 vs. 53±22mm Hg, respectively. Concordance of AVA and trans-aortic valve mean pressure gradient by each method were r=0.80, p<0.001 and r=0.78, p<0.001, respectively. Assuming appropriate estimation of EAVA as a difference between the two methods <0.15 cm H2O, 10 cases (31%) were overestimated (EAVA-CAVA, 0.28±0.07 cm H2O), 19 cases (59%) were appropriately estimated (EAVA-CAVA, -0.01±0.10 cm H2O), and 3 cases (9%) were underestimated. No significant differences in LVOT diameter (20.5±1.5 mm vs. 20.2±2.9 mm, p=NS), LVOT velocity time integral (27.7±10.1 cm vs. 23.1±5.4 cm, p=NS), and aortic regurgitation grade between the overestimation and appropriate estimation groups. Significantly more cases (70%) showed visual LVOT acceleration flow in the overestimation group than in the appropriate estimation group (36%; p<0.04). Visual LVOT acceleration flow was well predicted by LVOT peak velocity (cut-off value 0.98 m/s; sensitivity 100%, specificity 77%), LVOT peak velocity best predicted the overestimation of EAVA (cut-off value, 1.1 m/s; sensitivity 79%, specificity 70%) among various parameters.

Conclusion: Overestimation of EAVA was observed in 30% of cases due to LVOT acceleration flow in patients with severe AS. LVOT peak acceleration flow velocity greater than 1.1 m/s may be clinically useful as a cut-off value to avoid underestimation of AS severity.
CLINICAL IMPACT AND MODULATION OF ENDOTHELIAL (DYS)FUNCTION

P1110 | BEDSIDE
Medium term evolution of paravalvular leaks in the CoreValve percutaneous aortic valve prosthesis: echocardiographic assessment

M. Delgado Ortega, M. Puentes Chichacio, M. Ruiz Ortiz, D. Mesa Rubio, C. Ferreiro Quero, J. J. Sanchez Fernandez, E. Duran Jimenez, M. C. Morenate Navio, M. Pan Alvarez Osorio, J. Suarez De Lezo Cruz Conde. Department of Cardiology. Reina Sofia University Hospital, Cordoba, Spain

Background and aim: Transcatheter aortic valve implantation (TAVI) has become a routine procedure in patients with severe aortic stenosis and high risk for surgical aortic valve replacement. Postprocedural aortic regurgitation (AR) is common following a successful CoreValve implantation, but there are few studies investigating the course of periprosthetic leaks following the implantation. Our aim was to study the evolution of the degree of AR after a successful transcatheter aortic valve implantation and to study the evolution of the degree of AR at one year of follow up.

Methods: From April/2008 to March/2014 a total of 189 symptomatic aortic valve stenosis underwent TAVI with the CoreValve prosthesis in our department. We selected 115 patients (mean age 78±5 years. 45% male, mean Lognistic Euroscore 10±7%) who had completed, at least, 1 year of clinical and echocardiographic follow up. Clinical and echocardiographic examination were performed at discharge, at 1, 6 and 12 months, and annually thereafter. Postprocedural AR was graded by means of the classification system according to paravalvular leak into grades I, II, III and IV. Mean clinical follow up was 3.5±1.3 years, and echocardiographic follow up 3±1.3 years.

Results: Any degree of AR was present in the echocardiographic study at discharge in 90 patients (78%); grade I: 53 patients (46%), grade II: 28 patients (24%), grade III: 8 patients (7%) and grade IV: 1 patient (1%). At last echocardiographic follow up there was a significant reduction in the number of patients with postprocedural AR; any degree of AR was observed in 67 patients (58%); grade I: 31 patients (27%); grade II: 24 patients (21%); grade III: 10 patients (9%), and grade IV: 2 patients (2%), p<0.03.

Conclusions: At discharge, a high percentage of patients who underwent a successful implantation with the CoreValve prosthesis in our institution had any degree of echocardiographic postprocedural AR. Beyond the first year of follow up, we observed a significant reduction in the paravalvular regurgitation (disappearing any degree of AR in some patients), probably related to the high adaptability and self-expandability of the nitinol prostheses.

P1111 | BENCH
Critical role of PTNP18 in endoplasmic reticulum stress-induced endothelial dysfunction

P.A. Theibault1, D. Coquere1, E. Deile1, F. Tamir2, V. Richard3 on behalf of InsERM U1096, INSERM U1096, ROUEN, France; 1University Hospital of Rouen, Rouen, France

Protein tyrosine phosphatase 1B (PTP1B) negatively regulates tyrosine-kinase receptors and has been shown by our team to inactivate Nitric Oxide (NO) Synthase, resulting in impaired NO production and endothelial dysfunction. Indeed we demonstrated that pharmacological or genetic PTP1B inhibition restored NO production and improved endothelial dysfunction in a mouse model of heart failure. Recent evidence suggested that PTP1B also plays a major role in Endoplasmic Reticulum Stress (ERS) regulation, a conserved pathway involved in cell homeostasis control. PTP1B expression is induced under ERS conditions, such as misfolded protein accumulation in the ER lumen, and can inactivate the PERK branch and activate the IRE1 branch of ERS. Moreover, recent studies suggested that ERS plays a role in endothelial dysfunction via increased oxidative stress and impaired NO production.

To assess the role of ERS in PTP1B-mediated endothelial dysfunction, we used two different models of ERS induction, involving either in vivo intraperitoneal injection of the ERS inducer Tunicamycin (TN) or in vitro incubation of mesenteric arteries with TN. Endothelial function was assessed by measuring flow-mediated dilatation (FMD) in phenylephrine-preconstricted, isolated, perfused mesenteric arteries. Arterial ERS markers were analyzed by Western Blot.

In wild type (WT) mice, both in vivo and in vitro TN induced a severe endothelial dysfunction, (Maximal FMD, %: TN in vivo: Untreated 24±1.2±0; TN 3±0.9 p<0.01; TN in vitro: Untreated 20±5±1.3; TN 8±2±1.7, p<0.01). This endothelial dysfunction was associated with an increase in the ERS markers GRP78 (+136%) and ATF6α (+60%) in mesenteric arteries. In contrast, PTP1B(-/-) mice showed no alteration of endothelial function when treated with TN (in vivo: 22±5±0, p<0.01 vs. TN WT, p<0.01 vs. untreated WT, TN in vitro: 23±5±2.3, p<0.01 vs. untreated WT). This endothelial protection was associated with a lesser increase in GRP78 (+70%) and ATF6α (+25%) expressions. Interestingly, ATF6α was basally upregulated in PTP1B(-/-) mice, when compared to WT mice, suggesting a negative regulation of ATF6α expression by PTP1B.

This work confirms that ERS induces endothelial dysfunction in resistance arteries. It also demonstrates for the first time that PTP1B is a crucial actor of ERS in the endothelium and that the beneficial effect of PTP1B inhibition on endothelial dysfunction largely involves a reduction of endothelial ERS, potentially revealing powerful new targets for endothelial protection.
P1113 | BENCH
SIRT3 deficiency induces endothelial insulin resistance and vascular dysfunction in obese mice and human subjects

L. Yang, J.L. Zhang, W.J. Xing, Z. Zhang, J. Xu, X.N. Ning, H.F. Zhang, J. Li, F. Gao on behalf of Insulin. Fourth Military Medical University, Department of Physiology, Xi’an, China, People’s Republic of

**Background:** Recent evidence implicates SIRT3 as a central regulator of mitochondrial redox balance and metabolic homeostasis but the contribution of SIRT3 to vascular function remains unknown.

**Purpose:** The aim of this study was to investigate the role of SIRT3 in obesity-induced endothelial insulin resistance and subsequent vascular dysfunction.

**Methods:** Both vascular response to insulin and SIRT3 expression were detected in ob/ob mouse and human subjects undergoing bariatric surgery and non-obese controls. Male SIRT3 knockout mice and wild type littermates were fed with a standard chow diet or a high fat diet (HFD) for 24 weeks.

**Results:** We found an impaired insulin-induced mesenteric vasoconstriction (82.46±18.5% vs. 54.93±16.6%, n=8–12, P<0.05) and concomitantly a 50% reduced vascular SIRT3 expression in morbid obese human subjects compared with non-obese controls. Downregulation of SIRT3 either by siRNA or by palmitate exposure in cultured human endothelial cells resulted in overproduction of mitochondrial reactive oxygen species (mtROS) and impaired insulin signaling as indicated by decreased phosphorylation of Akt and eNOS and subsequent reduced NO bioavailability. Additionally, ob/ob mouse fed by 24-week HFD displayed an impaired endothelium-dependent vasoconstriction to insulin (46.84±3.29% vs. 29.56±2.99%, n=6, P<0.01) and acetylcholine (75.59±4.93% vs. 100.59±2.35%, n=6, P<0.01), which was further exacerbated by gene deletion of SIRT3 (P<0.05). Moreover, lentivirus-mediated restoration of vascular SIRT3 rescued HFD-induced endothelial dysfunction in SIRT3 knockout mice (46.84±3.29% vs. 29.56±2.99%, n=6, P<0.01 for response to insulin; 75.59±4.93% vs. 72.52±3.81%, P<0.01 for response to acetylcholine). Elimination of mtROS with MitoTEMPO not only restored insulin-stimulated NO production in SIRT3 knockout cells but also improved insulin-induced vasorelaxation in SIRT3 knockout mice fed with HFD.

**Conclusions:** We suggest that SIRT3 positively regulates endothelial insulin sensitivity and show that SIRT3 deficiency and resultant mtROS overproduction contribute to vascular dysfunction in obesity.

---

P1114 | BENCH
Platelet endothelial aggregation receptor-1: a novel modifier of angiogenesis

C. Vandenbriele1, A. Kauskot1, I. Vandersmissen1, M. Criell1, S. Craps1, A. Lutten1, S. Janssens2, M. Hoyaerts2, P. Verhamme1.* KU Leuven, Center for Molecular and Vascular Biology, Department of Cardiovascular Sciences, Leuven, Belgium; 2 KU Leuven, Cardiology, Department of Cardiovascular Sciences, Leuven, Belgium

**Objective:** Platelet Endothelial Aggregation Receptor-1 (PEAR1) is a cell membrane protein, expressed on platelets and endothelial cells (ECs). PEAR1 sustains s irrIg3-activation in aggregating platelets and attenuates megakaryopoeisis via controlling the degree of phosphorylation of Akt. Its role in EC biology is unknown.

**The aim of this study was to compare the expression of PEAR1 in human endothelium of various tissues and to determine its role for EC function in vitro and for angiogenesis in Pear1–/– mice.

**Methods:** All studies were done in human cultured ECs and it coincided with CD31 in various tissues. PEAR1-expression was variable in ECs of different origin. Lentinial knockdown of PEAR1 in cultured ECs by 70% double-celled EC proliferation, in turn enhancing in vitro formation of matrigel through the AkT/PEN-dependent p21/CCD2-pathway. Even when physiologically blood vessel formation was unaffected in Pear1–/– mice, neangiogenesis in these mice was significantly increased both in a hind limb ischemia ligation model (4.7-fold increase in capillary density in the ligated limb of Pear1–/– mice compared to ligated limbs in WT mice) and in a skin wound healing model (resulting in a 2-fold faster wound closure in Pear1–/– mice compared to WT littermates).

Conclusions: We established an inverse correlation between endothelial PEAR1-expression and EC proliferation driven vascular assembly both in vitro and in vivo. These findings identify PEAR1 as a novel modifier of neoangiogenesis.

---

P1115 | BENCH
Dual Antithrombotic Effects of Ticagrelor in Arterial Thrombosis: An Antiplatelet Agent With Anticoagulant Properties

M.F. Reiner1, A. Akhmedov1, S. Stivala1, S. Keller1, G. Savarese1, M. Glanzmann1, T.F. Luescher2, G.G. Camici1, J.H. Beer3.* University of Zurich, Center for Molecular Cardiology, Schlieren, Switzerland; 2 Cantonal Hospital of Baden, Internal Medicine, Baden, Switzerland; 3 University Heart Center, Department of Cardiology, Zurich, Switzerland

**Background:** Arterial thrombosis is the key event in myocardial infarction development. The P2Y12 antagonist ticagrelor reduced mortality in patients with acute coronary syndrome (ACS) compared with clopidogrel. Off-target effects for both ticagrelor and clopidogrel have been reported; however, endothelium-specific effects and their underlying mechanisms and potential implication in arterial thrombosis remain unknown.

**Methods:** Human aortic endothelial cells (HAECs) were treated with increasing concentrations of ticagrelor (10–7, 10–6, 10–5 M) or clopidogrel active metabolite (CAM, 1.5x10–8, 10–7, 10–6 M), and stimulated with tumor necrosis factor-alpha (TNF-α, 10 ng/mL). Effects on pro-coagulant tissue factor (TF) expression and activity, its counter-player TF pathway inhibitor (TFPI) and the underlying mechanisms as well as potential receptors, including the equilibrative nucleoside transporter 1 (ENT1), an additional target of ticagrelor, were investigated. To test the functional in vivo relevance of our findings, 12-week-old male C57BL/6 mice were treated with vehicle, ticagrelor (0.15% w/w) or clopidogrel (0.06% w/w) suplemented in chow. After 2 weeks, arterial thrombosis of the common carotid artery was examined following laser injury.

**Results:** Ticagrelor, but not CAM, reduced TF-induced TF expression and activity via PI3 and p70S6 kinase without affecting TFPI. TF reduction was regulated through post-translational decrease of protein stability rather than transcriptional modifications or TF mRNA half-life. Neither P2Y12 mRNA nor protein was detected in HAECs. Inhibition of ENT1 by dipyridamole did not mimic the observed effect. In line with this, adenosine receptor antagonists against A1, A2a, A2b or A3 did not reverse ticagrelor-mediated TF reduction. C57BL/6 mice treated with ticagrelor or clopidogrel exhibited equal and next to complete inhibition (-95%) of ADP (10cM)-induced platelet aggregation; however, ticagrelor significantly prolonged time to arterial occlusion as compared with clopidogrel (94.13±6.75 min vs 72.14±6.55 min; n=8/7; P<0.05).

**Conclusions:** Ticagrelor, unlike CAM, exhibits endothelial-specific anticoagulant properties independently of P2Y12 and ENT1 and reduces arterial thrombosis compared with clopidogrel. These mechanisms may explain the superior effects of ticagrelor in clinical trials and may provide new therapeutically options of the drug.

---

P1116 | BEDSIDE
The impact of flavonoid supplementation on acute smoking-induced vascular dysfunction and fibrinolytic impairment

E. Kokkou, G. Siasos, E. Okononofos, A. Verenovitis, N. Gouliopoulos, K. Zisimos, M. Zaromytidou, A. Millou, K. Mourouzis, D. Toussulis. University of Athens Medical School, 1st Cardiology Department, "Hippokration" Hospital, Athens, Greece

**Background:** Smoking is associated with vascular dysfunction and impairment of fibrinolytic status. Concord grape juice (CGJ), a rich source of flavonoids, can modify cardiovascular risk factors. Endothelial function and arterial stiffness are surrogate markers of arterial health.

**Purpose:** To evaluate the impact of CGJ on endothelial function, arterial stiffness and fibrinolytic status in healthy smokers.

**Methods:** We studied the effect of 2 weeks oral treatment with CGJ in 26 healthy smokers on three occasions (day 0: baseline, day 7 and day 14) in a randomized, placebo-controlled, double-blind, cross-over design. Measurements were carried out before (pSm), immediately (Sm0) and 20 minutes after (Sm20) cigarette smoking. Endothelial function was evaluated by flow-mediated dilation (FMD) of the brachial artery. Carotid-femoral pulse wave velocity (PWV) was measured as an index of aortic stiffness. Serum levels of plasminogen activator inhibitor 1 (PAI-1) were measured at each study day immediately before smoking and 20 minutes later as a biomarker of fibrinolytic status.

**Results:** Treatment with CGJ resulted in a significant improvement in FMD from 8.57±2.23% to day 0 to 9.15±2.1% day 7 to 9.1±2.7% day 14, p=0.02 and PWV (from 6.13±0.61/sec day 0 to 5.86±0.63/sec day 7 to 5.63±0.56/sec day 14, p=0.04). Treatment with placebo had no impact on FMD values (p=NS) and PWV (p=NS). Compared to placebo, CGJ treatment prevented the acute smoking induced decrease in FMD in day 7 (p=0.07) and in day 14 (p<0.04). Treatment with CGJ prevented the smoking induced elevation of PWV, after 7 p=0.055) and 14 p=0.04) days of treatment. Smoking induced an elevation in PAI-1 levels after smoking compared to smoking-produced levels in all study days and in both arms (CGJ and placebo) of the study (p<0.05, for all). Importantly, treatment with CGJ decreased pSm values of PAI-1 from 102 (65–134) ng/mL day 0 to 58 (42–75) ng/mL day 7 to 0.39 (20–47) ng/mL day 14, p<0.001 while placebo had no impact on PAI-1 levels (p=0.2). Moreover CGJ significantly ameliorated the acute smoking
induced increase in PAI-1 levels [from 24 (13–55)ng/ml day 0 to 14 (7–31)ng/ml day 7 to 13 (7–23)ng/ml day 14, p < 0.001] while placebo had no impact on the acute smoking induced increase in PAI-1 levels (p = 0.17).

Conclusions: Concord grape juice consumption improved endothelial function and vascular elastic properties of the arterial tree during the acute phase of smoking, and affected accompanied by improvements of antithrombotic status of mononuclear cells. These findings shed further light on the favorable mechanisms of Concord grape juice in atherosclerosis.

P1117 | BEDSIDE
Transradial catheterisation: a clinical translational model of human arterial injury in vivo

Introduction: Circulating endothelial progenitor cells (EPCs) are thought to play an important role in endothelial reconstitution following injury. However, investi-
gation of the biology of these cells in humans has been limited by the lack of a safe and accessible in vivo model of arterial injury. To address this, we charac-
terised the structural damage and functional impairment of the radial artery in patients undergoing transradial cardiac catheterisation as well as the EPC profile accumulating at the injury site.

Methods: Patients undergoing elective angiography were enrolled (n=21). Ra-
dial arterial injury was assessed using optical coherence tomography (OCT). Arte-
sial sheaths were examined for endothelial cells. Radial flow-mediated dilatation (FMD) was assessed bilaterally at baseline, 24 hours, 1, 4 and 12 weeks. Circu-
lating EPCs were assessed at baseline and 24 hours using flow cytometry.

Results: Radial injury was observed in 4 patients (19%). Despite the low in-
cidence of injury, FMD was attenuated in the catheterised vs non-catheterised arm (p = 0.04 vs 10.74±5.56 p < 0.05) but not at 4 and 12 weeks. Arterial sheaths yielded signif-
cant numbers of cells (mean 6.3x10^5 ±4.6x10^5) a significant proportion of which were endothelial (40.0±3.7%). Compared to baseline, transradial catheterization was associated with significant mobilisation of CD34+ cells (0.05% ± 0.02 vs 0.09% ± 0.06 of mononuclear cells p < 0.05).

Conclusions: Even in the absence of injury detectable by OCT, transradial catheterization is associated with endothelial denudation, radial artery vasmotor dysfunction, and mobilization of naïve progenitor cells. The radial artery thus of-
ters a unique model with which to examine arterial injury and therapies targeting cellular repair in vivo in man.

ADVANCES IN CARDIOMYOPATHIES

P1118 | BEDSIDE
New sudden cardiac death risk score in hypertrophic cardiomyopathy - clinical application in a referral clinic and correlation with clinical, genetic and imaging data

Introduction: Hypertrophic cardiomyopathy (HCM) is a major cause of sudden cardiac death (SCD) in the young, which can be prevented by implanted car-
dioverter defibrillators (ICD). We aim to introduce a new 5-year risk model in the new ESC guidelines, with a class IIa indication for ICD implantation if score ≥ 6%. Our aim was to evaluate the use of the new score in clinical practice, compare with previous recommendations and study the associations of a high score with pa-
rameters not included in the model.

Methods: Consecutive index HCM cases were studied and evaluated accord-
ing to the guidelines with genetic testing, ECG, echocardiogram, magnetic res-
sonance, Holter and treadmill stress ECG or echo. Conventional SCD risk fac-
tors were included in the model.

Results: 113 patients (pts) aged 57±18.3 years, 62 (55%) males, MLWVT 19.3±4.8 mm, left ventricular outflow tract obstruction in 31%. Positive genetic test-
s for sarcomere genes in 39%. Follow-up 31.8±29 months. Number of C-SCDRF: maximal left ventricular wall thickness (MLWVT) >30 mm; non-
sustained VT (NSVT); syncope; family history of SCD (FH-SCD); abnormal blood pressure response to exercise (ABPRE). The new risk score was calculated and correlated with clinical, electrocardiographic, imaging and follow-up parameters.

Results: 113 patients (pts), aged 57±18.3 years, 62 (55%) males, MLWVT 19.3±4.8 mm, left ventricular outflow tract obstruction in 31%. Positive genetic test-
s for sarcomere genes in 39%. Follow-up 31.8±29 months. Number of C-SCDRF: maximal left ventricular wall thickness (MLWVT) >30 mm; nonsustained VT (NSVT); syncope; family history of SCD (FH-SCD); abnormal blood pressure response to exercise (ABPRE). The new risk score was calculated and correlated with clinical, electrocardiographic, imaging and follow-up parameters.

Conclusion: Despite similar baseline characteristics, higher use of beta-blockers and less intraoperative hemodynamic shifts, HCM patients who undergo interme-
diate and high-risk noncardiac surgery have significantly worse outcomes com-
pared to a matched group of patients undergoing similar noncardiac surgery.

P1119 | BEDSIDE
Outcomes of hypertrophic cardiomyopathy patients undergoing non-cardiac surgery: A cohort study with matched non hypertrophic cardiomyopathy patients

Background: Data on peri-procedural outcomes of hypertrophic cardiomyopathy (HCM) patients undergoing noncardiac surgery are lacking.

Purpose: We sought to compare outcomes of HCM patients undergoing noncar-
diac surgery with a matched group of non-HCM patients.

Methods: In a cohort study, consecutive HCM patients (n = 92) undergoing in-
termediate and high-risk noncardiac surgery between 1/07 and 12/2013 were identified (excluding < 18 years, prior sepsis myocardial infarction, low-risk surgery) and matched (based on age, gender, type and time of noncardiac surgery) in a 1:2 fashion with non-HCM patients (n = 184). Clinical, intra-operative and post-operative data were obtained. A composite end-point of 30-day post-
operative death, myocardial infarction, stroke and congestive heart failure was recorded. Post-operative atrial fibrillation (AF) within 30-days was recorded.

Results: The 2 groups were well-matched for relevant non-HCM related base-
line characteristics, as shown in Figure 1. 58% HCM patients had provokable left ventricular outflow obstruction (>30 mm Hg) and 62% had systolic anterior mo-
tion of mitral valve. At 30 days post-operatively, a significantly higher proportion of HCM patients had AF, while none occurred in non-HCM patients (p < 0.03). Similarly, 4% HCM patients had AF, while none occurred in non-HCM pa-
tients (p < 0.01). At 30-days, there were 3 deaths each in HCM and non-HCM groups.

Conclusion: Despite similar baseline characteristics, higher use of beta-blockers and less intraoperative hemodynamic shifts, HCM patients who undergo interme-
diate and high-risk noncardiac surgery have significantly worse outcomes com-
pared to a matched group of patients undergoing similar noncardiac surgery.

P1120 | BEDSIDE
Prognosis in dutch mybpc3 founder mutation carriers is defined by phenotype
H.G. Van Velzen, A.F.L. Schinkel, R.A. Oldenburg, M.A. Van Slegtenhorst, I.M.E. Frohn - Mulder, M. Michels on behalf of Erasmus Medical Centre. Erasmus Medical Center, Cardiology, Rotterdam, Netherlands

Background: In the Netherlands, founder mutations in MYBPC3 are responsible for 35% of hypertrophic cardiomyopathy (HCM) cases. Functional studies show that these mutations cause haploinsufficiency and have similar effects on sarcomere function.

Purpose: To determine phenotypic expression and prognosis of MYBPC3 founder mutation carriers.

Methods: Subjects carrying a Dutch founder mutation in MYBPC3 known at our cardio genetics department were included. Survival curves were determined using Kaplan Meier analysis.

Results: There were 274 MYBPC3 founder mutation carriers (125 (46%) c.237dupG; 88 (32%) c.2827C>T and 11 (22%) c.2864_2865delCT); 144 index patients (age 45±14 years) and 130 relatives (age 44±15 years). Index patients

plantation using the new score is lower compared to the conventional assess-
ment. The presence of angina, lower longitudinal myocardial deformation, con-
centric or apical hypertrophy patterns and lower LV end-diastolic dimension were associated with a higher SCD risk score at 5 years.
presented with HCM (n=137; 95%), non-compaction cardiomyopathy (n=4; 3%) and dilated cardiomyopathy (n=3; 2%). At median follow up of 8 (range 1 to 25) years, 43 (30%) index patients underwent septal reduction therapy (SRT) and 32 (22%) received an implantable cardioverter defibrillator. All-cause mortality, heart failure-related mortality and sudden cardiac death (SCD) in index patients were 26%, 10% and 8% respectively. SCD occurred at a median age of 49 (range 12 to 74) years. At presentation, 52 (40%) relatives had phenotypic expression. At median follow up of 7 (range 1 to 17) years, 4 (3%) relatives underwent SRT and 5 (4%) received an ICD. All-cause mortality, heart failure-related mortality and SCD for affected relatives was 10%, 0% and 11% respectively. Cardiac mortality was absent in phenotype-negative carriers (median age 48, range 14 to 91).

Purpose: To compare the prognostic impact of liver transplantation in TTR-FAP. Methods: Prospective study of consecutive TTR-FAP patients evaluated between September 1998 and November 2014. Since the prognosis crucially depends on the clinical stage of the disease, we performed a nested case-control analysis comparing the clinical outcome of patients undergoing transplantation with non-transplanted, matching patients based on the neurophysiological score determined prior to transplantation (difference of neurophysiological score < 5%).

Results: We evaluated 284 TTR-FAP patients, of whom 153 were women (53.3%). During follow-up, 43 patients (15.1%) were treated with tafamidis and excluded from analysis of liver transplantation. It was possible to perfectly match 88 patients (44 transplanted with 44 non-transplanted) whose mean age was 47±15 years. The median neurophysiological and clinical scores were identical in both groups, 25 (IQR 7.85–51.25) and 24 (IQR 12–34), respectively. Non-transplanted patients had more often late onset disease (47.3% vs. 38.7%, p=0.011) and were older (54±15 vs. 39±22, p<0.001). During a median follow-up of 76 months, 21 patients died (6 transplanted and 15 non-transplanted). Mortality was significantly higher among the non-transplanted patients (13.6% vs. 34.1%, p=0.024), and their risk of death was four times higher (Hazard Ratio=4.03; 95% CI 1.46–11.15, p=0.007). The benefit of liver transplantation in terms of overall survival was found 48 months after the procedure.

Conclusion: Liver transplant significantly improves the long term survival in TTR-FAP patients.

P1123 | BEDSIDE

Genetic spectrum of end stage idiopathic restrictive cardiomyopathy

M. Gallego Delgado1, L. Montserrat2, M.J. Ruiz-Canó3, V. Brossa-Loidí4, J. Palomo5, R. Marzoa-Rivas6, F. Perez-Villa7, J. Salazar8, L. Alonso-Pulpon1, P. Garcia-Pavia1, 1Hospital Universitario Puerta de Hierro, Cardiology, Madrid, Spain; 2Hospital Universitario 12 de Octubre, Cardiology, Madrid, Spain; 3Hospital de la Santa Creu i Sant Pau, Cardiology, Barcelona, Spain; 4Hospital Universitario Gregorio Marañón, Cardiology, Madrid, Spain; 5Complejo Hospitalario Universitario de A Coruña, Cardiology, A Coruña, Spain; 6Hospital Clinic de Barcelona, Cardiology, Barcelona, Spain; 7Hospital Universitario de Bellvitge, Cardiology, Barcelona, Spain

Background: Restrictive cardiomyopathy (RCM) is the least common type of cardiomyopathy. The genetic basis of the condition is largely unknown as genetic sequencing has been challenging and limited to a number of genes associated to a limited number of genes. We sought to determine the genetic basis of RCM and to establish the yield of modern Next Generation Sequencing (NGS) technologies in this setting.

Methods: A total of 32 unrelated patients with end-stage idiopathic RCM (4±11 years, 44% males) underwent NGS genetic evaluation with a panel of 299 genes related to cardiovascular diseases (77 specifically associated with cardiomyopathies). Familial evaluation was performed in available family members. Genetic variants were initially classified as pathogenic mutations or as variants of uncertain significance (VUS). Final pathogenicity status was determined by familial cosegregation studies.

Results: Definite disease-causing mutations were identified in 18 patients (56%). Mutated genes included MYH7 (4), DES (3), MYBPC3 (3), LMNA (2), FLNC (2), TNNT3 (2), TNNT2 (1), TPM1 (1) and LAMP2 (1). A total of 12 patients (38%) exhibited genetic variants of unknown significance and 2 patients (6%) did not show any possible disease-causing mutation. Evaluation of 90 relatives from 25 families identified 18 affected individuals and 6 mutation carriers without clinical phenotypes. Familiar evaluation confirmed the pathogenicity of disease-causing mutations in 8 cases. Furthermore, familial evaluation also allowed reclassification of 4 VUS: 2 as pathogenic mutations and 2 as not pathogenic variants. Genetic study plus familial evaluation revealed a genetic basis of the condition in 23 (72%) cases.

Conclusion: Idiopathic RCM is primarily a genetic disease. The genetic spectrum of the condition is heterogeneous and multiple genes are involved. MYBPC3 and FLNC are new genes associated with RCM. Current genetic techniques plus detailed familial studies allow identification of causative mutations in a high number of RCM patients.

P1124 | BEDSIDE

Rest and exercise pulmonary hypertension in hypertrophic cardiomyopathy

J. Abellard1, J.N. Trochu1, C. Cueff1, A.S. Polge2, C. Bauters2, P. De Groote2, M. Gallego Delgado1, L. Montserrat2, M.J. Ruiz-Canó3, V. Brossa-Loidí4, J. Palomo5, R. Marzoa-Rivas6, F. Perez-Villa7, J. Salazar8, L. Alonso-Pulpon1, P. Garcia-Pavia1, 1Hospital Universitario Puerta de Hierro, Cardiology, Madrid, Spain; 2Hospital Universitario 12 de Octubre, Cardiology, Madrid, Spain; 3Hospital de la Santa Creu i Sant Pau, Cardiology, Barcelona, Spain; 4Hospital Universitario Gregorio Marañón, Cardiology, Madrid, Spain; 5Complejo Hospitalario Universitario de A Coruña, Cardiology, A Coruña, Spain; 6Hospital Clinic de Barcelona, Cardiology, Barcelona, Spain; 7Hospital Universitario de Bellvitge, Cardiology, Barcelona, Spain

Background: Heart failure is a common symptom of hypertrophic cardiomyopathy (HCM) and can be related to several known mechanisms but could also be explained by pulmonary hypertension (PH), which may be secondary to elevation of left-sided diastolic pressures. The main aim of this study was to examine determinants and prognostic significance of PH at rest and during exercise in patients with HCM.

Methods and results: We have included 235 patients referred for evaluation of HCM in this retrospective study. We have measured rest PH in 214 patients (48±16 years, 161 males). One hundred eighty-eight patients performed a symptom-limited semi-supine bicycle exercise including 108 in which exercise...
PH was measurable. Resting PH was present in 56 patients (26.2%) and exercise PH in 38 patients (35.2%). Resting PASP was significantly correlated with sinus rhythm (β = −0.15, P = 0.021), left ventricular obstruction tract (LVOT) maximal gradient (β = 0.22, P = 0.001) and left atrial volume (β = 0.39, P = 0.0001). Exercise PASP was significantly correlated with resting PASP (β = 0.28, P = 0.001), grade of mitral regurgitation (MR) at rest (β = 0.49, P = 0.0001) and resting LVOT peak gradient when MR was eliminated from the analysis. Considering progonis, patients with rest PH had a worse event-free survival at 4 years (24.8±8.8 vs 66.2±5.2%, P = 0.0001), survival without heart failure (55.6±10.5 vs 81.8±4.3%, P = 0.005), and overall survival after 6 and P = 0.001 and resting PH. In univariate Cox analysis rest PASP was a predictor of event-free survival (HR: 1.04; 95% CI; 1.02–1.06, P = 0.001), survival without heart failure (HR: 1.05; 95% CI; 1.02–1.07, P = 0.001), and overall survival (HR: 1.07; 95% CI; 1.03–1.01, P < 0.001).

Conclusion: In patients with HCM, the main determinants of rest PH are sinus rhythm, LVOT maximal gradient and left atrium volume. Determinants of exercise PH are rest PASP, grade of MR and rest LVOT gradient (without MR). Rest PH is associated with increased risk of events, heart failure and overall mortality in univariate analysis.

MANAGING LIPIDS – STATINS AND BEYOND

PI1125 | BEDSIDE
Intensive intervention by specialised nurses after an acute coronary event improves lipid levels and reduces readmissions: a randomized controlled trial
S. Ruiz Bustillo1, I. Ivern Diaz, N. Badosa Marco1, J. Bruguera Cortada, O. Merono Duenas1, D. Rodriguez Anton2, B.A. Perez1, A. Fernandez Gasalla1, E. Marco Navarro2, J. Comin Colet1, J. Hospital del Mar, Cardiology, Barcelona, Spain; 2Hospital del Mar, Physical Medicine and Rehabilitation, Barcelona, Spain

Introduction: Patients recently hospitalized for an acute coronary syndrome (ACS) have an increased risk of recurrent events and low density lipoprotein cholesterol levels (cLDL) with lipid-lowering drugs has been proven to reduce the risk of major adverse cardiac events. However, in the real-world setting, many patients do not achieve the target levels of cLDL recommended in clinical guidelines. Aim: We designed a prospective and randomised open label single center study to evaluate the impact on cLDL levels after an ACS of lipid-lowering drug optimisation by specialised nurses (intervention group, IG) compared to usual care (control group, CG). The primary end-point was the proportion of patients achieving cLDL levels <70 mg/dL at 6 months post discharge. Secondary end-points included changes in blood lipids, doses of lipid-lowering drugs achieved and clinical events (cardiovascular readmissions and death). All patients were followed in a comprehensive rehabilitation program that includes education by nurses and engagement in an exercise training program shortly after hospital discharge. In the CG, the primary care physician or the primary care cardiologist performed drug optimisation. In the IG, optimisation of lipid-lowering drugs was undertaken by specialised nurses following specific protocols and algorithms.

Results: 78 patients were included in the study, 31 patients in the IG and 39 in the CG. The overall survival (84.2±7.1% vs 97.1±2.7%) and 6 months follow-up rate of patients in both groups were similar (97.7% vs 94.9%) with no significant differences. Age 63±13 years, males 84%, 75% had hypertension, 30.8% diabetes mellitus and 18% were smokers. No differences were present in baseline cLDL levels (109±41 vs 114±39 mg/dl) and all the patients used statins at discharge. After 6 months, 38% of patients using statins in the IG were in target LDL-C levels and 30.8% in the CG, without significant differences (100% IG vs 95% CG). In the IG the equivalent dose of statin is significantly higher (51±24 vs 39±16, P<0.008) as well as the percentage of changes in lipid-lowering drugs depending of cLDL level (28.8±8.0 vs 1.3±4.5, P<0.007). We see a significant decrease in cLDL levels in the IG (87±16 vs 88±38 mg/dl, P=0.01) and 60% of patients in the IG vs 35% in the CG achieve the target cLDL level of <70 mg/dl (P<0.047). The readmission rate after 6 months due to ACS was significantly lower in the IG (0.2±10% vs 10%, P<0.04).

Conclusion: The intensive follow up and optimisation of lipid-lowering therapy guided by cLDL levels by specialised nurses after an ACS, improves the quality of the therapy and reduces the cLDL levels and the readmissions due to a recurrent coronary event.

PI1126 | BEDSIDE
A combination of three specific Lactobacillus plantarum strains reduces low-density lipoprotein cholesterol and improves other cholesterol and lipid parameters in adults with hypercholesterolemia
A. Ibarsa1, J. Cune2, O. Hasselwander2 on behalf of HOWARU Cardio Team. 1DuPont Nutrition & Health, Active Nutrition, Kotkaniemi, Finland; 2AB-BIOTICS, Barcelona, Spain; 3DuPont Nutrition & Health, Reigate, United Kingdom

Introduction: Substantial evidence indicates that the consumption of certain live microorganisms may significantly lower low-density lipoprotein cholesterol (LDL-C) and ameliorate the levels of other lipid parameters. Three specific strains of Lactobacillus plantarum selected for probiotic activity to hydroxymethylglutaryl-CoA reductase (HMG-CoA) without receiving cholesterol-lowering treatments, were randomized to receive either a placebo or the three strains combination (>1.2E+09 CFU) administered in one capsule a day during 12 weeks. Cholesterol, lipid and safety parameters were assessed at baseline and after 12 weeks of intervention. A follow-up of 4 weeks without treatment was also carried out after the intervention.

Results: There were no adverse events or changes in safety parameters during the study. After 12 weeks, and as compared to the placebo, the combination of the three strains reduced LDL-C by 8.4% and -0.63 mmol/L, for the placebo and L. plantarum strains respectively, P<0.001 and increased high-density lipoprotein cholesterol (HDL-C) by 5.5% (0.01 and 0.08 mmol/L, P<0.001), thus lowering TC by 9.0% (−0.27 and 0.08 mmol/L, P<0.001). Consequently, the strain combination reduced the LDL-C:HDL-C ratio by 12.8% (−0.26 and −0.77, P<0.001) and lowered the level of oxidized LDL-C by 11.3% (−1.04 and −7.45 U/L, P<0.001). In addition, the three L. plantarum strains reduced triglycerides by 14.3% (−0.05 and −0.33 mmol/L, P<0.05). No further changes were observed during the follow-up period.

Conclusions: This is the first specific strains of L. plantarum reduces LDL-C and improves the levels of other cholesterol and lipid parameters without altering safety. These results indicate that these strains in combination may be a potential agent to reduce the risk of coronary heart disease.

PI1127 | BEDSIDE
Impact of adding eicosapentaenoic acid to strong statin therapy on serum pentraxin X3 level: a six-month, randomized, controlled study
S. Tani, A. Hirayama, W. Atsumi, T. Yagi, S. Nizuma, K. Kawauchi, K. Nagao. Nihon University School of Medicine, Tokyo, Japan

Background: Multiple factors that affect coronary artery disease (CAD) risk may be affected by the intake of omega-3 fatty acids including eicosapentaenoic acid (EPA). We hypothesized that EPA combined with strong statin therapy might reduce pentraxin X3 (PTX3), a marker of coronary atherogenesis and plaque instability. The aim of this study was to assess the impact of adding EPA to a strong statin therapy on the serum PTX3 level.

Methods: We conducted this 6-month, single-center, prospective, randomized and open-label clinical trial, to investigate the effects of concomitant use of EPA and strong statin therapy on the serum PTX3 level in patients with CAD. We assigned statin-treated CAD patients to an EPA group (n=53) or a control group (n=53). Subjects in the EPA group were administered a 900-mg capsule containing EPA ethyl ester of ~98% purity twice a day (total daily dose, 1.800 mg).

Results: In the EPA group, strong statin therapy significantly reduced the serum PTX3 level, compared with moderate statin therapy (~11% vs. 44%, P<0.028), while no significance change in the PTX3 level was noted between the two therapies in the control group. A multiple-logistic analysis identified a reduction in the PTX3 level after adjustments for the coronary risk factors (Figure).

Conclusion: These results suggest that the concomitant use of EPA and strong statin therapy could reduce the PTX3 level, possibly leading to coronary plaque stabilization. Furthermore, combination therapy of strong statin and EPA may be a potential treatment option to prevent CAD.

PI1128 | BENCH
Predictive value of microvascular shedding in high cardiovascular risk subjects with and without future presentation of a major cardiovascular event
G. Chiva-Blanch1, R. Suades1, J. Crespo1, R. Estruch1, L. Badimon1. 1Barcelona Cardiovascular Research Center (CSIC-ICCC), IIB-Sant Pau, Hosp Sant Pau, UAB, Barcelona, Spain; 2Hospital Clinic de Barcelona, Department of Internal Medicine, Barcelona, Spain

Background: Vascular cells are key players in the pathogenesis of atherothrombosis. Circulating microparticles (cMPs) are small phospholipid microvesicles shed by activated cells that play a pivotal role on cell signalling related to the pathogenesis of atherothrombosis.

Purpose: To investigate the predictive value of MPs shed from different vascular
cells for CVE presentation (CVE = myocardial infarction, stroke or cardiovascular death).

Methods: Fifty subjects from the arm of the PREDMED trial supplemented with nuts were included in the study. Twenty-five individuals that did not suffer a CVE (no-CVE) and 25 individuals with the same risk profile of classical risk factors that were to suffer a future CVE in a mean of 3.8±1.5 years (CVE) were selected. Two sample measurements were considered: at baseline and after one year of dietary intervention. Annexin V positive (AV+) cMPs from platelets (CD61), endothelial cells (CD146), leukocytes (CD45), monocytes (CD14), lymphocytes (CD3), erythrocytes cells (CD235a/CD34) and smooth muscle cells (SMA-a) were characterized and quantified by flow cytometry.

Results: After one year of dietary intervention, no-CVE patients showed decreased MP shedding from activated platelets (CD62P) and endothelial cells (CD146 and CD146CD62E) compared to CVE patients, who showed increased shedding. After one year of dietary intervention, there was a decrease in AV+cMPs with PAC-1, tissue factor (CD142), CD61, CD63 and CD11a in no-CVE patients, while in CVE patients the diet did not influence MP shedding except for CD235ab/CD34 MP, which increased after one year. A ROC-curve analysis, to identify the threshold level of cMPs capable of predicting a future CVE, showed that at one year of intervention, CD235ab/CD34 MP at a cut-off point of 13.1 MP/μl of platelet free plasma (PFP), P=0.009, best predicted a future CVE with a 66.4% sensitivity and 64% specificity [area under de curve (AUC)=0.714 (95% CI 0.570, 0.859)], followed by CD142/CDMPs at a cut-off point of 102.6 MP/μl (P=0.045), with a 56% sensitivity and 70% specificity [AUC=0.669 (0.512, 0.825)]. When both type of MPs were considered together, the predictive power of a future CVE was increased (P=0.009, AUC=0.720 (0.573, 0.863), ROC analysis for classical risk factors (BP, HDLc and LDLc) did not achieve statistical significance.

Conclusions: In a high cardiovascular risk subset of patients from a controlled diet intervention study-PREDMED, cMPs derived from activated platelets and erythrocytic cells are predictive of future CVE.

P1130 | BEDSIDE
Usefulness of low-density lipoprotein cholesterol/ high-density lipoprotein cholesterol ratio on secondary prevention in the drug-eluting stent era

I. Matsumoto, S. Yokoyama, A. Misaki, M. Kurozumi, T. Nanba, Y. Takagi. KKR Takamatsu Hospital, Takamatsu, Japan

Objectives: Some clinical studies have demonstrated that a low-density lipoprotein cholesterol/ high-density lipoprotein cholesterol (LDL-C/HDLC) ratio was an excellent predictor of cardiovascular diseases. The aim of this study was to determine whether the LDL-C/HDLC ratio can affect outcomes after percutaneous coronary intervention (PCI) in the era of drug eluting stent (DES).

Methods: We enrolled 842 patients who underwent successful DES implantation and divided them into the following three observation groups: those with LDL-C/HDLC ratio of less than 1.5, between 1.5 and 2, and more than 2. Amongst the three groups, the incidence of major adverse cardiac events (MACE) during the five years after PCI was measured. MACE was defined as cardiac death, non-fatal myocardial infarction, new stenosis and restenosis.

Results: Kaplan-Meier analysis demonstrated that patients with the LDL-C/HDLC ratio of less than 1.5 had a significantly lower incidence of MACE than the other two groups (Figure). Cox proportional hazards analysis indicated that the LDL-C/HDLC ratio was significantly associated with the incidence of MACE (odds ratio=1.49, 95% CI: 1.26–1.79; P<0.001).

Conclusion: The LDL-C/HDLC ratio was a valuable predictor of cardiovascular events in patients even in the DES era. Furthermore, it is desirable to maintain the LDL-C/HDL-C ratio to be less than 1.5 for the secondary prevention after DES implantation.

P1131 | BEDSIDE
Prospective evaluation of cancer: in 18,144 patients randomized to ezetimibe vs placebo: a prespecified analysis from the IMPROVE IT trial

R.P. Giugliano1, S.D. Wiviott1, C.S. Fuchs2, A.J. Wagner2, W. Goessling2, J.A. White2, T.A. Musliner1, A.M. Tershakovec4, M.A. Blazing3, E. Braunwald1 for the IMPROVE IT Investigators. J.A. White3, T.A. Musliner4, A.M. Tershakovec4, M.A. Blazing3, E. Braunwald1 1Duke Clinical Research Institute, Durham, United States of America; 2Dana Farber Cancer Institute, Boston, United States of America; 3Duke Clinical Research Institute, Durham, United States of America; 4Mercer & Co., Kenilworth, United States of America

Background: The SEAS study in 1873 pts with aortic stenosis reported more cancers in pts randomized to ezetimibe-simvastatin (E/S) compared to placebo, while the SHARP trial in 9270 pts with chronic kidney disease did not. We prospectively conducted a systematic analysis of cancer in the IMPROVE IT trial to reassess this issue in a larger dataset with longer follow-up.

Methods: 18,144 patients post ACS were randomized to E/S or S alone. All suspected tumors (benign or malignant) reported by investigators or identified from a thorough review of adverse event terms were submitted using standardized forms for adjudication by independent oncologists blinded to treatment. The primary endpoint was the KM rate at 7 yrs of a new, relapsing or progressive malignancy (excluding non-melanotic skin cancers) that became clinically apparent after randomization.

Results: 1480 pts (8.2%) developed a new/worsening malignancy over 6 yrs av- erage follow-up (1.56 per 100 yrs exposure); 86% had pathology reports available. Pts developing a new/worsening malignancy were more likely older (67 v 63 yrs), male (80% v 75%), and current smoker (37% v 33%) (p=0.001 for each). There was no difference in the 7-year KM rate of the primary malignancy endpoint (10.2% in each group, P=0.57), nor in other secondary analyses (Table). There were no differences in location, including the 3 cancers (skin, prostate, stomach) that accounted for the imbalance in SEAS. Deaths due to malignancy were similar (280 vs 272, p=0.71).

The incidence of MACE

Conclusion: The LDL-C/HDLC ratio to be less than 1.5 for the secondary prevention after DES implantation.

The incidence of MACE

Cancers by Treatment Group

<table>
<thead>
<tr>
<th>E/S (n=9067)</th>
<th>Simva (n=9077)</th>
<th>Hazard ratio</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Primary malignancy endpoint*</td>
<td>748 (8.2%)</td>
<td>732 (8.1%)</td>
<td>1.03</td>
</tr>
<tr>
<td>New, relapsing, or progressive</td>
<td>10.2 (9.5, 10.9)</td>
<td>10.2 (9.5, 11.0)</td>
<td>0.93</td>
</tr>
<tr>
<td>Above + non-melanotic skin cancer</td>
<td>909 (10.0%)</td>
<td>915 (10.1%)</td>
<td>1.00</td>
</tr>
<tr>
<td>New malignancies only**</td>
<td>12.4 (11.7, 13.3)</td>
<td>12.7 (11.9, 13.5)</td>
<td>0.91</td>
</tr>
<tr>
<td>Prostate</td>
<td>854 (9.4%)</td>
<td>863 (9.5%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Colon</td>
<td>11.8 (11.0, 12.6)</td>
<td>12.1 (11.3, 13.0)</td>
<td>0.90</td>
</tr>
</tbody>
</table>

*Excludes non-melanotic skin cancers (basal and squamous cell), **Excludes relapsing and progressive malignancies.

Conclusions: No differences in cancer were observed with ezetimibe compared to placebo on a background of simvastatin in the IMPROVE IT trial after ~100,000 pt-years of follow-up. This systematic detailed approach to evaluate cancer allows for a more accurate assessment to identify or refute a cancer signal in large RCTs than traditional methods of spontaneous reporting.

ASSESSING PERCUTANEOUS TREATMENT OPTIONS FOR PAD

P1132 | BEDSIDE
How repeat endovascular therapy influence on outcomes of critical limb ischemia with tissue loss?

N. Kobayashi, T. Muramatsu, R. Tsukahara, Y. Itô, H. Ishimori, K. Hirano, M. Nakano. Saiseikai Yokohama City Eastern Hospital, Yokohama, Japan

Background: Endovascular therapy (EVT) has become first-line approach for critical limb ischemia (CLI), however, its high restenosis rate remains as a major problem. Generally, restenosis is associated with poor wound healing course, so usually repeat EVT is needed for clinical restenosis case. The clinical impact of repeat EVT on outcomes of CLI with tissue loss remains unclear. The aim of this study was to investigate the clinical influence of repeat EVT for CLI patients with tissue loss.

Methods: Between April 2007 and August 2013, 206 CLI patients (241 limbs) with tissue loss were treated by EVT in our institution. Patients were divided into the 2 groups, repeat EVT group (n=75) and non-repeat EVT group (n=166). Wound healing rate at 1 year, limb salvage rate at 3 years and major amputation free survival rate at 3 years in repeat EVT and non-repeat EVT group.
Conclusions: Post-EVT FFR is useful to predict future restenosis.

Methods: Between January 2013 and February 2014, FFR measurement was performed for 39 SFA lesions after EVT. We calculated both mean FFR (distal mean pressure/proximal mean pressure) and systolic FFR (distal systolic pressure/proximal systolic pressure) after EVT. All of these lesions were investigated for primary patency at 12 months. Cut off point of FFR for primary patency at 12-months were evaluated using Receiver Operating Characteristics (ROC) curve analysis.

Results: The area under the ROC curve was 0.925 in mean FFR and 0.900 in systolic FFR. Cut off point of mean FFR for primary patency at 12 months was 0.90. The primary rate at 12 months was significantly lower in high FFR group (-0.90) compared to low FFR group (-0.90) (23.3% vs. 66.7%, P=0.035).

Conclusions: Post-EVT FFR is useful to predict future restenosis.

Background: Post-stenting fractional flow reserve (FFR) is a predictor of repeat target vessel revascularization after percutaneous coronary intervention. However, little is known about the clinical impact of post-procedural FFR on future restenosis in patients with superficial femoral artery (SFA) disease after endovascular treatment (EVT).

Methods: From 2007 to 2009, 246 consecutive CLI patients (246 first treated limbs) on HD (age, 69±10 years; 70% male; 45% non-ambulatory status; 69% with limb ischemia due to infragenual lesions (178 EVT and 68 BSX)) were retrospectively enrolled. Overall survival rate after revascularization was evaluated by Kaplan-Meier analysis. Predictors of 2-year mortality after revascularization were determined using a Cox hazards model.

Results: Overall survival rate was 77% at 1 year, and 66% at 2 years. Predictors of 2-year mortality after revascularization were age > 75 years (hazard ratio [HR] 95% confidence interval), 1.82 [1.14–2.91], albumin < 3g/dL (2.31 [1.39–3.84]), and ejection fraction < 50% (1.73 [1.06–2.83]). Patients with more predictors had a higher incidence of death within 2 years after revascularization.

Conclusions: Post-EVT FFR is useful to predict future restenosis.

Methods: From Jan 2010-Mar 2013 total 675 consecutive procedures who suc-

Results: Kaplan-Mayer analysis revealed that the, Clinical driven TLR and primary patency (PSVR 2.5) rate were significantly higher (logrank, p=-0.02, 0.01) in patient with TP-Trunk pain than in patient with TP-Trunk stenosis. Multi-varant analysis shows that TP-Trunk patency were remained independently factors as-

Conclusion: TP-trunk patency reduce TLR rate in patients treated EVT for Femoro-popliteal lesions.

Results: The mean follow-up period was 32.6±27.3 months. At 2 years, freedom from ReISR rates were 15.1% in the POBA group, 32.5% in the BMS group, 58.2% in the DES group and 65.0% in the BSX group, respectively (p<0.01, log-rank test). Freedom from ReTLR rates and Reocclusion were 22.8% and 37.1% in the POBA group, 40.4% and 56.5% in the BMS group, 64.7% and 77.1% in the DES group, and 70% and 75.8% in the BSX group, respectively (p<0.01 and 0.03, log-rank test). Among EVT groups, on multivariate analysis by Cox proportional hazard ratio, body mass index (HR, 1.16; P<0.01), and use of DES (HR, 0.23; P<0.01) were the independent predictors of ReISR in-stent occlusion after FP stenting.

Conclusion: Although BSX was feasible for in-stent occlusion after FP stenting, the use of DES is also a good option because ReTLR and Reocclusion were similar.
**P1137 | BEDSIDE**

Relationship between primary patency and lesion length following bare nitinol stent placement for femoropopliteal artery disease

Y. Soga1, M.T. Takahara2, O.i. Iida1, K.H. Hirano1, K.S. Suzuki2, K.A. Ando1, Y. Soga1, M.T. Takahara2, O.i. Iida1, K.H. Hirano1, K.S. Suzuki2, K.A. Ando1, 1Kokura Memorial Hospital, Kitakyushu, Japan; 2Osaka University Graduate School of Medicine, Metabolic Medicine, Osaka, Japan; 3Kansai Rosai Hospital, Amagasaki, Japan; 4Saiseikai Yokohama City Eastern Hospital, Yokohama, Japan; 5Sendai Kosei Hospital, Sendai, Japan

Background: It remains unclear whether primary patency decreases proportionally to lesion length and whether lesion length was significantly associated with MACE free rate. We evaluated the relationship between 1-year primary patency and lesion length in patients with femoropopliteal disease who underwent bare nitinol stenting and to detect.

Methods: Between January 2004 and December 2011, consecutive 1373 limbs underwent femoropopliteal stenting with nitinol bare-metal stent and obtained 1-year follow-up data were identified and analyzed in this study.

Results: The mean age of the subjects was 72 years and female subjects represented 26%. The mean vessel diameter was 5.3 mm and the mean lesion length was 142 mm. The lower limit of the 95% CI for the unadjusted 1-year primary patency was 83.2% (95% Confidential Interval [CI]: 79.8 to 86.1%). The 1-year primary patency decreased linearly with the extension of lesion length. The 1-year primary patency decreased linearly with the extension of lesion length. The 1-year primary patency was 83.2% (95% CI: 71.7 to 80.5%) at 200 mm, and 70.7% (95% CI: 62.4% to 77.7%) at 300 mm, respectively. The maximum lesion length providing a significantly higher 1-year primary patency than 66% was 263 mm.

Conclusion: The 1-year primary patency of patients treated with bare nitinol stents for femoropopliteal lesion decreased linearly with the extension of lesion length. The maximum lesion length providing a higher primary patency rate than 66% of the OPG was approximately 25 cm.

**P1138 | BEDSIDE**

Impact of patient’s activity on clinical outcome after femoropopliteal intervention

H. Muranishi, Y. Soga. Kokura Memorial Hospital, Cardiology Department, Kitakyushu City, Japan

Background: Several studies have already reported some predictors of major adverse cardiac events (MACE) in patients with peripheral artery disease, but the impact of patient’s activity is unknown. The aim of this study is to examine the associations between patient’s activity and clinical outcome after femoropopliteal (FP) intervention.

Methods: Retrospective analysis of a prospectively maintained database for FP intervention in our center was performed. Patient’s activity was classified into two groups, ambulatory group or wheel chair and bed ridden group. The study endpoints were MACE, defined as stroke, myocardial infarction, and cardiac death. Results: A total of 1100 consecutive patients were performed with FP intervention (male 69.2%, 73.1±9.2 years old, mean follow up period 2.7±2.3 years). MACE free rate was significantly higher in ambulatory group (96.3%, 92.6% and 86.2% at 1, 2 and 4 years) than that in wheel chair and bed ridden group (86.8%, 83.4% and 63.3% at 1, 2 and 4 years; P<0.0001). In univariate analysis, patient’s activity, critical limb ischemia, hemodialysis, a history of coronary artery disease, atrial fibrillation, and heart failure showed significant associations with MACE free rate. Cox proportional hazards analysis, wheel chair and bed ridden group significantly affected MACE free rate (hazard ratio 1.99, 95% confidence interval, 1.16–3.39; P=0.0127).

Conclusion: Patient’s activity may be an independent predictor of MACE after FP intervention.

**MYOCARDIAL FUNCTION**

**P1139 | BEDSIDE**

ST2-R2 score: degree of reverse remodelling and 4-year survival in patients with heart failure. A multicenter study

S. Sanders-Van Wijk1, J. Lupon2, J.L. Januzzi3, M. De Antonio2, H.P. Brunner-La Rocca1, H. Gagg1, A. Galan2, R. Shah3, M. Pister3, A. Bayes-Genis2, 1Maastricht University Medical Centre (MUMC), Maastricht, Netherlands; 2Germans Trias i Pujol University Hospital, Badalona, Spain; 3Massachusetts General Hospital, Boston, United States of America; 4University Hospital Basel, Basel, Switzerland

Introduction: Recently, the ST-R2 score (ST2-R2 score: degree of reverse remodelling and LV size changes. Based on the specified subgroups a significant association was observed between LVEF recovery and LV reduction at one year according to the ST2-R2 score and its prognostic implications up to 4 years.

Methods: A total of 1100 consecutive patients were performed with FP intervention. Patient’s activity may be an independent predictor of MACE after FP intervention.

Results: A linear relationship was observed between ST2-R2 scoring and LVEF and LV size changes. Based on the specified subgroups a significant association was observed between LVEF recovery and LV reduction at one year according to the ST2-R2 score and its prognostic implications up to 4 years.

Conclusions: The ST2-R2 score, which includes the novel biomarker ST2 and five conventional risk parameters, reasonably predicts degree of R2 in HF patients and was useful to prognosticate mortality up to 4 years.
and non-PH group. The SPP was 87.3±3.2 mmHg in the PH group as compared to 107.1±24.8 in the no-PH group (p<0.001). The DPP was similar in both groups, 62.9±17.2 vs 62.9±12.9 mmHg, respectively (p=0.97). No difference in the mortality event rate according to SPP quartiles was observed (p=0.33). In contrary, in DPP quartile analysis, the death rate in the two lower quartiles was significantly increased (37.4% and 28.8%, as compared with 16.2% and 17.6% in the higher quartiles (p=0.002). In a multivariate analysis, the adjusted hazard ratio (HR) for all-cause mortality was 3.27 (95% Confidence Interval (CI) 1.31–8.18, p=0.01), 2.76 (95% CI 1.10–6.86, p=0.029) and 0.81 (95% CI 0.42–1.56, p=0.53) for the first, second and third DPP quartile, respectively, as compared with the highest quartile.

Conclusion: The results of our study suggest that the diastolic, and not systolic, RV myocardial perfusion pressure is a strong predictor for all-cause mortality in patients with chronic LHF and PH.

P1141 | BENDSIDE

The impact of left ventricular function and balloon aortic valvuloplasty on paravalvular leakage in patients undergoing TAVI

M. Drakopoulou1, K. Tountouzas1, G. Latsios1, A. Synetos1, K. Chatzoglouanni1, A. Mastrokostopoulos1, S. Yuecil2, U. Gerckens2, E. Grube2, D. Tousoulis1.

1Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece; 2Gemeinschaftskrankenhaus, Bonn, Germany; 3University Hospital, Dept of Medicine II, Bonn, Germany

Background: Direct transcatheter aortic valve implantation (TAVI) has shown to be a comparably success rate to TAVI with percutaneous balloon aortic valvuloplasty (BAV). However, little is known about the impact of direct TAVI on the paravalvular leakage (PVL) of patients based on pre-procedural left ventricular ejection fraction (LVEF).

Purpose: In the current study, we aimed to evaluate the impact of direct TAVI on the PVL of patients with impaired and patients with preserved ejection fraction.

Methods: Patients with severe and symptomatic aortic stenosis (effective orifice area [EOA] <1cm²) who were scheduled for TAVI were prospectively enrolled. Prospectively collected echocardiographic data before TAVI were retrospectively analyzed in all patients. The VARC-2 criteria were used for designing clinical outcomes. Patients were classified based on LVEF in patients with impaired (LVEF <50%) and patients with preserved LVEF (≥50%). The VARC-2 criteria were used for designing clinical outcomes.

Results: Two hundred and four patients (mean age: 81±7 years) were included in the study. From 130 patients with preserved LVEF, 62 patients (48%) underwent BAV and 68 patients (52%) underwent direct TAVI. Device success rate was equal in both groups (70% in the BAV group versus 74% in the direct TAVI group, p=0.24). The BAV group had higher moderate/severe paravalvular leakage (24% versus 6%, p<0.04) compared to the direct group. From 74 patients with impaired LVEF, 56 patients (70%) underwent BAV and 18 patients (30%) underwent direct TAVI. Device success rate was lower in the BAV compared to the direct TAVI group (70% versus 88%, p=0.04). The BAV group had higher moderate/severe paravalvular leakage (36% versus 6%, p=0.02) compared to the direct group.

Conclusions: Direct TAVI with the self-expanding bioprosthesis is safe and feasible and has lower paravalvular leakage rates compared to patients undergoing non-direct TAVI at 1-year.

P1142 | BENCH

Mechanically independent ventricular beta-2-adrenocceptor stimulation compensates for reduced contractile function in type-2 diabetes


Background: β-adrenocceptor (AR) expression and functional β-AR responsiveness are key components of contractile function contributing to impaired cardiovascular health in type 2 diabetes. Changes in β1-AR subtypes and the β1-AR associated stimulatory G (Gs) proteins evoke alterations in contractile response, whereas changes in β2-AR subtypes and downstream inhibitory G (Gi) proteins are suggested to evoke potential indirect functional and/or metabolic effects. However, the individual β-AR subtypes contribute to cardiac function in type 2 diabetes is unknown.

Purpose: We aimed to evaluate the responsiveness of specific myocardial β1- and β2-AR on contractile function in type-2 diabetes.

Methods: Left ventricular developed pressure (LVPdev), a measure of myocardial function, was assessed in isolated Langendorff-perfused hearts from 20-week old Zucker diabetic fatty (ZDF) rats compared with 16.5% and 17.6% in the higher quartiles (p=0.002). In a multivariate analysis, the adjusted hazard ratio (HR) for all-cause mortality was 3.27 (95% Confidence Interval (CI) 1.31–8.18, p=0.01), 2.76 (95% CI 1.10–6.86, p=0.029) and 0.81 (95% CI 0.42–1.56, p=0.53) for the first, second and third DPP quartile, respectively, as compared with the highest quartile.

Conclusion: The results of our study suggest that the diastolic, and not systolic, RV myocardial perfusion pressure is a strong predictor for all-cause mortality in patients with chronic LHF and PH.

P1143 | BENDSIDE

Relationship of extracardiac matrix regulation, collagen turnover and renin angiotensin system activity with myocardial dysfunction in patients with type 2 diabetes mellitus

J.H. Liu, Y. Chen, Z. Zhen, H.F. Tse, K.H. Yu. The University of Hong Kong, Medicine, Hong Kong, China, People’s Republic of

Background: Patients with type 2 diabetes mellitus (T2DM) have impaired myocardial function. However, the mechanism(s) mediating cardiac β2-AR activity in the large cohort of diabetic patients with heart disease may enhance myocardial metabolism and improve prognostic outcomes.

Purpose: Our data suggest that β2-AR indirectly support β1-AR-induced stimulation of myocardial function, most likely through an increase in metabolic efficiency.

Conclusion: The current study is the first one to report on the relationship between myocardial function, most likely through an increase in metabolic efficiency.

P1144 | BENCH

Comparative investigation of in vivo hemodynamics in rat models of physiological and pathological left ventricular hypertrophy


Background: Left ventricular (LV) hypertrophy is a physiological (PhyH) or pathological (PathH) response of LV myocardium to increased cardiac load and is associated with characteristic molecular changes. To date, a direct comparison of functional consequences of PhyH and PathH is missing.

Purpose: We aimed at investigating and comparing in vivo hemodynamic alterations in rat models of PhyH and PathH by using LV pressure-volume (P-V) analysis.

Methods: PhyH and PathH were induced in rats by swim training (athlete's heart) and by suprarenal abdominal aortic banding (AB), respectively. Morphology of the heart was investigated by echocardiography. A detailed characterization of cardiac function was performed by LV P-V analysis using a pressure-conductance-derived conductance micromanometer. In addition to in vivo experiments, histological and molecular biological measurements were performed. All data were normalized to the corresponding control group.

Results: As detected by echocardiography, myocardial hypertrophy was more pronounced in PathH (LV mass: +14.3±1.5% PhyH vs. +25.6±3.2% PathH, p<0.01), which was further confirmed by post mortem heart weight data. In AB we detected subendocardial fibrosis, while no fibrotic remodeling was present in PhyH. The SPP was 87.3±3.2 mmHg in the no-PH group compared to 107.1±24.8 in the PH group (p<0.001). The DPP was similar in both groups, 62.9±17.2 vs 62.9±12.9 mmHg, respectively (p=0.97). No difference in the mortality event rate according to SPP quartiles was observed (p=0.33). In contrary, in DPP quartile analysis, the death rate in the two lower quartiles was significantly increased (37.4% and 28.8%, as compared with 16.2% and 17.6% in the higher quartiles (p=0.002). In a multivariate analysis, the adjusted hazard ratio (HR) for all-cause mortality was 3.27 (95% Confidence Interval (CI) 1.31–8.18, p=0.01), 2.76 (95% CI 1.10–6.86, p=0.029) and 0.81 (95% CI 0.42–1.56, p=0.53) for the first, second and third DPP quartile, respectively, as compared with the highest quartile.

Conclusion: The results of our study suggest that the diastolic, and not systolic, RV myocardial perfusion pressure is a strong predictor for all-cause mortality in patients with chronic LHF and PH.

Conclusion: Our data suggest that β2-AR indirectly support β1-AR-induced stimulation of myocardial function, most likely through an increase in metabolic efficiency.

Conclusion: The current study is the first one to report on the relationship between myocardial function, most likely through an increase in metabolic efficiency.
fraction were detected in PaH, indicating the compensated nature of the observed hypotrophy. Active relaxation was ameliorated in athlete’s heart, while it showed a marked impairment in AB (Tau: -7.7±2.6% PhY vs. +4.2±11.1% PaH, p<0.01). Load-independent, sensitive indices of LV contractility were increased in both models, in parallel with the degree of hypertrophy. Stroke work increased in both models, whereas mechanical efficiency of LV was improved in PhY and remained unchanged in PaH (±20.8±4.7% PhY vs. +4.7±6.9% PaH, p<0.05).

Conclusions: In this project we provided the first detailed, comparative hemodynamic characterization of PhY and PaH in relevant rodent models. Increased LV contractility could be observed in both types of myocardial hypertrophy, characteristic differences were detected in diastolic function and LV mechanoenergetics.

P1145 | BENCH
Human iPSC-MSCs is superior to human ESC-CMs for improvement of left ventricular function in a porcine model of post-myocardial infarction heart failure
S.Y. Liao1, Q.P. Ting2, Z. Chen1, F. Luo1, Z.Y. Zhu1, Y. Liu1, A. Chen3, S. Oh3, H.F. Tse1,3. 1The University of Hong Kong, Medicine, Hong Kong, Hong Kong SAR, People’s Republic of China; 2Bioprocessing Technology Institute, Singapore, Singapore

Background: Cell-based therapies have been proposed as a novel treatment for post-myocardial infarction (MI) heart failure (HF), nevertheless, the optimal cell type remains unclear. This study sought to compare the safety and efficacy of direct intramyocardial transplantation of human embryonic stem cell-derived cardiomyocytes (hESC-CMs) versus human induced pluripotent stem cell derived mesenchymal stem cells (hiPSC-MSCs) in a porcine model of post-MI HF.

Methods and results: Eight weeks after induction of MI, animals developed HF with left ventricular ejection fraction (LVEF) <40% were randomly assigned to receive single intramyocardial injection of saline (MI group, n=8); saline + 200 million hESC-CMs (n=8) or 200 million hiPSC-MSCs (n=8). All the animals received immunosuppression with steroid and cyclosporine after transplantation. As compared to MI group, LVEF and +dP/dt were significantly improved in the hiPSC-MSC group after 8 weeks but not in the hESC-CM group (Figure 1A&B). The incidence of inducible ventricular arrhythmias was similar among 3 groups (83% vs. hiPSC-MSC group, 75% in hESC-CMs group vs. 75% in MI, P>0.05). Histological examination showed very limited number of hESC-CM or hiPSC-MSC over the myocardium and no tumor observed at 8 weeks after transplantation. Nonetheless, there was significantly increased in capillary density over the peri-infarct zone after hiPSC-MSCs but not hESC-CMs transplantation (Figure 1C).

Conclusions: Our results demonstrate that transplantation of hiPSC-MSCs and hESC-CMs are safe without risk of tumor formation, however, hiPSC-MSCs is superior to hESC-CMs for improvement of LV function and neovascularization in post-MI.

P1146 | BEDSIDE
An ingestible sensor and wearable patch tracking adherence and activity patterns identified underlying factors leading of persistent hypertension: a real-world registry study
L. Dicarlo1, R. Naik2, N. Macey3, R.J. West4, P. Godbehere5, S. Thurston6, R. Fox2, I. Singh1, Y.A. Kim1. 1Proteus Digital Health, Redwood City, United States of America; 2Far Lane Medical Centre, Sheffield, United Kingdom; 3Stowell, Salford, United Kingdom; 4Woolpit Health Centre, Suffolk, United Kingdom; 5North Brink Practice, Cambridgehire, United Kingdom; 6Wymondham Medical Practice, Norfolk, United Kingdom; 7The Health Centre, Oxon, United Kingdom

Background and introduction: Despite the availability of numerous therapeutic agents, as many as half of all hypertensive patients do not have their blood pressure (BP) at goal (HSCIC data). Novel CE-marked devices have been developed to capture and share information about medication-taking and activities of daily living (ADL) through an ingestible sensor (IS), a wearable patch, and a mobile app. This offering was used to identify the root cause of uncontrolled blood pressure BP amongst patients being managed in everyday practice.

Purpose: To evaluate the clinical and patient-reported outcomes of this digital health offering in patients with uncontrolled hypertension in an open-label, observational real-world registry study

Methods: The target sample size of the registry study was 150 patients with uncontrolled hypertension whilst prescribed ≥2 antihypertensives. Patients could incorporate any prescribed BP medications whilst simultaneously wearing the patch for 2 weeks. Clinic BP was measured on days 1 and 14. Adherence and ADL patterns were measured via the wearable patch and IS. Subjects returned to the clinic at week 4 to discuss the next steps in therapy based on the Proteus data.

Results: In this preliminary analysis, 140 patients met the inclusion/exclusion criteria, and 96% completed the trial. Out of those who completed the study, the root cause of persistent hypertension was identified in all patients: 39% of patients had inadequate medication adherence; 34% believed that the platform was easy to understand and convenient to use as measured by a patient satisfaction survey.

Conclusions: In patients with uncontrolled blood pressure in everyday practice, the inclusion of a digital health offering may help practitioners to identify the specific factors contributing to persistent hypertension, and to determine appropriate, patient-specific interventions to improve disease management.
P1148 | BEDSIDE Potential reduction in office and nocturnal blood pressure after renal denervation in patients with obstructive sleep apnea: a subgroup analysis of SYMPLECTIC HTN-3

K. Kario1, D. Bhatt2, R. Townsend2, J. Flack3, M. Negoița2, S. Oparil4, G. Bakris5 on behalf of SYMPLECTIC HTN-3 Investigators. 1Jichi Medical University Department of Cardiovascular Medicine, National Cardiovascular Center, Tochigi, Japan; 2Harvard Medical School, Boston, United States of America; 3University of Pennsylvania, Philadelphia, United States of America; 4Wayne State University, Detroit, United States of America; 5Medtronic, Inc., Santa Rosa, United States of America; 6University of Alabama Birmingham, Birmingham, United States of America; 7University of Chicago Medicine, Chicago, United States of America

Background: Obstructive sleep apnea (OSA) is associated with activation of the sympathetic nervous system and the development of resistant hypertension. Among OSA patients with hypertension a non-dipping pattern of nocturnal systolic blood pressure (SBP) is common and is associated with a higher risk for stroke and cardiovascular events.

Purpose: In a post hoc analysis, we examined the impact of catheter-based renal artery denervation (RDN) on changes in office and ambulatory blood pressure measures (ABPM) and on changes in nocturnal SBP defined by ABPM 6 months post-RDN in patients with OSA.

Methods: SYMPLECTIC HTN-3 is a prospective, randomized, blinded, sham-controlled trial of RDN for treatment of resistant hypertension. Patients were on a stable antihypertensive regimen of at least 3 drugs including a diuretic before randomization. Office and 24-h ambulatory blood pressure was determined at 6 months follow-up for patients with OSA. Average nocturnal SBP (1 am to 6 am), average peak nocturnal SBP (average of 3 highest SBPs between 1 am and 6 am) and maximum nocturnal peak SBP were calculated using previously published methods. All data were collected using Medtronic’s ProVue® monitoring system. Six-month changes in nocturnal SBP parameters were compared between RDN and control patients.

Results: A total of 94 OSA patients were in the RDN group vs. 54 OSA patients in the sham group. The groups were well balanced at baseline; a non-dipper SBP pattern was found in 54.8% of the RDN and 50.0% of the control OSA patients (p=0.610). The six-month change in office SBP was significantly greater in the RDN OSA patients compared with control patients (−17.0±22.4 mmHg vs −4.3±26.1 mmHg, p=0.011) while the 24-h ambulatory SBP change was not significantly different between the groups (−5.0±14.7 mmHg vs −0.8±17.9 mmHg, p=0.142). Average nocturnal SBP was reduced in the RDN but not in the control patients (−5.5±19.6 vs 1.6±21.5 mmHg, p=0.056). This pattern was also observed with average peak and maximum nocturnal peak SBP (−5.6±20.4 vs 3.2±22.4 mmHg, p=0.021 and −4.8±21.8 vs 4.5±24.6 mmHg, p=0.025, respectively).

Conclusions: Patients with resistant hypertension and OSA appeared to have greater reductions in office SBP and in average peak and maximum peak nocturnal SBP compared with control patients. These results require confirmation in future clinical research.

P1149 | BEDSIDE Effects of renal denervation on ADMA and sympathetic nerve activity in true resistant hypertensives

G. Seravalle1, R. Dell’oro2, D. Spaziani3, C. Auguardo4, P. Pizzini5, G. Tripepi6, F. Mallamaci6, G. Mancia7, C. Zoccali4, G. Grassi2, 1San Luca Hospital, Italian Institute for Auytorx (IRCCS), Milan, Italy; 2Clinica medica, Univ. Milano Bicocca, Monza, Italy; 3Department of Cardiovascular Medicine, Legnano, University of Milan, Legnano, Italy; 4Polyclinic of Monza, Interventional department, Monza, Italy; 5Bianchi Melacini Morelli Hospital (BMM), CNIR-IFCN, Reggio Calabria, Italy

Background and aims: Plasma concentrations of the endogenous inhibitor of nitric oxide synthase asymmetric dimethyl arginine (ADMA) are associated with sympathetic activity in patients with chronic disease. The driver of this association remains unknown. To solve the question it has been used the renal denervation of resistant hypertensive patients due to the marked reduction in whole-body norepinephrine spillover and sustained decrease in sympathetic nerve traffic (MSNA), thus representing an unique model to examine the hypothesis that sympathetic activity modulates circulating ADMA and its symmetric enantiomer (SDMA).

Methods: 14 true resistant hypertensives (ESH/ESC guidelines definition) were evaluated at baseline and 15, 30, 90, 180 days after renal denervation. In each session blood samples were taken and then we measured beat-to-beat finger blood pressure (Finapres) (fin). heart rate by HRM (noninvasive, Silynx). The global relationship between MSNA vs ADMA and SDMA was based on the calculation of the areas under the curves of these variables after renal denervation. Regression analyses were then performed.

Results: After renal denervation we observed a reduction in MSNA of ~17% (range: from ~66% to +10%). Changes in MSNA were strongly associated with the corresponding changes in plasma ADMA (r=0.69, p=0.005) and SDMA (r=0.87, p<0.001). Furthermore, changes in MSNA went along with simultaneous changes in systolic (r=0.79, p=0.001) and diastolic BP (r=0.82, p=0.001) and HR (r=0.68, p=0.01). All these relationships were largely independent of renal dysfunction.

Conclusions: These observations are compatible with the hypothesis that the sympathetic nervous system exerts an important role in modulating circulating levels of ADMA and SDMA in this condition.

P1150 | BEDSIDE Transforming the information highway for the clinical management of blood pressure using an ambulatory setting, objective assessment, and digital communication

L.Dicarlo1, R. Weinstein2, C. Morimoto3, G. Moon4, J. Savage5, Y.A. Kim1, T. Robertson6, K.Y. Au-Yeung1, 1Proteus Digital Health, Redwood City, United States of America; 2Diablo Clinic, Walnut Creek, United States of America

Background: For blood pressure (BP) management, objective information that BP may vary across time in an ambulatory setting is required to determine susceptible modification, medication use, and/or pharmacologic unresponsiveness should be the focus.

Purpose: Digital dose-forms of valsartan and telemetric data and communication system integrated and piloted in a true-resistant population. Objectives included summarization of (1) regularity and pattern of medication taking, daily step count, and daily BP and weight; (2) safety; and (3) patient acceptability. No data was used for diagnosis or treatment.

Methods: 37 subjects (23 males; age 62±9 years) used the system for 6 weeks. Two digital medicine prototypes consisted of valsartan 80 mg or 160 mg placed in a gelatin hemi-capsule having an exipient tablet as a “stopper”. On the external stopper surface, a poppy-seed size ingestible sensor (IS) made of foodstuff created a biogalvanic current upon ingestion to alert a prototype adhesive wearable device for display. Twice-daily BP and once daily weight (WT) were also integrated telemetrically for display. Automatic SMS reminders were sent whenever BP or WT was not received within a 24-hour period. During clinic visits, dosing was directly observed and compared to the accuracy of concurrent system detection of ingestion (PDA).

Results: In clinic, PDA versus observed dosing was 98%. Between clinic visits, mean dosing and scheduling adherence was 90% and 83% with some tapering at weeks 5 and 6. Activity averaged 2.0±1.5 hours/day with step count >60 steps/minute for 88% of subject-days. The morning BP was 132/78 and the mean evening BP was 127/73 during system use. Subjects appeared to be more compliant with taking WT than BP. SMS was sent and 100%-confirmed for 267 missed BPs or WT’s (6%). Mild and transient WS-related skin irritation (mostly pruritis) occurred in 14 subjects (40%), and no IS-related adverse events. Feedback–90% of patients did not mind swallowing the IS, and 75% had a positive experience with system use.

Conclusions: Automatically acquiring, integrating, displaying, and communicating (1) physiologic metrics, (2) activities of daily living, and (3) regularity and patterns of directly confirmed medication ingestion, appears to be feasible in an ambulatory setting. Versions of better tolerated WSS are now available, and development of medicinals having an IS within each tablet is underway.

P1151 | BENCH Renal sympathetic denervation using MR guided high intensity focused ultrasound in a porcine model

M.K. Koopmann1, J.S. Shea2, E.K. Kholomovski3, J.B. De Bever3, E.M. Minalga3, R.H. Hadley2, O.T. Owahn4, M.S. Salama5, N.M. Marrache6, A.P. Payne2, 1University of Utah, CARMA Center, Dept. of Cardiology, Salt Lake City, United States of America; 2University of Utah, Dept. of Surgery, University of Utah, Salt Lake City, United States of America; 3University of Utah, Dept. of Radiology, Salt Lake City, United States of America; 4University of Utah, Dept. of Pathology, Salt Lake City, United States of America; 5University of Utah, Dept. of Pathology, Salt Lake City, United States of America

Background: Cathereter-based strategies for renal sympathetic denervation (RSD) for the interventional management of treatment resistant hypertension (TRH) have recently been introduced into the clinical arena. However, the recent negative result of a large randomized trial suggests there is still need for pre-clinical evaluation.

Purpose: To evaluate the feasibility of using magnetic resonance guided high intensity focused ultrasound (MRgHIFU) to perform RSD in a porcine model.

Methods: Seven normotensive female Yorkshire pigs underwent unilateral RSD using MRgHIFU for safety and efficacy assessment. A fiberoptic temperature probe was invasively placed in the target renal artery to confirm energy delivery. The center of the thermal lesion was clearly visualized. Susceptibility weighted images showed demineralization and increased signal within the treated renal arteries. All animals tolerated the procedure well with no observed complications.

Results: Animals were sacrificed 5–9 days post-treatment and pathological analysis was performed. Norepinephrine present in the kidney medulla was assessed postmortem.

Conclusions: All animals tolerated the procedure well with no observed complications. Post-ablation a significant reduction (p<0.03) of cross-sectional area of nerve bundles between the treated and untreated renal arteries was observed in 85% of animals with treated nerves showing increased cellular infiltrate and fibrosis. A reduction of norepinephrine (p=0.14) in the kidney medulla tissue was also observed. No significant reduction in blood pressure was detected. There was no indication of tissue damage in arterial walls.
Non-invasive coronary flow reserve in patients with resistant hypertension

S. VOELZ1, S. SVERDUND2, B. ANDERSSON1, L.M. GAN2, B. RUNDVIST1
1 Sahlgrenska University Hospital, Department of Cardiology, Gothenburg, Sweden; 2 Sahlgrenska Academy, Department of Clinical Physiology, Gothenburg, Sweden

Resistant hypertension (RH) (office blood pressure (OBP) >140/90 despite treatment with three antihypertensive agents including one diuretic) is associated with increased risk for cardiovascular events. Coronary flow reserve (CFR) is impaired in patients with hypertension and is an independent predictor of cardiac mortality. However data on CFR in the subset of RH are scarce.

Aim: The aim of this study was to assess CFR in patients with RH.

Methods: Mean flow velocity was measured in the left anterior descending artery by transthoracic colour Doppler echocardiography at baseline and during Adenosine infusion (TDE-CFR). Thirty consecutive patients with RH, scheduled for renal denervation and 30 matched patients with controlled hypertension underwent TDE-CFR. The two groups were matched according to following variables: age, sex, ischemic heart disease, diabetes mellitus, smoking status and body-mass-index.

Results: Baseline mean flow velocities were similar in the two groups (Table). TDE-CFR was significantly lower in patients with RH as compared to individuals with non-resistant hypertension (2.7±0.6 vs. 3.1±0.8, p=0.01). There was no correlation between systolic or diastolic blood pressure and CFR or baseline flow velocities.

Conclusion: Successfully performing RSD non-invasively using MRgHIFU is feasible and safe. This approach may be a promising alternative to catheter-based strategies for TRH.

Symptom onset to reperfusion trends in patients with ST-elevation myocardial infarction across New York State from 2004 to 2010

Weill Cornell Medical College, Division of Cardiology, New York, United States of America

Introduction: Door-to-balloon time (DTB) has been the focus of local, regional, and national quality improvement initiatives in order to maximize myocardial salvage during ST-elevation myocardial infarction (STEMI). Recently published registry-driven data have shown a significant decrease in door-to-balloon time in patients with STEMI receiving percutaneous coronary intervention (PCI) over the past several years. However, there has been an increasing appreciation for the importance of symptom-onset to door time as an important quality measure.

Purpose: We sought to determine the trends in symptom-onset to door (OTD) time, symptom-onset to balloon (OTB) time, in addition to door-to-balloon (DTB) time in patients presenting with ST-elevation myocardial infarction across New York State between 2004 and 2010.

Methods: In our study, we retrospectively examined 28,330 patients receiving PCI for STEMI in New York State from 2004 to 2010. We compared median OTD, OTB and DTB times. Extreme outliers with OTD time <720 minutes and DTB time >180 minutes were excluded. We used non-parametric trend testing to determine statistical significance. In subgroup analysis, we examined the influence of age, gender, and the presence of co-morbid conditions on the trend of symptom onset to reperfusion time.

Results: There was a statistically significant trend towards shorter OTD, OTB, and DTB times in patients presenting with STEMI in New York State between 2004 and 2010 (median DTB time of 79 minutes (IQR 47, 114) in 2004 to a median time of 59 minutes (IQR 38, 81) in 2010, p<0.01 for trend from 2004 to 2010). In subgroup analysis, gender (male or female), age (<65 vs. >65), and the presence of co-morbid conditions (cerebrovascular disease, chronic obstructive pulmonary disease or diabetes mellitus) did not influence the trend in reperfusion times. A statistically significant trend towards shorter OTD times (p<0.04) was observed in patients with history of myocardial infarction but not in patients with prior CAGB. On the other hand, patients with prior CAGB had a statistically significant trend towards shorter OTD and DTB times (p<0.01) but non-significant OTD times (p>0.38).
Conclusions: Our results show a consistent, statistically significant trend towards shorter OTD, OTB, and DTB times from 2004 to 2010 in STEMI patients across New York State. This trend was significant regardless of age, gender and the presence of prevalent co-morbid conditions.

1198 | B E D S I D E
Impact of national PCI network on prognosis after acute myocardial infarction in Estonia
A. Saar1, T. Marandi2, T. Alinia3, M. Blondal4, K. Fischer4, J. Eha5.
1 University of Tartu, Department of Cardiology, Tartu, Estonia; 2 Regional Hospital of North Estonia, Quality Department, Tallinn, Estonia; 3 Regional Hospital of North Estonia, Centre of Cardiology, Tallinn, Estonia; 4 University of Tartu, Estonian Genome Centre, Tartu, Estonia; 5 Tartu University Hospital, Heart Clinic, Tartu, Estonia

Background: A study conducted in 2001 described shortages in the management of acute myocardial infarction (AMI) in Estonia: access to cardiac catheterization was poor and use of guideline-suggested medicines was low, especially in community hospitals. As a response, quality improvement measures were conducted, including establishing a percutaneous coronary intervention (PCI) network and publishing local ST-segment elevation myocardial infarction (STEMI) guidelines. Educational activities throughout the country highlighted the importance of early revascularization and the use of guideline-suggested medicines for the purpose of providing equal care to all AMI patients.

Purpose: Our aim was to analyze the changes in AMI management and outcomes of AMI patients undergoing cardiac artery disease (CAD) over time.

Methods: We included two random samples of AMI cases hospitalized in 2001 and 2011 (a third of annual cases). Data on baseline characteristics and in-hospital treatment were collected retrospectively from patient records and mortality data for 1 year were obtained from the Population Registry. Statistical analysis was performed using the "R" software.

Results: The study included 423 patients in 2001 and 665 in 2011. The mean age of patients has increased (68.3 vs 72.0 years, p < 0.001). Diabetes, hypertension and dyslipidemia were more prevalent in 2011 than in 2001. The concomitant in-hospital use of drugs from all five suggested cardiovascular drug groups (aspirin, P2Y12-inhibitors, beta-blockers, angiotensin converting enzyme inhibitors/angiotensin II receptor blockers and statins) increased from 3% to 29% (p < 0.001). Invasive management was more common in 2011 than in 2001 – the frequency of cardiac catheterization increased from 18% to 47% (p < 0.001) and PCI from 11% to 39% (p < 0.001). Reperfusion rates for STEMI did not change, but primary PCI (increased from 4% to 36%) has largely replaced thrombolysis (decreased from 10% to 45%). From the patients who were primarily hospitalized to community hospitals without catheterization facilities, more were referred for more advanced care (6% in 2001 vs 40% in 2011, p < 0.001). 30-day mortality after AMI decreased from 19% to 13% (p = 0.01) and 1-year mortality from 31% to 24% (p < 0.001). Invasive management was more common in 2011 than in 2001 – the frequency of cardiac catheterization increased from 18% to 47% (p < 0.001) and PCI from 11% to 39% (p < 0.001). Reperfusion rates for STEMI did not change, but primary PCI (increased from 4% to 36%) has largely replaced thrombolysis (decreased from 10% to 45%). From the patients who were primarily hospitalized to community hospitals without catheterization facilities, more were referred for more advanced care (6% in 2001 vs 40% in 2011, p < 0.001). 30-day mortality after AMI decreased from 19% to 13% (p < 0.001) and 1-year mortality from 31% to 24% (p < 0.001). The detected reduction in mortality rates persisted after adjusting for the differences in baseline characteristics.

Conclusion: Establishment of national PCI network and systematic educational activities led to the increased use of revascularization methods and guideline-suggested cardiovascular medicines resulting in improved prognosis after AMI over the period of 2001–2011 in Estonia.

1199 | B E D S I D E
Complete percutaneous coronary intervention versus culprit only percutaneous coronary intervention for acute ST elevation myocardial infarction with multivessel coronary artery disease: a meta-analysis
L.G. Almelo1, C. Fornage2, A. Dayag. Philippine Heart Center, Department of Adult Cardiology, Quezon City, Philippines

Background: Current guidelines recommend primary PCI in haemodynamically stable acute STEMI patients should be limited to the culprit vessel despite significant stenosis in non-culprit coronary arteries. Recent studies and meta-analyses provide conflicting data.

Objective: This review compared the efficacy of culprit (infarct-related artery only) primary PCI versus complete (infarct-related artery and at least one other artery with significant stenosis) primary PCI in acute STEMI patients with multivessel coronary artery disease (CAD).

Methods: The electronic databases MEDLINE and CENTRAL and the clinical trial registries ClinicalTrials.gov and ISRCTN registry were systematically searched for all published and unpublished randomised controlled trials (RCTs) comparing complete PCI versus culprit only PCI in patients presenting with ST-elevation myocardial infarction with multivessel CAD. Manual searching was done by reviewing the references of available studies. Data were extracted from full text reports of eligible trials and evaluated independently by the authors using the Cochrane Collaboration’s tool for assessing risk of bias. Statistical analyses were performed using RevMan 5.3 (The Nordic Cochrane Centre, 2014).

Results: Four RCTs (3 published, 1 unpublished) involving 979 patients were analysed. Complete PCI is associated with decreased risk for both cardiovascular (RR 0.45 [0.22,0.94] p = 0.03) and all-cause (RR 0.63 [0.37,1.05] p = 0.08) mortality, as well as with repeat revascularisation (RR 0.37 [0.26,0.53] p < 0.00001) and repeat non-fatal MI (RR 0.37 [0.19,0.71] p < 0.0003). No heterogeneity was detected (I2=0% for all outcomes).

Conclusion: Complete PCI is significantly associated with decreased risk of cardiovascular mortality, repeat revascularisation, and repeat non-fatal MI in patients with acute STEMI and multivessel CAD.

1200 | B E D S I D E
Impact of complete revascularization in a real world population of patients presenting with ST-elevation myocardial infarction

Aims: Complete revascularization during primary percutaneous coronary intervention (PCI) in patients with multivessel disease is associated with better outcome in highly selected cohorts. We intend to evaluate this subject in all-comers ST elevation myocardial infarction (STEMI) population.

Methods: Retrospective analysis of 1511 consecutive patients with STEMI, from a tertiary centre prospective registry between January 2004 and January 2014. We evaluated the impact of complete revascularization on clinical outcomes (by binary logistic regression) throughout a period with significant changes in STEMI standard of care.

Results: The mean age was 61.8 years (±12.4). 76.5% of patients were men, 19.5% were diabetic, 82% presented for primary PCI, 7% for facilitated PCI and 53% had multivessel disease (median affected segments 2, IQR [1–3] and 12.1% (n=183) were submitted to complete revascularization (number of intervened segments 1 IQR[1–2]).

Complete revascularization was associated with a lower rate of 30-day and 1-year major adverse cardiac events (MACE) (8.2% vs 15.1%, p<0.013 and 14.2% vs 23.6%, p<0.004, respectively) reflecting a lower rate in non-programmed revascularization and myocardial infarction. This effect is preserved even when corrected for other significant variables (OR 0.54, IC 95% 0.35–0.84, p<0.007). There was no difference regarding all-cause mortality at 1 year (8.2% vs 6.9%, p=0.5).

Conclusion: Even in broader real world population and including different PCI techniques over time, complete revascularization was associated with a better long-term outcome.

1201 | B E D S I D E
Frequency, reasons and predictors of unplanned cardiac rehospitalizations following primary PCI in STEMI patients: results of the Comfortable AMI trial
E. Spitzer1, L. Raebet1, S. Zaugg2, M. Ferl1, M. Magro3, A. Baumbach4, D. Tueller5, V. Volcovic6, H. Kelaeb3, S. Windlecker1, 1 Bern University Hospital, Cardiology, Bern, Switzerland; 2 University of Bern, Institute of Social and Preventive Medicine, Bern, Switzerland; 3 Erasmus Medical Center, Thoraxcenter, Rotterdam, Netherlands; 4 Bristol Heart Institute, Cardiology, Bristol, United Kingdom; 5 Freim Hilb Hospital, Cardiology, Zurich, Switzerland; 6 Clinical center of Serbia, Cardiology, Belgrade, Serbia; 7 Righospitalet - Copenhagen University Hospital, Cardiac Catheterization Laboratory, Copenhagen, Denmark

Introduction: Rehospitalizations after ST-elevation myocardial infarction (STEMI) carry a significant economic burden and may adversely impact long-term prognosis. Although coronary events leading to revascularization have been previously studied, data on any unplanned rehospitalizations is scarce.

Purpose: Our aim was to study the frequency, reasons and predictors for unplanned cardiac rehospitalizations (UCRH) after STEMI in patients undergoing primary PCI.

Methods: We performed a post-hoc analysis in the population of the COMFORTABLE AMI randomized controlled trial (NCT 00952416), which compared biolimus-eluting with bare-metal stents in STEMI patients undergoing primary PCI. All rehospitalizations after the index procedure were prospectively ascertained and reasons leading to rehospitalization adjudicated. Two reviewers independently categorized rehospitalizations into those related to cardiac or non-cardiac causes, and planned versus unplanned stays.

Results: A total of 1137 patients were included in the analysis. UCRH occurred in 133 patients (11.7%) at one year, with an estimated rate of 0.15 UCRH per patient per year (95%-CI 0.13–0.18) when taking into account multiple UCRH.

Conclusion: Complete PCI is significantly associated with decreased risk of cardiovascular mortality, repeat revascularisation, and repeat non-fatal MI in patients with acute STEMI and multivessel CAD.
year were angiographic Syntax MI score (UCRH: 16 vs No-rehosp: 13 points, p<0.002), LVEF (45% vs 50%, p=0.006), and age (62.5 vs 59.7 years, p<0.01). On multivariate analysis, LVEF (22% increase in the rate of UCRH per 10% decrease of LVEF, p<0.03) and angiographic Syntax MI score (34% increase in the rate of UCRH per 10 points increase in score, p<0.01) emerged as independent predictors of UCRH. Regional differences for UCRH rates were observed.

Conclusion: Among STEMI patients undergoing primary PCI, unplanned cardiac rehospitalizations occur in more than 10% at one year. Left ventricular ejection fraction and angiographic Syntax MI score are independent predictors of unplanned cardiac rehospitalizations and identify patient subgroups in need for improved secondary prevention.

1202 | BEDSIDE

Rarity of adverse events related to non-culprit coronary stenosis early after STEMI: implications for timing of additional revascularisation procedures
P. Rubartelli1, D. Bartolini1, S. Bellotti1, A. Iannone1, V. Fontana2. 1 Ospedale Villa Scassi, Genoa, Italy; 2 IRCCS San Martino IST, Genoa, Italy

Background: In patients with STEMI and multivessel disease (MVD), the indication to treat non-culprit lesions and the timing of complete revascularisation are controversial.

Purpose: The aim of this study is to compare the 30-day incidence of death or recurrent MI in patients with single vessel disease (SVD) or MVD and STEMI treated with primary PCI (pPCI).

Methods: From January 2006 to December 2014, 1379 patients underwent pPCI at our centre. According to our policy, non-culprit coronary stenoses were not treated before 30 days unless judged responsible for haemodynamic instability or heart failure. Therefore, only 39 (7.1%) of MVD patients underwent non-culprit revascularisation within 30 days.

Results: Patients with MVD were significantly older (69±13 vs 65±13 years), more often diabetic (32% vs 19%), experienced a longer median ischemic time (216 vs 180 minutes), and had a higher 30-day death or MI rate (11.5% vs 4.6%). However, at multivariate analysis, only age, TIMI risk index, total ischemic time, Killip class, TIMI flow before and after pPCI, but not MVD, were significantly associated with 30-day death or MI rate (Table).

The 30-day recurrent MI rate was low in both SVD (0.5%) and MVD (0.9%, P=NS), associated with 30-day death or MI rate (Table).

Summary: In MVD patients, 30-day recurrent MI due to non-culprit lesions was extremely rare. At multivariate analysis, MVD was not an independent predictor of death or MI. The mechanism underlying the potential benefit of early complete revascularisation in STEMI needs to be clarified.

1203 | BEDSIDE

Improved outcome in patients treated with GP IIb/IIIa inhibitors undergoing primary PCI for STEMI. Results of the prospective ALKK-Registry
J.G. Karcher1, R. Zahn1, M. Hochadel2, M. Brueck2, T. Budde3, S. Behrens4, V. Schaeching7, H. Darius1, B. Zrenner8, U. Zeymer9. 1 Heart Center Ludwigshafen, Department of Cardiology, Ludwigshafen am Rhein, Germany; 2 Heart Attack Research Center at the University of Heidelberg, Ludwigshafen am Rhein, Germany; 3 Clinic of Wetzlar, Wetzlar, Germany; 4 Alfred Krupp Hospital, Essen, Germany; 5 Vivantes Humboldt Klinikum, Berlin, Germany; 6 Clinic of Fulda, Fulda, Germany; 7 Vivantes Clinics for Health, Berlin, Germany; 8 Hospital Landshut-Achdorf, Landshut-Achdorf, Germany; 9 Herzcentrum Ludwigshafen, Institut f. Herzinfarktforschung Ludwigshafen at the Univ. Heidelberg, Ludwigshafen am Rhein, Germany

Background: There is still debate about the optimal antithrombotic therapy in patients undergoing primary PCI. Earlier randomized trials have shown a benefit of GP IIb/IIIa inhibitors in patients treated with heparin, with the highest benefit in high risk patients. Most recent trials did not support the earlier data. Therefore we evaluated the impact of GP IIb/IIIa inhibitors on outcome in patients with primary PCI for STEMI in real life in a large number of patients.

Methods: We used the data of the ongoing prospective ALKK-PCI registry and included patients with PCI for STEMI -<24 h duration treated with heparin in 40 centres. We excluded patients who were treated with bivalirudin.

Results: Between 2008 and 2012 a total of 15061 consecutive patients with PCI for STEMI without cardiogenic shock were included. Of these 8864 (58.9%) received a GP IIb/IIIa inhibitor. Baseline characteristics, procedural features and in-hospital outcomes are given in the table.

In a multivariate analysis GP IIb/IIIa inhibitors were associated with a reduced mortality (odds ratio 0.81, 95% CI 0.72–0.96).

Table 1

<table>
<thead>
<tr>
<th>GP IIb/IIIa Inhibitor</th>
<th>No GP IIb/IIIa Inhibitor</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=8864)</td>
<td>(n=6197)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.8, 66.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sex</td>
<td>24.8, 30.7</td>
<td>0.01</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>12.8, 16.1</td>
<td>0.02</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>7.8, 6.7</td>
<td>0.01</td>
</tr>
<tr>
<td>CKD</td>
<td>79.3, 71.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>P-urol or ticagrelor</td>
<td>19.0, 26.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Left main PCI</td>
<td>2.7, 2.4</td>
<td>0.22</td>
</tr>
<tr>
<td>TIMI 0 before PCI</td>
<td>72.2, 51.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>TIMI 3 after PCI</td>
<td>89.0, 90.0</td>
<td>0.7</td>
</tr>
<tr>
<td>Mortality</td>
<td>6.2, 7.3</td>
<td>0.13</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>2.2, 2.1</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Conclusions: In clinical practice GP IIb/IIIa inhibitors in Germany are used in more than 50% of the patients with primary PCI for STEMI treated with heparin. The use of these inhibitors proves to be associated with an improved mortality without an increase in bleeding complications. This data supports the results of randomized clinical trials and questions the use of heparin alone as intranasal antithrombotic agent.

1204 | BEDSIDE

Role of contrast volume adjusted for weight and renal function as a predictor of contrast induced nephropathy and mortality in STEMI patients undergoing primary PCI: a prospective multicentre coronary intervention study

G.M. De Ferrari1, A. Somaschini1, S. Cornara1, G. Crimi2, C. Pavesi3, R. Camporotondoto4, A. Repetto5, A. Potenza1, M. Gnecci6, M. Ferrario7. 1 Dept. of Cardiology - Fondazione IRCCS Policlinico San Matteo and University of Pavia, Pavia, Italy; 2 Dept. of Cardiology - Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Background: Contrast induced nephropathy (CIN) is associated with increased mortality in STEMI patients (pts) treated with primary PCI (pPCI).

Purpose: This study assessed whether a higher volume of contrast medium (CM) corrected for weight and renal function is a predictor of CIN and mortality (since this has never been assessed in appropriately sized studies).

Methods: We prospectively enrolled all consecutive STEMI pts undergoing pPCI in our center in 2007–2011 (n=807, after exclusion of pts without CM values). CIN was defined as an increase in creatinine >0.5 mg/dl in the first 72 hours; contrast-induced mortality (CIM) was defined as death before discharge (41.9% vs 33.8%, p<0.001) had more frequently anterior MI, a higher Killip class, a higher baseline eGFR, <0.05). CR >1 was a predictor of 1 and 2-year mortality (HR 2.08 95% CI 1.40–4.71, p<0.007) after adjusting for CKD, anterior acute MI, diabetes, prior MI, age, Killip class and haemoglobin values. CR >1 was associated with an increased 1-year (14.9% vs 3.3%, p<0.001), 1-year (26.6% vs 5.8%, p<0.001) and 2-year (34% vs 8.8%, p<0.001) mortality. At multivariable analysis CR >1 was a predictor of 1 and 2-year mortality (HR 2.08 95% CI 1.40–4.71, p<0.007 and 1.83% 95% CI 1.05–3.19, 0.03) respectively) after adjusting for LVEF, age, CK peak, haemoglobin, eGFR and diabetes.

Conclusions: CR >1 is strongly associated with both CIN and mortality in STEMI pts treated with primary PCI and could contribute to the identification of high risk pts. Our findings also underline the risk of exceeding the maximum dose of CM calculated for each patient.

1205 | BEDSIDE

New generation drug-eluting stents vs. bare metal stents for primary angioplasty in patients >75 years with ST elevated myocardial infarction: the ESTROFA MI+75 study

J.M. De La Torre Hernandez1, S. Brugaletta2, J.A. Gomez Hospital3, A. Perez De Prado4, R. Lopez Palop5, B. Cid6, A. Diego7, F. Gimeno De Carlos8. 1 Hospital de Valdecilla, Santander, Spain; 2 Hospital Clinic de Barcelona, Barcelona, Spain; 3 University Hospital of Bellvitge, Barcelona, Spain; 4 Hospital of Leon, Leon, Spain; 5 University Hospital San Juan de Alicante, Alicante, Spain; 6 University Hospital of Santander de Compostela, Santiago de Compostela, Spain; 7 Hospital Clinico Universitario, Salamanca, Spain; 8 University Hospital Clinic of Valladolid, Valladolid, Spain; 9 University Hospital Puerta de Hierro Majadahonda, Madrid, Spain; 10 University Hospital Clinic of Valencia, Valencia, Spain

Purpose: Primary angioplasty is the best reperfusion treatment in ST elevated myocardial infarction. The prevalence of very elderly patients (>75 years) un-
Inflammation and plaque vulnerability – Advanced insights from mouse and man

1215 | BENCH

Dendritic cells are involved in hypercholesterolemia after myocardial infarction

Z. Li, C. Wu, J. Yuan, H. Liu, W. Gao, A. Sun, Y. Zou, J. Ge. Zhongshan Hospital, Fudan University, Shanghai, China, People's Republic of

Background: Dyslipidemia during myocardial infarction (MI) has been reported but the mechanism is still unclear. Sterol regulatory element binding protein (SREBP) is a key lipogenic transcription factor and it adjusts the lipogenesis through the AMPK-mTOR-SREBP signaling pathway in hepatocytes. The signaling pathway inside hepatocytes could be altered by inflammatory signals secreted by inflammatory cells including dendritic cells (DCs). It has been known that DCs can directly interact post-MI, we therefore hypothesized that activated DCs post-MI might participate in the hypercholesterolemia.

Purpose: To define whether DCs play a role in the dyslipidemia post-MI through regulation of AMPK-mTOR-SREBP signaling in liver.

Methods: 1. Adult male C57BL/6 mice were randomly divided into three groups: 1) MI, 2) MI+24h, 3) Sham. MI was induced with ST elevated myocardial infarction undergoing primary angioplasty with implantation of new generation drug-eluting stents (DES) or bare metal stents (BMS) were included.

Results: A total of 2, 146 pts have been included, 1, 487 (69.3%) treated with BMS and 659 (30.7%) treated with new generation DES. After exclusion of patients presenting with cardiogenic shock or requiring cardiac surgery for mechanical complications (13%) a propensity score matching was performed yielding two comparable groups of 403 patients each with well balanced baseline clinical or angiographic characteristics. All patients completed one year follow up. Outcomes at 12 months were the following: cumulative incidence of cardiac death and MI was 9.6% in BMS group and 4.7% in DES group (p=0.02), TLR was 3.5% in BMS and 1.5% in DES (p<0.01), definite or probable stent thrombosis was 4.6% in BMS and 2.5% in DES (p<0.01), definite stent thrombosis 3.9% in BMS and 1.4% in DES (p=0.05) and incidence of bleeding BARC ≥2 was 0.6% in BMS and 1.1% in DES (p=0.5).

Conclusions: In this registry of patients over 75 years undergoing primary angioplasty, most were treated with BMS. After propensity score matching the observed clinical outcome (BARC ≥2) with new DES without significant increase in severe bleeding events in follow up from the RELAX-AHF study showed significant improved dyspnea symptoms and significant mortality benefits within patients with acute heart failure. It is unclear whether serelaxin has an effect on atherosclerosis. Therefore, we investigated the effect of serelaxin in human coronary artery smooth muscle cells (HCASMCs) and in a mouse model of atherosclerosis.

Methods and results: In vitro, we investigated the effects of serelaxin on oxidative stress (LO–12, DCF) in human coronary artery smooth muscle cells (HCASMC). Serelaxin incubation of HCASMC reduced significantly angiotensin II– induced ROS production (veh: 100%, angII:127.3±7.2%, angII+RLX (10ng/ml, 24h): 108.9±6.1%, p=0.044 vs. angII). Female 6–8-week-old apolipoprotein E– deficient (C57BL6.ApoE–/–) mice were fed a high-fat (21%) diet containing 1.25% cholesterol for 6 weeks and received a continuous treatment with serelaxin in two different doses (0.1μg/g and 0.05μg/g) using subcutaneously implanted osmotic mini-pumps. Additionally, one group of female ApoE–/– mice served as control group treated with vehicle through osmotic mini-pumps. Total cholesterol, fasting blood glucose, blood pressure and heart rates were no different between the groups. Vascular oxidative stress (L012–chemiluminescence) was significant reduced in both serelaxin–treated mice (veh: 322.7±39.6 U/L vs. RLX 0.05μg/g: 119.76±14.27 U/L (p=0.03 vs. veh), RLX 0.1μg/g: 109±22.2 U/L (p=0.002 vs. veh)). Serelaxin treatment in both concentrations significantly improved endothelium–dependent vasodilatation (organ chamber experiments) without influencing endothelium-independent vasorelaxation as compared with sere-

Conclusion: The presented data demonstrate novel effects of serelaxin on vascular oxidative stress and atherosclerotic plaque development. Therefore, Serelaixin could serve as a new drug class for treating atherosclerosis–related diseases.

1217 | BENCH

Loss of hematopoietic DPP4 ameliorates atherosclerosis and vascular inflammation by non-catalytic mechanisms

J. Zhong1, X. Rao1, S. Oghumu2, J. Deuluis1, A.R. Satoskar2, M. Friemen1, S. Rajagopalan1, 1 University of Maryland, Department of Medicine, Baltimore, United States of America, 2 The Ohio State University, Columbus, United States of America

Background: Dipeptidyl peptidase-4 (DPP4) is a transmembrane protein that is widely expressed in a vast number of tissues. DPP4 is a key enzyme in the degradation of incretin hormones GLP-1 and GIP. The role of DPP4 non-catalytic function in the enzymatic degradation of the incretins or other enzymatic targets remains insufficiently characterized.

Purpose: In this study we attempted to understand the contribution of DPP4 non-catalytic function and the role of hematopoietic DPP4 in regulating atherosclerosis progression.

Methods and results: DPP4 was highly expressed on T cell and monocytes with expression increased in patients with stable established cardiovascular disease vs. controls [T cells 48.06±1.96% vs. 27.46±2.67%, p<0.0001; peripheral monocytes 5.76±0.44% vs. 4.2±0.44%, p=0.037 respectively]. Expression was highest on CD4+ T cells. DPP4+/− mice transplanted with wild-type (WT) bone marrow and fed high fat diet (HFD) displayed increased plasma DPP4 activity and impaired response to oral glucose challenge after 12 weeks. Ldlr−/− mice transplanted with Dpp4−/−/bone marrows were protected from atherosclerosis compared with Ldlr−/−/chimeras with wild-type bone marrows (Plaque/aorta area ratio [Mean ± SD]: 54.8±11.4% vs. 31.3±10.5% for wild-type vs. Dpp4−/−, p<0.05). T cell infiltration in aortic plaque was reduced in chimeras with Dpp4−/− bone marrows. Both in vivo and in vitro chemotaxis assays suggested that lack of DPP4 non-catalytic but not catalytic function impaired T cell motility.

Conclusion: Our results suggest a potential role for non-catalytic function of hematopoietic DPP4 in vascular inflammation and atherosclerosis.
SYSTOLIC HYPERTENSION

1237 | BEDSIDE
Rising systolic blood pressure leads to a continuous progression towards hypertensive heart disease: a prospective population study
A. De Marvao1, T. Dawes1, W. Shi1, D. Rucker1, S. Cook1, D. O'Regan1, 1Imperial College London, Medical Research Council Clinical Sciences Centre, London, United Kingdom; 2Imperial College London, Department of Computing, London, United Kingdom; 3Duke-NUS Graduate Medical School Singapore, Singapore, Singapore

Background: Left ventricular (LV) hypertrophy and remodeling occur in response to hemodynamic stress but little is known about how these phenotypic changes are initiated.

Purpose: Using high-resolution 3-dimensional cardiac magnetic resonance (3D-CMR) we define the anatomical and functional LV properties associated with increasing systolic blood pressure (SBP) in a drug-naive cohort.

Methods: 1534 volunteers (54.9% females, 74.8% Caucasian, mean age 41.3±13.0 years) without self-reported cardiovascular disease underwent 3D-CMR combined with computational modelling. The relationship between SBP wall thickness (WT), relative wall thickness (RWT), end-systolic wall stress (WS) and fractional wall thickening (FWT) were analysed using 3D regression models adjusted for body surface area, gender, race, age and multiple testing. Significantly associated points in the LV model (p<0.05) were identified and the relationship with SBP reported as mean β coefficients.

Results: SBP varied widely in the cohort: 7.5%, systolic hypertension (SBP ≥140 mmHg); 37.1%, pre-hypertension (SBP 120–139 mmHg) and 55.4%, normotension (SBP <120 mmHg).

There was a continuous relationship between SBP and asymmetric concentric hypertrophy of the septum and anterior wall with associated normalisation of WS. In the lateral wall an increase in WS with rising SBP was not balanced by a commensurate hypertrophic response. In normotensives, SBP was positively associated with WT (β=0.08) and RWT (β=0.06) in the septal and anterior walls, and this regional hypertrophic response was progressively stronger amongst pre-hypertensives (β=0.08) and hypertensives (β=0.21). Males had a greater hypertrophic response than females with the most robust interaction between SBP and gender in the septum (β=0.67). FWT was positively associated with SBP in the inferior and lateral walls (β = 0.10) but not where SBP-associated hypertrophy was predominant.

Conclusions: SBP is associated with a continuous progression towards the hypertensive cardiac phenotype, which we show to be defined by concentric hypertrophy of the septum and eccentric remodeling of the lateral wall. We observed that rising SBP is associated with a normalisation of WS in the septum where concentric hypertrophy is predominant. However, in the majority of the left ventricle the increase in WS with rising SBP was not balanced by a proportionate increase in RWT. These findings challenge the conventional understanding of compensated hypertrophy in pressure overload and suggest disease mechanisms.

1238 | BEDSIDE
Association of orthostatic hypertension with cardiovascular and all cause mortality in the elderly program
J.B. Kostis1, D. Sargsyan1, W.J. Kostis2. 1Rutgers Robert Wood Johnson Medical School, Cardiovascular Institute, New Brunswick, United States of America; 2Massachusetts General Hospital, Division of Cardiology, Boston, United States of America

Background: Orthostatic hypertension, an increase in systolic blood pressure (SBP) upon standing, occurs in some older individuals, but has not been studied extensively, is usually not appreciated by clinicians, and there are no long-term data in placebo controlled trials.

Purpose: We examined the relationship between orthostatic hypertension, increase in SBP by more than 15 mm Hg after standing (oHyper) in the randomized, placebo-controlled Systolic Hypertension in the Elderly Program (SHEP) trial in older patients with isolated systolic hypertension.

Methods: Of the 4,736 participants, 22 did not have data on orthostatic change, 203 had oHyper, 4073 had a normal response, and 438 had orthostatic hypotension (SBP decrease by 20 mm Hg or more, oHypo).

Results: Compared with normal response, oHypo was associated with higher 17-year cardiovascular death in an analysis adjusted for age, gender and SBP (HR 1.16, 95% CI 1.06–1.27, p=0.001). Similar findings were observed for all-cause mortality. The higher risk was no longer significant after additional adjustment for creatinine, diabetes, body mass index, smoking, left ventricular failure, and HDL cholesterol. The higher mortality associated with oHyper was observed at the end of the randomized phase (4.5 years; 1.38, 1.10–1.72, p=0.005) and at 8.5 (1.27, 1.10–1.46, p<0.001), at 12.5 (1.18, 1.06–1.32, p=0.003) as well as at 17-years after randomization. The well-known effects of orthostatic hypotension were also observed in this analysis.

Conclusions: Orthostatic hypertension may be associated with increased cardiovascular and all-cause mortality in older persons with isolated systolic hypertension. Attention to this easily determined risk factor may be used to refine cardiovascular risk estimation.

SYNCOPE AND SUDDEN DEATH

1320 | BEDSIDE
Management and outcomes of out of hospital cardiac arrest according to its time of occurrence: results from the paris sdc study
N. Karam, E. Marjion, L. Offredo, F. Begantone, L. Lamhaut, F. Dumas, C. Spaulding, A. Cariou, X. Jouven. Inserm U970 - Paris Cardiovascular Research Center (PRHCC), Cardiovascular Epidemiology-Sudden Death, Paris, France

Background: Prognosis of STEMI is worse during off hours compared to working hours. A similar relationship has never been assessed in out-of-hospital cardiac arrest (OHCA)

Comparison of OHCA by occurrence time

<table>
<thead>
<tr>
<th>Comparison of OHCA by occurrence time</th>
<th>N</th>
<th>p.value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Working hours</td>
<td>Off hours</td>
</tr>
<tr>
<td>Number (%)</td>
<td>11430</td>
<td>4190 (36.65)</td>
</tr>
<tr>
<td>Age (mean (median))</td>
<td>11378</td>
<td>71 (74)</td>
</tr>
<tr>
<td>Call-to-EMS arrival delay (mean (median))</td>
<td>12843</td>
<td>11 (9)</td>
</tr>
<tr>
<td>Home location</td>
<td>11295</td>
<td>73.57</td>
</tr>
<tr>
<td>Witness presence</td>
<td>9965</td>
<td>72.05</td>
</tr>
<tr>
<td>Bystander BLS-initiation</td>
<td>7570</td>
<td>48.90</td>
</tr>
<tr>
<td>AED use</td>
<td>4906</td>
<td>3.04</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>2291</td>
<td>50.27</td>
</tr>
<tr>
<td>ROSIC</td>
<td>8623</td>
<td>31.59</td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>2379</td>
<td>55.56</td>
</tr>
<tr>
<td>Coronary angioplasty</td>
<td>1330</td>
<td>36.28</td>
</tr>
<tr>
<td>On-site death</td>
<td>11430</td>
<td>74.30</td>
</tr>
<tr>
<td>Death</td>
<td>11113</td>
<td>94.04</td>
</tr>
</tbody>
</table>

ABSTRACT WITHDRAWN
Purpose: To compare OHCA management and outcomes according to whether they occur during off or working hours.

Methods: Data was taken between May 2011 and 2014 from the our Sudden Cardiac Death Expertise Center (SDEC) prospective registry that includes all patients who present OHCA in Paris and suburbs. Patients were classified according to whether they presented OHCA during off hours (weekends, holidays and nights) or working hours.

Results: Of the 11430 reported OHCA, 7240 (63%) occurred during off hours. Witnesses were more often present but less frequently initiated BLS and used AED; bystanders were more often in hospital discharge, despite similar rates of hypothermia, coronary angiography and angioplasty.

Conclusion: Survival rates of OHCA were lower during off hours mainly due to a lower rate of witness-initiated BLS and AED use rather than a difference in hemorrhagic complications. The results of public awareness and training programs in improving OHCA prognosis during off hours were presented within 50 days of WCD use, and 90% of all therapies occurred within 80 minutes, in addition to BPM during physical examination (PE) and BPM before and after a meal.

Conclusions: We recommend routine prehospital BPM during PE and standing test. We urgently need more research on orthostatic and postprandial blood pressure testing that includes clinical outcomes.

Introduction: In the elderly, orthostatic hypotension (OH) and postprandial hypotension (PPH) are common causes for syncope. Blood pressure measurements (BPM) in the supine and upright position for 3 minutes is part of the diagnostic tests in the ESC guidelines, but meal testing for PPH is not. We evaluated the diagnostic yield in elderly patients with syncope of active standing during 10 minutes, in addition to BPM during physical examination (PE) and BPM before and after a meal.

Methods: In a multidisciplinary program for the evaluation of unexplained falls and/or syncope in elderly patients we investigated all patients for OH and PPH. This diagnostic program of 2 days included a comprehensive geriatric assessment without the Risks of PPH (RAPH) assessment. The first 10 minutes of the standing test and BPM were performed. On a second day, the patients arrived in the morning after an overnight fast for orthostatic- and postprandial BPM. Patients started with an active standing tests for 10 minutes, followed by a meal and postprandial BPM. Blood pressure (BP) was measured at the right upper arm using a Welch Allyn vital signs monitor 300 device. For PPH, patients were measured in the sitting position and a standardized 292-kcal liquid meal was used. BP was measured every 5 minutes for 75 minutes after the start of the meal. Patients were asked about possible symptoms during both tests.

Results: Of 262 patients evaluated, 117 patients had syncope and 12 patients were diagnosed with pre-syncope, mean age 80.5 years. In 120 patients of the 129 patients, orthostatic BPM were performed both during PE and standing test.
49 patients had OH at PE and 49 patients had OH during the standing test. Only 32 patients had OH at both tests. Compared to BPM at PE, we found 17 additional patients with OH during the standing test of whom 15 patients were symptomatic. In addition, 7 patients had delayed OH during the standing test, 5 symptomatic and 2 asymptomatic. In 123 patients a meal test was done. 66 patients (54%) had PPH and 38 patients were symptomatic.

**Conclusions:** In these very elderly patients, we found a significant number of patients with OH during the second test. This well-known variability of OH indicates that for the diagnosis of OH more active standing BPM should be performed in the whole 3 up of syncope. The active standing tests should be performed for at least 10 minutes to identify patients with a delayed OH. BPM before and after meals for the diagnosis of PPH should be added to the diagnostic tests in the ESC syncope guidelines.

### 1327 | BESIDE

**Epileptic seizures are frequent in patients with long QT syndrome type 2**

I. Dahl1, P.G. Larsson2, K.H. Haugaa3, E. Taubøl4, 1University of Oslo, Faculty of Medicine, Oslo, Norway; 2Oslo University Hospital, Section of Neurophysiology, Dept. Neurosurgery, Rikshospitalet, Oslo, Norway; 3Oslo University Hospital, Dept. Cardiology, Rikshospitalet, Oslo, Norway; 4Oslo University Hospital, Dept. Neurology, Rikshospitalet, Oslo, Norway

**Background:** The long QT-syndrome (LQTS) is caused by cardiac ion channel dysfunction predisposing to ventricular arrhythmias. Cerebral ion channel dysfunction may lead to idiopathic epileptiform discharges. Essential ion channels are co-expressed in the heart and in the brain. Accordingly, current theories suggest that some cases of syncope in patients with LQTS may in fact be caused by a coexisting cerebral channelopathy (i.e. epilepsy). Case reports and small-scale studies have indicated that LQTS patients with LQTS type 2 (LQT2) have an increased prevalence of cerebral affection compared to other LQTS subcategories.

**Purpose:** We aimed to describe the semiology of loss of consciousness in LQT2 patients. In addition, we evaluated for alterations in the electroencephalograms (EEG) of these patients.

**Methods:** We studied 15 patients (age: 43 (21–72), 12 women) with a genotyped diagnosis of LQT2. We performed a standard medical history with emphasis on the semiology of previous syncopes and a clinical neurological examination. A 1hr 64-channel awake EEG has so far been analysed in 9 patients. The EEGs were assessed visually and the frequency of abnormalities was recorded.

**Results:** Of the 15 patients, 11 (73%) had experienced syncopes, of which 6 (55%) had experienced tonic-clonic activity or spells and urine incontinence. One of the 11 (9%) had experienced urine incontinence in absence of tonic-clonic activity or spells. Two patients (13%) had been diagnosed with epilepsy and received anti-epileptic medication prior to their LQTS diagnosis. EEGs showed an increased frequency of theta activity fraction-centrally in 7 of the 9 examined patients, including one patient with confirmed epileptic activity.

**Conclusion:** Synapses in LQT2 patients were frequently associated with tonic-clonic activity, spells and urine incontinence, which could also be consistent with epilepsy. In addition, 2/15 had co-existing diagnoses of epilepsy and LQT2. The majority of the EEGs showed minor to moderate changes with intermittent theta activity or spells. Two patients (13%) had been diagnosed with epilepsy and received anti-epileptic medication prior to their LQTS diagnosis. EEGs showed an increased frequency of theta activity fraction-centrally in 7 of the 9 examined patients, including one patient with confirmed epileptic activity.

The active standing tests should be performed for at least 10 minutes to identify patients with a delayed OH. BPM before and after meals for the diagnosis of PPH should be added to the diagnostic tests in the ESC syncope guidelines.

### 1328 | BESIDE

**Cumulative risk of symptoms in pediatric patients with long QT syndrome (LQTS) who were diagnosed by school-based screening programs in Japan**

M. Yoshinaga1, H. Ogata2, H. Suzuki3, H. Ushinohama4, N. Sumitomo5, H. Horigome6, S. Tateno3, S. Sato6, N. Tauchi6, M. Nagashima7, 1National Hospital Organization Kagoshima Medical Center, Kagoshima, Japan; 2Centers for Public Health Research, National Institute of Public Health, Wako, Japan; 3Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan; 4Fukuoka Children’s Hospital and Medical Center for Infectious Diseases, Fukuoka, Fukuoka, Japan; 5Saitama Medical University, Saitama, Japan; 6University of Tsukuba, Tsukuba, Japan; 7Chiba Cerebral and Cardiovascular Center, Chiba, Japan; 8Niigata City General Hospital, Niigata, Japan; 9Aichi Saiseikai Rehabilitation Hospital, Nagoya, Japan

A nationwide school-based ECG screening program is active in 1st, 7th, and 10th graders in Japan. The prevalence of children with prolonged QT intervals diagnosed by the program is close to 1:1200 at 7th grade. However, the cumulative risk of symptoms in patients with LQTS who were diagnosed by the programs is still unclear. A total of 451 pediatric patients (≥20 years of age at the time of diagnosis) included 275 subjects who were screened (screened group), 79 subjects who visited with symptoms (clinical group) and 97 subjects who were diagnosed by family study or by chance (miscellaneous group). Cumulative risk of symptoms by Kaplan-Meier method was 100%, 35%, and 28% in the clinical, miscellaneous, and screened groups, respectively (Figure).

**Results:** Log-rank test revealed significant differences between groups (screened vs clinical, p=0.000; screened vs miscellaneous, p=0.000). Multiple regression analysis showed that a longer observation period was a sole predictor of symptoms (p=0.03) in the screened group. The cumulative risk of symptoms in the screened group is not so low. Thus, we suggest that, like clinically identified patients, screened patients should receive follow-up assessments.

### 1329 | BESIDE

**Antidiuretic autoimmunity in postural tachycardia syndrome and vasovagal syncope**

A. Fedorowski1, R. Sutton2, O. Melander3, H. Li1, X. Yu1, D.C. Kern3, 1Dept. of Clinical Sciences, Lund University, Malmö, Sweden; 2Imperial College Healthcare NHS Trust, London, United Kingdom; 3University of Oklahoma, Dept. of Medicine, Oklahoma City, United States of America

**Background:** Postural tachycardia syndrome (PoTS) affecting predominantly young females is characterized by upright tachycardia, adrenergic symptoms, and sporadic syncope. We previously reported a possible pathophysiological role for activating autoantibodies (AAbs) to the alpha-1 (α1AR) and beta-1 and -2 adrenergic receptors (β1/2AR) in PoTS.

**Purpose:** To examine the AAB profile of a representative cohort of PoTS and determine if these AAbs are also present in patients with recurrent vasovagal syncope (VVS) compared with normals.

**Methods:** Sera (with consent) from 18 PoTS patients (16F, 26±9 years), 7 with recurrent VVS (5F, 31±19 years), and 13 normal controls (all F, 29±5 years) without past history of syncope and with normal postural hemodynamics were analyzed. Sera and/or IgG were examined for the ability to activate α1AR and β1/2AR in...
transected Chinese Hamster ovary cells. Data were expressed as % rise over buffer baseline (BB) or relative luminescence units (RLU).

Results: As can be seen in Table 1, α1AR activity was significantly higher in PoTS patients than controls (p<0.01) but not VVS (p=0.35). The PoTS group demonstrated heterogeneity as 12/18 subjects had higher α1AR activity than the controls. In contrast, α2AR activity in PoTS was more homogeneous and higher than both VVS and controls (p<0.05) while VVS also was higher than the control group (p<0.01). Moreover, sera from PoTS shifted α1AR-phenylephrine dosage curves to the right.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Alpha-1AR AAb (% above BB)</th>
<th>Beta-1AR AAb (RLU)</th>
<th>Beta-2AR AAb (RLU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n=13)</td>
<td>63±2.7</td>
<td>3901±157</td>
<td>4212±251</td>
</tr>
<tr>
<td>PoTS (n=18)</td>
<td>78±1.4*</td>
<td>5209±95*</td>
<td>6534±251*</td>
</tr>
</tbody>
</table>

Conclusions: These data support a pathophysiological relationship between α1 and β2 adrenergic AAs and PoTS; and suggest they are not restricted to classic PoTS alone but may also be present in other forms of dysautonomia such as recurrent VVS as a part of an autonomous spectrum.

Acknowledgments: The Ernhold Lundström’s Research Foundation; Acknowledgement/Funding:

---

1329 | BEDSIDE

Increased risk of occupational accidents following syncope: a Danish nationwide study

A. Nume1, M.H. Ruwald1, K. Kragholm Soerensen2, D. Zahir1, C. Torp-Pedersen3, G. Glisason1,1, Gentotte University Hospital, Department of Cardiology, Hellerup, Denmark; 2Aalborg University, Department of Health Science and Technology, Aalborg, Denmark

Background: Performing hazardous working activities by individuals suffering from syncope may be associated with increased risk of serious accidents.

Purpose: We sought to identify whether there is an excess risk of occupational accidents in a nationwide cohort of patients with syncope compared with that of the general population and secondly, whether it is associated with increased short-term mortality.

Methods: All individuals aged 18–65 years with a first-time diagnosis of syncope in 2008–2012 were identified and included. The primary endpoint was defined as first event of an occupational accident requiring hospitalization. As for secondary endpoint, we investigated all-cause mortality within 30 days after an occupational accident. We assessed risk using multivariable Poisson regression analyses adjusted for age, sex, calendar year, socioeconomic status and comorbidities, with the total Danish population as reference.

Results: Out of 3,474,709 Danish residents we identified 20,911 patients with syncope (median age 46 years [IQR 31–58]; 51% women) who experienced 1,080 (5.2%) occupational accidents during a median follow-up time of 2.3 years (95% CI 1.1–3.6). Crude incidence rates of occupational accidents among the syncope and general population were 20.3/100,000 (95% CI 19.1–21.7) and 14.2/100,000 (95% CI 14.1–14.2) per 1,000 person-years respectively. The rate ratios (RR) of occupational accidents were significantly increased (p<0.0001) among patients with syncope compared with the general Danish population in all age groups. The RR's were 1.15 (95% CI 1.03–1.28) among 18–27 year olds, 1.48 (95% CI 1.34–1.63) among 28–52 year olds and 1.51 (95% CI 1.35–1.69) among 53–65 year olds respectively. However, there was no difference in all-cause mortality within 30 days from the occupational accident between the syncope and general population: RR 1.31 (95% CI 0.53–3.20, p=0.56).

Conclusions: In this nationwide cohort of syncope patients we found a significant increased risk of occupational accidents following syncope, especially among the younger population, however, not accompanied by increased short-term mortality. Increased physician awareness on risk of occupational accidents following syncope might be warranted.

BEST POSTERS SESSION 2

P1331 | BEDSIDE

Neurological outcomes in children transported to hospital without a prehospital return of spontaneous circulation after out-of-hospital cardiac arrest

Y. Goto1, T. Maeda1, A. Funada1, Y. Nakatsu-Goto2, Kanazawa University Hospital, Section of Emergency Medicine, Kanazawa, Japan; 2Yawata Medical Center, Department of Cardiology, Komatsu, Japan

Background: Obtaining favourable neurological outcomes is extremely difficult in children transported to hospital without a prehospital return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest (OHCA). However, the crucial prehospital factors for long-term survival with favourable outcomes in this cohort remain unclear.

Purpose: We aimed to determine the prehospital factors for long-term survival and favourable neurological outcomes (cerebral performance category score, categories 1 or 2; CPC 1–2) in children transported to hospital without a prehospital ROSC after OHCA.

Methods: Of 9093 OHCA children, 7332 children (age, <18 years; 80.6% of the total) without prehospital ROSC after attempting resuscitation, were eligible for enrolment into the present study. Data were obtained from a prospectively recorded national Utstein-style database from 2008 to 2012 (5 years). The primary endpoint was 1-month CPC 1–2 after cardiac arrest.

Results: The rates of 1-month survival and 1-month CPC 1–2 were 6.92% (95% CI 6.58%–7.27%) and 0.99% (97% CI 0.89%–1.10%), respectively. The proportions of the following prehospital variables were significantly higher in the 1-month CPC 1–2 cohort than in the 1-month CPC 3–5 cohort: age (median, 3 year [interquartile range (IQR) 0–14] vs. 1 year [IQR 0–11], P<0.001), initial shockable rhythm (28/73 [38.3%] vs. 180/7259 [2.52%, P<0.0001]), initial shockable rhythm (28/73 [38.3%] vs. 180/7259 [2.52%, P<0.0001]), presumed cardiac causes (42/73 [57.5%] vs. 2385/7259 [32.8%, P<0.0001]), and actual shock delivery (25/73 [34.2%] vs. 314/7259 [4.3%, P<0.0001]). Multivariable logistic regression analysis indicated that the following prehospital factors were associated with 1-month CPC 1–2: (1) initial non-astiole rhythm (ventricular fibrillation [VF]/pulsless ventricular tachycardia [VT]: adjusted odd ratio [aOR] 15.9; 95% confidence interval [CI] 8.05–32.0, pulseless electrical activity [PEA]: aOR 5.18; 95% CI 2.76–9.82), (2) bystander-witnessed arrest (aOR 3.21; 95% CI 1.95–5.45) and (3) bystander-witnessed arrest (aOR 3.17; 95% CI 2.26–4.67). In witnessed-arrest children with an initial VF/pulseless VT rhythm, the rate of 1-month CPC 1–2 was significantly higher than that in those with other initial cardiac rhythms (15.6% vs. 2.27% for PEA and 1.18% for asystole, P<0.001).

Conclusions: The crucial prehospital factors for 1-month favourable neurological outcomes after cardiac arrest were initial non-astiole rhythm and bystander-witnessed arrest in OHCA children transported to hospital without a prehospital ROSC.

194 Syncope and sudden death / Best Posters in sudden death
P1334 | BEDSIDE
Survival improved for men but not women, despite increased bystander CPR and first responder defibrillation for both: results form a statewide quality improvement initiative

C. Malta Hansen1, K. Kragholm1, D.A. Pearson2, C. Tyson1, L. Monk1, D. Nelson3, M.E. Dupre3, J.G. Jolli1, B. McNally1, C.B. Grainger1, 1Duke Clinical Research Institute, Durham, United States of America; 2Carolina HeartCare, Winston-Salem, United States of America

Purpose: Bystander and first responder intervention and survival increased after out-of-hospital cardiac arrest following a quality improvement initiative in North Carolina (2010–2013). We assessed whether statewide efforts to improve survival have narrowed gender-related differences in care and outcome according to gender.

Methods: Through the CARES registry, we identified out-of-hospital cardiac arrests during 2010–2013 from counties in North Carolina with complete case capture (population ~3 mio). Multivariable Poisson regression models examined changes in survival across years.

Results: Of 6243 cardiac arrests, 61.4% were male. Women were older, had more often non-shockable heart rhythm (83.1% vs 70.0%), unwitnessed arrest (48.9% vs 42.6%) and arrest in private homes (83.1% vs. 77.7%) but similar response time. From 2010–2013, bystander CPR and first responder defibrillation increased for men but not women. Future research is needed to elucidate gender-related differences in treatment response in this population.

Conclusions: Following a statewide quality improvement initiative, increased bystander CPR and first responder defibrillation were associated with increased survival in men but not women. Future research is needed to elucidate gender-related differences in treatment response in this population.

P1336 | BEDSIDE
Long-term mortality and risk of myocardial infarction associated with presence and extent of coronary artery disease in diabetic and non-diabetic patients

K.K.W. Olesen1, M. Madsen2, G. Egholm1, T. Thim1, L.O. Jensen3, H.E. Boetker1, H.T. Soerensen2, M. Maeng1, 1Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark; 2Aarhus University Hospital, Department of Clinical Epidemiology, Aarhus, Denmark; 3Odense University Hospital, Department of Cardiology, Odense, Denmark

Introduction: Patients with medically treated diabetes mellitus have a risk of myocardial infarction (MI) equivalent to non-diabetic patients with a previous MI, and it has been suggested prophylactically treat these patients with aspirin and statins.

Purpose: We aimed to examine long-term clinical outcomes in patients with and without coronary artery disease stratified for presence/absence of diabetes at first presentation and angiography (CAD).

Methods: We performed a population-based cohort study of every CAG registered in the Western Denmark Heart Registry from January 1st 2003 to December 31st 2012. Patients with prior history of MI, percutaneous coronary intervention, or coronary artery bypass operation were excluded. In case of multiple CAG examinations during the period, only the first CAG was included. Patients were stratified according to presence of obstructive coronary artery disease (CAD) defined as ≥50% lumen narrowing in ≥1 coronary artery. Patients were further stratified according to presence of diabetes. Patients were followed for a maximum of 7 years. End-points, including all-cause mortality, cardiac death and MI were obtained through cross-linkage of national Danish registries. The total number of events was counted and Kaplan-Meier curves were constructed.

Crude and adjusted hazard ratios were estimated using Cox proportional hazards model.

Results: 71,424 patients were eligible for analysis of which 8,541 (12%) had diabetes at the time of evaluation. CAD was present in 41,010 (n=5,475 diabetic patients, while 30,414 had no CAD (n=3,066 diabetic). Mean follow up was 4.3 years. Diabetic patients with CAD at CAG exhibited the highest risk of MI during follow-up followed by non-diabetic patients with CAD. However patients without CAD, despite presence or absence of diabetes, exhibited similar low rates of MI. In terms of all-cause death, diabetic patients with CAD were at highest risk, followed by non-diabetic patient with CAD and diabetic patients without CAD showing equally high mortality risk, with non-diabetic patients without CAD at the lowest risk of death.

Conclusions: Patients with diabetes but no CAD exhibited the same low risk of MI as non-diabetic patients without CAD. This challenges the general assumption of diabetic patients as a uniform group of high-risk patients with regard to risk of future MI.

P1337 | BEDSIDE
Long-term risk of myocardial infarction and mortality in patients without obstructive coronary artery disease by coronary angiography

K.K.W. Olesen1, M. Madsen2, G. Egholm1, T. Thim1, L.O. Jensen3, H.E. Boetker1, H.T. Soerensen2, M. Maeng1, 1Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark; 2Aarhus University Hospital, Department of Clinical Epidemiology, Aarhus, Denmark; 3Odense University Hospital, Department of Cardiology, Odense, Denmark

Introduction: Chest pain despite the absence of obstructive coronary artery disease (CAD) has previously been associated with favorable long-term risk of death and future myocardial infarction (MI). However, recent large-scale studies are suggesting otherwise, leaving risk assessment of these patients unclear.

Purpose: Examine long-term risk of myocardial infarction (MI) and all-cause mortality in patients without obstructive CAD verified by coronary angiography (CAG) compared to a sampled background population from the Western Danish population.

Methods: Population-based retrospective cohort study. Patient cohort was established using every CAG procedure from January 1st 2003–December 31st 2012 in the Western Denmark Heart Registry. Analyzes were restricted to patients without obstructive CAD at time of premier CAG examination, further stratified according to procedural priority: acute/subacute or elective procedures. Further sensitivity analyzes was performed in elective patients with stable angina pectoris. Patients with prior history of MI, PCI or CABG were excluded. Subcohorts were compared to background population matched sample without prior history of MI from the Western Denmark population. Maximum follow up of 7 years with endpoints of MI and death. Total number of endpoints were counted. Cumulated event curves were constructed. Short-term risk difference and relative risk were estimated for the
initial 6 months after CAG. Crude and adjusted long-term HR were generated using Cox’s proportional hazard regression analyses.

Results: 31,805 patients undergoing first time CAG were eligible for analyses of whom 9,241 were acute/subacute procedures and 22,493 were elective procedures. In sensitivity analyzes 13,110 elective patients had stable angina pectoris, while 22,493 were elective procedures. In sensitivity analyzes 13,110 elective patients had stable angina pectoris, while 22,493 were elective procedures. In sensitivity analyzes 13,110 elective patients had stable angina pectoris, while 22,493 were elective procedures. In sensitivity analyzes 13,110 elective patients had stable angina pectoris, while 22,493 were elective procedures. In sensitivity analyzes 13,110 elective patients had stable angina pectoris, while 22,493 were elective procedures.

Background and aim: Number of PCI performed by center is a determinant of the rate of prehospital reperfusion-decisions in the ambulance setting. This study was performed in 18,063 STEMI patients managed by 41 mobile intensive care units.

Methods: The e-MUST registry was set-up in 2003 by the regional health authority of the Paris region in France (12-million population) to prospectively collect data on all STEMI patients transported by the physician-staffed MICU dispatched on site. Median time for testing and/or better ways to titrate the negative response beyond classical physiology. Previous studies have suggested a decline in positivity of myocardial perfusion imaging in North-America, suggesting the need for developing better strategies for test selection to achieve acceptable cost-effectiveness balance.

Methods: We assessed the rate of sensitivity and specificity of 4087 patients evaluated in a tertiary care referral center from 1991–1999. We performed 3159 patients were more likely to be younger without diabetes mellitus than non-spasm patients. However, in a group of non significant organic stenosis, ACh-positive patients were more likely to be older smokers with dyslipidemia and to have a family history of ischemic heart disease than non-spasm patients. ACh-positive patients with significant organic stenosis were divided into 2 groups: patients with coronary spasm at the sites of organic stenosis (n=192) and those with coronary spasm except the sites of organic stenosis (n=41). Multiple logistic regression analysis identified ST-segment elevation during angina attacks, significant organic stenosis in left anterior descending (LAD) artery and multivessel spasm to correlate with the ACh-provoked spasm at the sites of organic stenosis. Kaplan–Meier survival curve indicated worse 5-year survival rates free from major adverse cardiovascular events (MACEs) in patients with ACh-provoked coronary spasm at the sites of organic stenosis compared with those except the sites of organic stenosis and without organic stenosis (P=0.048, P=0.001, respectively). Multivariate Cox hazard regression analysis identified ACh-provoked spasm at the sites of organic stenosis (HR: 2.28; 95% CI: 1.22 to 4.25; p=0.010) and use of nitrates (HR: 1.94; 95% CI: 1.02 to 3.67; p=0.043) as significant predictors for MACEs in patients with coronary spasm.

Conclusions: ACh-induced coronary spasm occurred at the sites of significant organic stenosis was frequently observed in patients with ST-segment elevation during angina attacks, significant organic stenosis in left anterior descending (LAD) artery and multivessel spasm, and was a significant predictor for MACEs. These results suggest the need to identify the site of coronary spasm in patients with significant organic stenosis.

BEST POSTERS IN STRESS ECHOCARDIOGRAPHY

P1341 | BEDSIDE
The declining frequency of inducible myocardial ischemia during cardiac stress testing in the last 39 years (1970-2009)
C. Carpeggiani, P. Landi, R. Sicari, E. Picano. CNR Institute of Clinical Physiology, Pisa, Italy

Objective: To assess the rate of positivity during cardiac stress testing by stress echo (SE) and exercise-electrocardiography test (EET) over time in the last 39 years.

Background: Previous studies have suggested a decline in positivity of myocardial perfusion imaging in North-America, suggesting the need for developing better strategies for test selection to achieve acceptable cost-effectiveness balance.

Methods: We assessed the rate of SE and EET positivity in 4087 patients evaluated in a tertiary care referral center from 1970 to 2009, who performed 3159 EET and 2007 SE as screening test for coronary artery disease. Acute coronary syndrome, history of myocardial infarction and/or coronary revascularization were exclusion criteria. We divided the 39-year period into four decades and compared the changes in tests results.

Results: There was a progressive decline in the rate of positivity in the last 39 years for all markers and all forms of stress testing. EET positivity (by ECG criteria) fell from 46% in the first decade (1970–1979) to 23% in the last one (2000–2009) (P<0.001). Likewise, SE positivity declined from 42% (1986–1989, 1986 was the first year of extended clinical use) to 6% (2000–2009). The proportion of angina declined during both tests (p<0.001).

Conclusion: Over the last 39 years, we observed a steady decline of positivity for all stress tests - imaging and non-imaging, exercise and pharmacological, based on highly specific signs of ischemia (such as wall motion abnormalities) and less specific signs such as ECG changes. We probably need refined criteria of referral for testing and/or better ways to titrate the negative response beyond classical physiology.
P1342 | BEDSIDE

Dobutamine stress contrast echo in diabetic patients: the prognostic impact of appropriateness criteria indication

C. Aggeli, I. Felekos, V. Panagopoulou, S. Kastellanos, P. Koudounis, A. Aggelis, K. Zisimos, D. Tousoulis. Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Purpose: The aim of the current study was to evaluate the prognostic impact of diabetes in patients with known or suspected CAD, undergoing Dobutamine stress contrast echo (DSCE), according to appropriateness indication.

Methods: We studied 2380 (58.8±9.9 years) patients who were referred for DSCE. Ischemic response was defined as wall-motion deterioration and/or perfusion abnormality in two or more consecutive myocardial segments. Patients were classified as diabetics and non-diabetics. Furthermore, they were stratified as appropriate (A), uncertain (U) and inappropriate (I). Mean follow-up lasted 57±10 months. End points included all-cause mortality, cardiac death, the need for late revascularization (<3 months) and hospitalizations.

Results: Out of 2380 patients, 45.6% were classified as appropriate, 31.7% as inappropriate and 22.7% as uncertain. Ischemic response to DSCE was elicited in 20.6% of the patients. During follow-up end-points were noted in (9.9%) patients. Moreover, appropriate and uncertain setting combined was more predictive for a positive DSCE result than the inappropriate class (χ²=9518.0, p<0.005), with the most positive response being noted in the appropriate setting (28.1%). Multivariate analysis revealed that DSCE response was the strongest predictor for adverse outcomes (OR 51.7, p<0.05). Log-Rank test revealed that diabetics had more events than non-diabetics in the Appropriate class (χ² = 8.53, p<0.05). On the contrary, there was no statistically significant difference in outcomes between the two groups in the Inappropriate setting (χ² = 3.55, p=NS).

Conclusion: Dobutamine stress contrast echo is a strong predictor of end points in patients with known or suspected CAD. Patients being classified as appropriate fare worse, especially if they are diabetics.

P1344 | BEDSIDE

Objective criteria of LAD lesion during exercise stress echocardiography: coronary flow velocity reserve during exercise

A. Zagatina, N. Zhuravskaya. Cardiocenter Medika, Saint Petersburg, Russian Federation

Stress echocardiography is always reproached with subjective interpretation. Assessment of coronary flow reserve is a method of objectivity of coronary artery lesions. This method is used during pharmacological tests, but supine bicycle tests have enabled the application of coronary flow assessment during exercise. The purpose of the study was to establish the parameters of the anterior descending artery (LAD) coronary flow, which can attribute to the significant narrowing of this artery during exercise test.

Methods: We enrolled 302 patients: 1) 232 non-selective subjects who were referred to stress echocardiography before coronary angiography; 2) 70 controls without CAD who were not significantly different from the main group according to age and gender distribution (mean age 59±8 vs. 57±10 years, 71% vs. 59% men, p=NS). All the patients performed a supine bicycle symptoms-limited echocardiography test. Coronary flow velocities were measured at the medium segment of the LAD before and at the peak of exercise. The differences between the peak and rest velocities (ΔV) and coronary flow velocity reserve (CFVR) were calculated.

Results: The patients with proximal lesions of LAD had significant differences between velocity flow data regarding the subgroup without proximal stenosis of this artery: velocity in LAD at the peak of exercise (49±29 vs. 66±22 cm/s, p=0.00003), ΔV (16±20 vs. 28±20 cm/s, p=0.00007), and CFVR (1.5±0.6 vs. 1.9±0.7, p=0.00001). The patients with the middle lesions of LAD had the significant higher velocity at rest versus group without such LAD lesions (42±23 vs. 33±15 cm/s, p=0.003). The patients with LAD lesions had a lower flow velocity at the peak of exercise (55±30 vs. 74±18 cm/s, p=0.00005), a lower ΔV (19±21 vs. 42±16 cm/s, p=0.0000001), and a lower CFVR (1.6±0.7 vs. 2.4±1.6, p=0.0000001) in comparison with the control group. The cut-off values were 55 cm/s, 28 cm/s, and 1.8 for the peak velocity, ΔV, and CFVR, respectively.

Conclusion: It could be helpful to use the coronary artery flow velocity parameters for coronary artery disease diagnosis.

BEST POSTERS IN STEM CELLS AND CELL THERAPY

P1346 | BENCH

Optical action potential recordings in healthy and diseased induced pluripotent stem cell-derived cardiomyocytes

D. Sinnecker, Z. Chen, L. Dreizhenter, T. Dorn, A. Goedel, A. Moretti, K.L. Laugwitz. Technical University of Munich, Klinikum rechts der Isar, I. Medical Department, Munich, Germany

Background: Cardiomyocytes from patient-specific induced pluripotent stem cells (iPSCs) recapitulate key features of heritable disorders. Assays for drug-induced QT prolongation are a promising application. Conventional electrophysiology is restricted by limited throughput. We aimed at establishing optical action potential (oAP) recordings as a non-invasive, scalable alternative.

Methods and results: iPSCs were generated from skin fibroblasts of controls and individuals affected by long-QT syndrome type 1 and 2 and catecholaminergic polymorphic ventricular tachycardia (CPVT1) and differentiated to cardiomyocytes. A genetically-encoded FRET-based membrane potential sensor (VSVF- CPR4) was subcloned into a lentiviral expression vector, which efficiently transduced iPSC-derived cardiomyocytes (Fig. 1A). Simultaneous donor and acceptor visualization allowed AP imaging. Ventricular and non-ventricular cardiomyocytes were identified by AP shapes (Fig. 1B). AP characteristics were consistent with values obtained using patch clamp electrophysiology (Fig. 1D). AP duration of spontaneously-beating cells was rate-dependent. In patient-specific cardiomyocytes, arrhythmias at a single-cell level were frequently observed (Fig. 1C). QT interval-prolonging drugs (e.g. Sotalol, Cisapride) prolonged APs in control iPSC-derived cardiomyocytes. An even more pronounced AP prolongation was observed in LQT1 cardiomyocytes, consistent with a reduced repolarization reserve in these cells.

Conclusion: Optical AP imaging in iPSC-derived cardiomyocytes is suitable to...
Methods: AT-MSCs from the adipose tissue of aged (12-month-old) male C57BL/6 mice were transduced with lentiviral vectors encoding TERT and MYOCD. Twelve month-old C57 mice underwent coronary artery ligation (Lig), followed by randomization into 4 groups (n=5/group): Sham operation, MI control (saline 20 μL), MI followed by intramyocardial injection with mock-transduced AT-MSCs (2.5x10^5 cells/20 μL), or aged AT-MSCs overexpressing TERT and MYOCD (2.5x10^6 cells/20 μL).

Results: AT-MSCs overexpressing TERT and/or MYOCD decreased the area of fibrosis (Figure A-D) and increased arteriogenesis (Figure A’-D’) and myocardial fractional shortening when transplanted into the infarcted hearts of C57 mice (n=5, P<0.05, by ANOVA). These effects were accompanied by increased number of Ki-67 positive cells and cardiac-resident c-kit cells (n=5, P<0.05, by ANOVA), and enhanced expression of cardiac actin, GATA4, Nkx2.5, MEF2c and myocardin A (Figure E).

Conclusions: The delivery of the TERT and MYOCD genes into AT-MSCs promotes cardiomyogenic program, vasculogenesis and stem cell survival, and may have applications in patients with MI.

P1349 | BENCH
Prolyl hydroxylase inhibition induces SDF-1 and CXCR4 expression to increase CXCR4+ cell homing and myocardial repair
S.K. Ghadge1, T.H. Pham2, M. Messner1, M. Doppelhammer2, B. Husse1, W.M. Franz3, M.M. Zaruba1,1, Innbruck Medical University, Department of Internal Medicine III, Innsbruck, Austria;2 Ludwig-Maximilians University, Medical Department I, Munich, Germany

Objective: Stabilization of the cardiac SDF-1/CXCR4 axis preserves myocardial function and attenuates ischemic cardiomyopathy. However, HIF-1α dependent SDF-1 upregulation lasts only for 48–72 hours after MI limiting the targeting of regenerative cells to ischemic myocardium. To overcome this caveat, we aimed to activate the HIF-1α target genes SDF-1 and CXCR4 by stabilization of HIF-1α through inhibition of prolyl hydroxylase with the ratio to stimulate myocardial repair.

Methods: To evaluate the effects on HIF-1α mediated SDF-1 and CXCR4 expression, genetically tagged SDF1-EGFP and CXCR4-EGFP mice were subjected to optimal doses (80mg/kg i.p.) of the prolyl hydroxylase Inhibitor dimethyloxalyl-glycine (DMOG). To examine the time frame of SDF-1 and CXCR4 expression in vitro (HEK cells) and in vivo (BM & heart), DMOG was treated at different dosing regimens (50μM to 1000μM & 80mg/kg i.p.) and time intervals (1 to 6 hrs), FACS and immunohistochemical analyses of CXCR4+ bone marrow (BM), peripheral blood, and heart cells as well as infarct size measurements were performed under normoxaemic and ischemic conditions with and without DMOG treatment.

Results: SDF1-EGFP mice treated with DMOG showed robust induction of SDF-1 in heart vessels. In vitro, SDF-1 was transiently upregulated within 60 mins to 2 hrs after DMOG treatment, followed by significant decrease after 6hrs. CXCR4 was significantly elevated at late time points (6h). In vivo, CXCR4 expression was significantly upregulated in BM (6h) after DMOG treatment. FACS analyses of transgenic CXCR4-EGFP BM and hearts revealed that CXCR4+ was frequently expressed on CD11b+ monocytes, and to a less amount on angiogenic CD31+, CD34+, c-kit+, and Flk1+ cells, as well as stem cell populations like ACC133+ and Lin-/c-kit+/Sca-1+. Treatment with DMOG revealed a robust upregulation of CXCR4+ cell populations in the ischemic heart, predominantly of angiogenic CXCR4+/CD11b+ monocytes. Further analysis of the latter showed that DMOG treatment leads to a shift of the CD206+/CD86+ ratio in favor of M2 macrophages associated CD206+ population in infarcted hearts associated by attenuated infarct remodeling.

Summary and conclusion: Our data suggest that inhibition of prolyl hydroxylase may be a promising target for HIF-1α mediated SDF-1 activation to increase CXCR4+ cell homing and myocardial repair.

P1348 | BENCH
Improved vascularization and increased expression of contractile protein mediate beneficial effects of transplantation of adipose tissue mesenchymal cells expressing telomerase and myocardin in murine R. Madonina1, L. Petrov2, M.A. Teberino1, M. Doppelhammer2, B. Husse1, W.M. Franz3, M.M. Zaruba1,1, Innbruck Medical University, Department of Internal Medicine III, Innsbruck, Austria;2 Ludwig-Maximilians University, Medical Department I, Munich, Germany

The success of stem cell therapy is hampered by poor survival of transplanted stem cells in the microenvironment of the host tissue. This may be improved by genetically reprogramming the stem cells to delay apoptosis and enhance their regenerative properties. Myocardin (MYOCD), a promyogenic transcription factor with anti-apoptotic activity, and telomerase (TERT), an anti-senescence protein, may promote survival and cardiomyogenesis of adipose tissue mesenchymal stromal cells (AT-MSCs).

Objectives: We examined the therapeutic efficacy of transplanted AT-MSCs overexpressing MYOCD and TERT in a murine model of myocardial infarction (MI), and underlying mechanisms.
Lack of progression or regression of left ventricular hypertrophy in children with sarcomeric gene disease

M. Pieroni1, P. Notarstefano1, A. Camporeale1, R. Guida1, S. Grotti1, T. Rio1, C. Nucci1, A. Fraticelli1, A. Carnevali3, L. Bolognese1, G. Frisso1, M. Ribino1, A. Bologna1, S. San Donato Hospital, Rome, Italy; 2 Catholic University of the Sacred Heart, Rome, Italy; 3 San Donato Hospital, Pathology Department, Arezzo, Italy

Background: Clinical application of endomyocardial biopsy (EMB) to the study of patients with ventricular arrhythmias (VA) is limited by low sensitivity due to sampling error. Three-dimensional electroanatomic voltage mapping (EAM) has been proposed as a tool to guide EMB, but the impact of EAM-guide on EMB diagnostic yield has never been prospectively assessed.

Methods: Fifteen patients (9 M, 47 ± 13 years) with repetitive VA originating from right ventricle, underwent EAM and EAM-guided EMB. Electroanatomic guide was obtained by live visualization of biotome in the electroanatomic map during biopsy procedure, connecting biotope to the mapping system with alligator clips pinching a screw inserted in the biotope handle. In all patients bipolar and unipolar map were reconstructed and low-voltage areas identified according to established thresholds. In each patient EMBs were drawn from the conventional septal-apical region (≥2 biopsies) and from areas with low voltages (<2 biopsies) at both bipolar and unipolar map or low voltages at unipolar map in case of normal bipolar map. Histological diagnosis was obtained analyzing all fragments retrieved in each patient. Myocarditis and arrhythmogenic right ventricular cardiomyopathy (ARVC) were diagnosed according to current historical criteria.

Results: Five patients had a non-invasive diagnosis of ARVC, 2 pts presented with VA in clinically suspected myocarditis while 8 patients had apparently idioventricular rhythms. EAM-guided EMB was performed in 7 patients because of A-V block of 4th degree. The number of samples collected from conventional site was higher compared to EAM-guided biopsy (44 vs. 38, P = 0.014), without significant difference in sample size (3.51 ± 0.34 vs 3.57 ± 0.34 mm², P = 0.75). Histological diagnosis was active myocarditis in 6 patients. ARVC in 5 patients, healed myocarditis in 3 patients, normal myocardium in 1. The number of diagnostic samples obtained from conventional site and EAM-guided site was 21/44 (49%) and 33/38 (87%) with a mean number of diagnostic samples of 1.4±1.3 vs 2.2±0.7 (P = 0.04), respectively. EAM-guided diagnostic biopsy of EMB to 87% sensitivity of the conventional approach. In particular performing EMB only in the conventional site, the histological diagnosis would have been missed in 6 (40%) patients. There were no major complications of EMB.
Results: MHO in adulthood was not less likely in those who were overweight (RR: 0.76, 95% CI: 0.59–0.99; WC RR: 0.69, 95% CI: 0.52, 0.90). Childhood overweight and obesity were not associated with a decreased risk of MHO.

Purpose: Using data from the Childhood Determinants of Adult Health study, we aimed to examine whether childhood adiposity or change in adiposity from childhood to adulthood predicted MHO 20 years later. We hypothesised that individuals would be less likely to be MHO if they were overweight or obese in childhood, or had larger increases in body mass index (BMI) or waist circumference (WC) from childhood to adulthood.

Methods: A national sample of 2,410 Australian participants had height, weight and WC measured in 1985 (aged 7–15 years) and 2004–06 (aged 26–36 years). A fasting blood sample was also taken in 2004–06. MHO was defined as BMI ≥30 kg/m², normal fasting glucose (<1.04 mmol/L, men; <1.30 mmol/L, women); blood pressure <130/85 mmHg; and no medication for these conditions. Children were classified as being healthy weight, overweight or obese using standard age- and sex-specific cut points. Relative risks (RR) for MHO by childhood overweight or obesity, or a one standard deviation (SD) increase in BMI or WC from childhood to adulthood were calculated, adjusted for sex, childhood age and, for estimates of the effects of change, for baseline BMI or WC.

Results: Of the 323 obese individuals at follow-up, 79 (24.5%) were MHO. Childhood overweight and obesity were not associated with a decreased risk of MHO (RR: 1.07, 95% CI: 0.72–1.58). A 1 SD increase in BMI or WC from childhood to adulthood was associated with a significantly decreased likelihood of MHO (BMI RR: 0.76, 95% CI: 0.59–0.99; WC RR: 0.69, 95% CI: 0.52, 0.90).

Conclusion: MHO in adulthood was not less likely in those who were overweight or obese in childhood but it was less likely in those obese adults who had greater gains in BMI or WC since childhood.

BEST POSTERS IN OBESITY

P1357 | BEDSIDE

Association of body mass index with the incidence of stroke and death in real-world atrial fibrillation patients: The Fushimi AF Registry

Y. Hamatani1, H. Ogawa, D. Takagi, Y. Yamashita, M. Easot1, Y.H. Chun2, H. Wada, K. Hasegawa, M. Abe1, M. Nakao1 on behalf of The Fushimi AF Registry investigators. 1Kyoto Medical Center, National Hospital Organization, Kyoto, Japan, 2Lijnkai Takeda General Hospital, Kyoto, Japan

Background: Atrial fibrillation (AF) increases the risk of stroke/systemic embolism (SE) and death. Regarding the impact of body mass index (BMI) on the incidence of stroke/SE and death in AF patients is limited.

Methods: The Fushimi AF Registry, a community-based prospective project, was designed to enroll all of the AF patients in Fushimi-ku, which represents a typical urban community in Japan. We started to enroll patients from March 2011. The value of BMI and follow-up data were available for 2,913 patients as of November 2014. We compared the backgrounds and outcomes during the median follow-up of 781 days between those with underweight (BMI <18.5), normal (18.5 ≤BMI ≤25), and overweight (BMI >25).

Results: The mean BMI was 23.0±4.0 kg/m². Underweight, normal, and overweight groups included 325 (11%), 1,775 (61%), and 813 (28%) patients, respectively. The prevalences of male, hypertension, diabetes mellitus, and oral anticoagulant prescription were higher in overweight, whereas those of the elderly, heart failure, and history of stroke/SE were higher in underweight. A total of 156 stroke/SE and 532 death occurred during follow-up. The Kaplan-Meier curves for the incidence of death/stroke/SE and those of stroke/SE are shown in the figure. Even after adjustment by sex, components of CHADS2 score, and oral anticoagulant prescription, overweight was associated with lower risk of death/stroke/SE as compared with normal (hazard ratio: 0.60, p<0.01), whereas underweight was associated with higher risk of death/stroke/SE (hazard ratio: 1.89, p<0.01).

Conclusion: In real-world Japanese AF patients, overweight was significantly associated with lower risk of death/stroke/SE, whereas underweight was significantly associated with higher risk of death/stroke/SE.
Further data collected in a subset of participants through periodic resurveys to estimate usual intake levels for the whole cohort. Cox regression models were used to yield adjusted hazard ratios (HRs) among 474,191 participants free of major prior diseases at baseline.

Results: At baseline, 18% reported consuming fresh fruit on a daily basis (daily consumers) and 6% never or rarely consumed (non-consumers). There was a strong inverse log-linear dose-response relationship of usual habitual fruit consumption with all-cause mortality and mortality from a range of cardiovascular and non-cardiovascular diseases. Comparing daily to non-consumers, the adjusted HRs (95% confidence interval) were 0.68 (0.67–0.70), 0.66 (0.60–0.73), 0.59 (0.54–0.74), 0.64 (0.55–0.74) respectively for all-cause, total cardiovascular, ischemic heart disease, and stroke mortality, and 0.45 (0.35–0.57) for mortality from chronic obstructive pulmonary disease (COPD) (Figure). For cancer, the overall risk reduction by daily fruit consumption was 19% (HR 0.81, 0.75–0.87), with particularly large reductions for esophagus, stomach and colorectal cancer. These risk reductions appeared to be similar in both genders and across different age groups.

Conclusions: In Chinese adults, daily consumption of fresh fruit was associated with about 30% reduced risk of overall mortality and nearly 40% reduction of CVD mortality. There will be substantial health gain in China from increased consumption of fresh fruit, even though daily consumption of fresh vegetables is almost universal.

P1363 | BEDSIDE
Comparison of physiological coronary artery stenosis severity assessed by fractional flow reserve and optical coherence tomography findings in stable angina pectoris
Tsukuba Kyodo Hospital, Tsukuba, Japan.

Background and aim: Acute coronary syndromes were widely believed to result from rupture of thin-capped fibroatheroma (TCFA) and thrombosis at the site of plaque rupture of TCFA evenly results in coronary artery occlusion. However, lesions responsible for acute coronary syndromes are mild in the concept that lesions are associated with non-ST-segment elevation acute myocardial infarction patients, the relationship between target lesion characteristics and microvascular function remains elusive.

Purpose: We evaluated the optical coherence tomography (OCT) findings of the culprit lesions and their relationship with microvascular function after PCI in patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS).

Methods and results: Forty-five hemodynamically stable NSTE-ACS patients (male: N=36, age: 64.0±10.4 years, unstable angina: N=19, NSTEMI: N=26) with single de novo culprit lesion were enrolled in this study. OCT examination after PCI was performed immediately after PCI with the use of a pressure-temperature sensor wire. The median IMR value was 24.0 (interquartile range [IQR]: 11.2–35.6). IMR value after PCI was significantly associated with age (P<0.03). There was no significant relationship between post-PCI IMR values and cardiac troponin I (cTnl) levels at all measurements (on admission, before PCI and after PCI). There was a significant relationship between high post-PCI IMR values and the presence of plaque rupture (P=0.00), whereas the presence of OCT-derived thin-cap fibroatheroma, and red thrombus showed weak correlation with high IMR values (P>0.07, respectively).

Conclusion: High IMR values after PCI in the target vessel were significantly associated with OCT-derived high-risk lesion characteristics, although there was no significant correlation between post-PCI OCT and microvascular function.

P1364 | BEDSIDE
FFR gray zone and clinical outcome

Background: Fractional flow reserve (FFR) inversely assesses the ischemic potential of coronary stenosis and predicts the expected improvement by revascularisation. An FFR value of 0.75 has been validated against ischemic testing, while an FFR value of 0.80 has been widely accepted to guide clinical decision making. Whether, and in which patients (pts) revascularization should be proposed when FFR is between 0.75–0.80 “gray zone” is still debatable. We studied the clinical outcome of pts with an isolated stenosis and an FFR value in the gray zone.

Conclusions: Drug-eluting stents exhibited greater trends for atherosclerotic changes occurring in earlier time point than BMS. High LDL-cholesterol and CRP levels may be risk factors for NA development in patients treated with coronary stents. Moreover, the presence of NA was independently associated with MACE.
P1367 | BEDSIDE
Central apneas and chemoreflex activation influence on pulmonary hypertension in heart failure: role of adrenergic activation
V. Raglanti, A. Del Franco, G. Mirizzi, A. Aimo, C. Taddei, F. Bramanti, G. Iudice, C. Passino, M. Emini, A. Giannoni, Gabriele Monterasio Foundation, Cardiology and Cardiovascular Medicine, Pisa, Italy

Background: Pulmonary arterial hypertension (PAH) is an established prognostic factor in patients with heart failure (HF). Beyond a “passive” component due to the increased left ventricular pressure, an “active” component due to pulmonary vascular reactivity may be present. The mechanism behind pulmonary vasoconstriction being not fully understood, we hypothesized that central apneas (Cheyne-Stokes respiration – CSR) through chemoreflex stimulation may contribute to PAH in HF.

Methods: We studied 54 systolic HF patients (left ventricular ejection fraction <50%), on stable guideline recommended pharmacological treatment, without increased left ventricular pressure (excluding patients with mitral prostheses, and those with grade III either mitral insufficiency or diastolic dysfunction). All patients underwent echocardiographic and neurohormonal assessment, 24-hour cardiorespiratory screening for CSR (patients with obstructive events were excluded) and chemoreflex test for hypoxic (HVR) and hypercapnic (HCVR) ventilatory responses (by rebreathing technique).

Results: Eleven patients (20%) showed significant CSR, as defined by a 24-hour apnea/hypopnea index >AHI > 15. HF patients with CSR, compared with patients with normal breathing, presented with higher systolic arterial pulmonary pres- sure (54.5 ± 11.6 vs. 51.9 ± 11.9 mmHg, p < 0.01), with no difference in systolic and diastolic function. Furthermore, patients with central apneas also presented with enhanced HVR (median 0.79, interquartile range -0.62 to 1.27 vs. 0.43, IR 0.19–0.69 L/min/mmHg, p < 0.05) and HCVR (1.16, IR 1.10–1.31 vs. 0.73, IR 0.51–0.95 L/min/mmHg, p < 0.01) as well as increased plasma norepinephrine level (559, IR 446–770 vs. 367, IR 229–508.5 Î¼g/L, p < 0.05). sPAP was indeed correlated with AHI (Spearman’s rho, R=0.6, p < 0.001), HCVR (R=0.48, p < 0.001), HVR (R=0.35, p < 0.001) and noradrenaline (R=0.25, p < 0.05). At univariate regression analysis sPAP was associated with AHI, HVR, HCVR, norepinephrine, NT-proBNP. At multivariates analysis only AHI maintained its predictive value (p < 0.014).

Conclusions: The severity of CSR occurring either at night- or daytime, likely via recurrent hypoxia and hypercapnia cycles, may determine a chemoreflex-activated adrenergic activation in patients with systolic HF, and as a consequent pulmonary vasoconstriction, responsible of the undesirable increase in pulmonary arterial pressure.

P1368 | BENCH
Impaired immune phenotype of circulating endothelial-derived microparticles in non-diabetic patients with chronic heart failure
A. Berezin, A. Krenzer. State Medical University, Zaporozhye, Ukraine

Background: Increasing attention has been paid to insulin resistance (IR) as a distinct cause of cardiac dysfunction and CHF in diabetic and non-diabetic patients. The causality role of different immune phenotype in IR developing among chronic heart failure (CHF) subjects has not determined obviously. The aim of the study was to assess relationship between IR and immune phenotype of circulating endothelial-derived microparticles (EMP) in patients with CHF.

Methods: The study retrospectively involved 300 CHF patients aged 46 to 62 years who were undergone multiphasic computed tomography angiography or coronary angiography. All the patients have given written informed consent for participation in the study. Biomarkers were measured at baseline of the study. End points were defined as activated and activated microparticles were phosphorylated by flow cytometry.

Results: These were not significant differences between both cohorts patients in EMPs labeled as CD144+CD31+, CD144+/annexin V+, and CD62E+ microparticles between 2 groups (p=0.80). Higher concentrations of CD144+CD31+/annexin V+ EMPs and CD144+CD31+/annexin V+ EMPs were found in IR subjects when compared with non IR patients. Using multivariate logistic regression analyses, we found that HOMA-IR (OR=1.1, 95% CI: 1.08–1.21, P=0.001), NT-proBNP (OR=1.07, 95% CI: 1.04–1.10, P=0.001, hs-CRP (OR=1.04, 95% CI: 1.02–1.07, P=0.001), and NYHA class (OR=1.05, 95% CI: 1.02–1.09, P=0.001) significantly predicted elevation of MACE’s. Among patients with an FFR between 0.81 and 0.85, MACE’s were more frequent after MT than after revasc (11 [21%] vs. 53 [12%], respectively, p=0.026). Among patients with an FFR between 0.70 and 0.75, MACE’s were more frequent after MT than after revasc (11 [21%] vs. 53 [12%], respectively, p=0.057). Among patients with an FFR between 0.65 and 0.70, MACE’s were more frequent after MT than after revasc (11 [21%] vs. 53 [12%], respectively, p=0.01). The presence of grade II or III mitral insufficiency or diastolic dysfunction, or any revascularization up to 5 years. Data were also analyzed according to their lesion location (proximal versus distal).

Conclusions: The study reveals that an FFR <0.70 is valid to guide clinical decision making with lesion located in proximal coronary segments, while distal coronary stenosis with FFR in the gray zone might be safely deferred to MT.

BEST POSTERS IN BIOMARKERS

P1369 | BENCH
Lysyl oxidase overexpression impacts cardiovascular remodeling
M. Galan1, S. Varona1, M. Orriols1, S. Aguilo1, A. De Diego2, J. Osada3, J. Martinez-Gonzalez2, C. Rodriguez1. Catalan Institute for Cardiovascular Science, Barcelona, Spain;2 Aragones Institute of Health Sciences, Zaragoza, Spain;3 University of Zaragoza, Zaragoza, Spain

Introduction: The disturbance of extracellular matrix (ECM) composition and structure plays an important role in cardiovascular remodelling and in the progression of heart failure. Lysyl oxidase (LOX) is a key enzyme in ECM remodelling.

Methods: From Feb 1997 to Jun 2013, all pts presenting with single segment disease at coronary angiography and FFR between 0.70–0.85 were included. Pts with previous bypass surgery, in-stent restenosis, myocardial bridge, or heart transplantation were excluded. According to FFR values, pts were divided into the following strata: a) 0.70–0.75, b) 0.76–0.80, c) 0.81–0.85. Study endpoints consisted of major adverse cardiovascular events (MACE: death, myocardial infarction or any revascularization) up to 5 years. Data were also analyzed according to their lesion location (proximal versus distal).

Results: Of total 17380 pts undergoing FFR measurement: a) 2781 (16%) pts presented lesions with FFR in the gray zone; b) 1459 fulfilled the inclusion/exclusion criteria and were included in the present analysis: 449 treated with revascularization (revasc) and 1010 with medical therapy (MT). Clinical characteristics were similar among pts treated with revascularization or MT, except for male gender. Di-aminopimelic acid urinary values were higher in the revasc group (p < 0.0001). In pts with an FFR between 0.70 and 0.75, MACE’s were more frequent after MT than after revasc (11 [21%] vs. 53 [12%], respectively, p=0.026). In pts with an FFR between 0.81 and 0.85, MACE’s tended to be less frequent after MT than after revasc (11 [21%] vs. 53 [12%], respectively, p=0.057). Among pts treated with MT alone, a progressive increase in MACE was observed in the 3 FFR strata (FRF, 0.70–0.75: n=11 [21%] vs. FFR, 0.76–0.80: 35 [13%] vs. FFR, 0.81–0.85: 58 [8%], p < 0.0001). For stenoses located in proximal or mid segments, decreasing FFR values were paralleled by an increase in overall mortality (p < 0.0001).

Conclusions: These data suggest that an FFR <0.80 is valid to guide clinical decision making with lesion located in proximal coronary segments, while distal coronary stenosis with FFR in the gray zone might be safely deferred to MT.
Purpose: Because LOX deficiency is lethal, we have developed a transgenic mouse model to study the impact of LOX overexpression on cardiovascular remodeling.

Methods and results: A new mouse model that over-expresses human LOX was generated by conventional methods. Transgene expression was determined by real time PCR in 8 different tissues including aorta, heart, kidney, white adipose tissue (WAT), brown adipose tissue, lung, liver and skeletal muscle. The maximum expression of human LOX was found in aorta followed by heart and WAT. Neither the expression of endogenous LOX nor that of other LOX-like (LOXL) isoenzymes was modified by transgene expression in aorta, heart, kidney or WAT. We tested the impact of LOX over-expression on cardiovascular remodeling in TgLOX mice and their wild-type (WT) littermates after chronic infusion with Ang II (1.4 μg/kg/min) or saline by using osmotic minipumps (n=10 per group). Ang II-induced aortic diameter dilation studied by echography was similar in TgLOX and WT mice after Ang II infusion. However, the mortality rate due to aortic rupture was higher in WT mice (20%) compared to TgLOX mice (0%). Cardiac function was evaluated by echocardiography. We observed that Ang II infusion decreased ejection fraction (EF) and fractional shortening (FS) in TgLOX mice, while they were augmented in WT mice. A stronger hypertrophic response induced by Ang II was observed in TgLOX mice as evidenced the increased LV mass and left ventricle posterior wall thickness in diastole and systole and the higher HW/SW ratio compared with WT mice. Accordingly, the left ventricular inner diameter (LVID) in systole and diastole was significantly lowered in both groups. Finally, LOX overexpression impaired cardiac function under hypertensive conditions.

Conclusion: This study demonstrated that LOX overexpression has a pro-atherogenic effect in WT mice, but is not deleterious in Ang II-induced hypertension, consistent with a possible protective role of LOX in the heart under stressed conditions. This work was supported by a grant from the Japanese Society for the Promotion of Science (2015-2018).
P1374 | BEDSIDE
Blood Pressure control, pressure of depressive symptoms and clinical outcomes at 4 years in patients with cardiometabolic disease
B. Jan1, S. Barry1, J. Cavanagh1, G. Der1, N. Sattar2, F. Mair1, 1University of Glasgow, Institute of Health and Wellbeing, Glasgow, United Kingdom; 2University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom

Background: The health hazards of uncontrolled Blood Pressure (BP) as well as the potential beneficial effect of tight BP control have been extensively studied for high cardiovascular risk patients (Coronary Heart Disease (CHD), Diabetes, previous stroke) -“J-shaped curve”. The relationship between BP control and depression remains unknown. Depressed patients (Coronary Heart Disease (CHD), Diabetes, previous stroke)-“J-shaped curve.”

Purpose and methods: The aim of this project is to study interaction between depression and BP control in predicting adverse outcomes in 4 years in a primary care cohort (N=35537) of cardiometabolic disease patients (CHD/Diabetes/Stroke). Patients underwent depression screening using the hospital anxiety and depression score (HADS-D) in 2008–09. Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) were recorded concurrently and classified into uncontrolled (SBP >140, DBP >90), normal control (SBP 130–139, DBP 80–89), and tightly controlled (SBP <130, DBP <80). We recorded subsequent vascular events (myocardial infarction/stroke) and used Cox’s proportional hazards survival analysis.

Results: Out of 35537 patients, 2068 (5.8%) had at least one vascular event during the 4-year follow-up. Depression (defined as HADS-D>7) had a significant interaction with SBP (p=0.04) and DBP (p=0.01) in predicting a new vascular event. In the sub-group analysis based on SBP control categories, patients with uncontrolled SBP and depression had a higher risk of a new vascular event (Hazard Ratio HR 1.38, 95% Confidence Interval (CI) 1.14–1.67, p<0.001) compared to those with uncontrolled SBP but without depression. Similarly, patients with tightly controlled SBP and depression had a higher risk of a subsequent vascular event (HR 1.42, 95% CI 1.17–1.71) compared to those with tightly controlled SBP and without depression. Depression without SBP control had a higher risk of a new vascular event (HR 2.14; 95% CI 1.41–3.25), as compared to those with uncontrolled DBP without depression. All results were adjusted for age, gender, socioeconomic status, number of comorbid conditions, total cholesterol values, body mass index and antidepresant initiation.

Conclusion: There may be potential benefits from closer monitoring of BP in those with cardiometabolic disease and comorbid depression. Further research is needed to understand the relationship between BP control and depressive symptoms in patients with existing cardiometabolic disease.

POSTER SESSION 2
MECHANISMS AND PREDICTORS OF SUDDEN CARDIAC DEATH
P1375 | BEDSIDE
Novel Right-sided vectorcardiographic methods detect electrocardiographic defects in patients with arrhythmogenic right ventricular cardiomyopathy in the absence of conventional depolarization or repolarization criteria
D. Cortez1, J. Carlson2, S. Gawr3, F. Brun4, A. Spezzacatene4, L. Mestroni3, F. Del Carpio, S.M. Gharacholou, G.S. Scott, V.T. Nkomo, F. Lopez-Jimenez, P1375 | BEDSIDE

1 University of Colorado, Pediatric Cardiology, Aurora, United States of America; 2University of Colorado, Pediatric Cardiology, Aurora, United States of America; 3University of Colorado, Aurora, United States of America; 4University of Trieste, Trieste, Italy

Introduction: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is associated with sudden death risk, however its diagnosis remains challenging. We aimed to establish whether vectorcardiographic (VCG) parameters specific to the right heart would help to differentiate ARVC with otherwise normal ECG’s from control subjects.

Methods: 12-lead resting ECGs from 115 patients meeting Task Force 2010 diagnostic criteria were assessed. 52 (age 41.3±13.9 years, 64% males) did not fulfill depolarization or repolarization criteria and were compared with age- and gender-matched control subjects (n=52, age 42±16 years, 63% males). A 3-dimensional spatial QRS-T (SQRS-T) angle, a right-sided adjacent spatial QRS-T (RT SQRS-T) angle and a root mean square of both left and right sided depolarizing features, were calculated. 56.1±12.6 vs. 86.5±33.9 degrees ms, p<0.01). Nine parameters were selected from the pseudo orthogonal lead system based on the leads V1, V5 and II and which utilized specific maximum QRS voltages into their calculations (ie. Twave of V1, 5-wave of V5).

Conclusions: Measurement of TW-AD in left precordial leads is able to stratify SCID risk in general population.

Acknowledgement/Funding: This study was funded in part by the Finnish Foundation for Cardiovascular Research.

P1376 | BEDSIDE
QRS fragmentation induced by ventricular pacing predicts appropriate defibrillator therapies and total Mortality in subjects with cardiomyopathy
F. Del Carpio, S.M. Gharacholou, G.S. Scott, V.T. Nkomo, F. Lopez-Jimenez, S.J. Asirvatham, Mayo Clinic, Cardiovascular Diseases, Rochester, United States of America

We examined total mortality and appropriate ICD therapy predictive value of QRS fragmentation (QRSf) induced by right ventricular (RV) pacing in subjects with left ventricular (LV) dysfunction undergoing electrophysiology studies (EPS).

Methods: Subjects with LV dysfunction (EF ≤50%) undergoing EPS since 2002 until 2011 were included. QRSf during RV pacing was defined as the presence of >2 notches on the RV waves identified in ≥2 contiguous standard ECG leads representing anterior (V1–V5), inferior (II, III, aVF), and lateral (I, aVL, V6) myocardial segments. Patients were followed for appropriate ICD therapies and total mortality until December 2014.

Results: All were included in the analysis, mean age 65 years, 80% men, 61% with ischemic cardiomyopathy, mean EF 33.7% (±9.4), 244 subjects have an implanted defibrillator, followed for a mean of 4 years (±3.3). RV pacing induced QRSf was observed in 159 subjects in any myocardial segment. On multivariate analysis RV pacing induced QRSf was associated with higher mortality and appropriate ICD therapies. On multivariate analysis RV pacing induced QRSf was associated with a higher total mortality (p<0.01, HR
Methods and results: In 35 rabbit hearts, risperidone (5 and 10 μM, n=12), quetiapine (5 and 10 μM, n=12) or cilazapril (2 μM and 4 μM, n=11) were infused after obtaining baseline data. Eight endo- and epicardial monophasic action potentials and a simultaneously recorded 12-lead ECG showed a significant prolongation of the QT-interval after application of risperidone as compared with baseline (2 μM: +29ms, 4 μM: +35ms, p < 0.05) accompanied by an increase of action potential duration (APD90, +25 ± 5 ms with 5 μM risperidone, +30 ± 10 ms with 10 μM risperidone, p < 0.05). Administration of risperidone also significantly increased spatial dispersion of repolarization (2 μM: +16ms, 4 μM: +19ms; p < 0.05). Lowering of potassium concentration in bystander AV-blocked hearts provoked early afterdepolarizations (EAD) in 8 of 12 hearts and polymorphic ventricular tachycardia resembling torsade de pointes in 6 of 12 hearts (49 episodes). The results were compared to rabbits treated with either quetiapine or citalopram. Cilazapril led to an increase in QT-interval (5 μM: +10ms, 10 μM: +29ms; p < 0.05) and APD90 (2 μM: +13ms, 4 μM: +29ms; p < 0.05) without significant effects on dispersion of repolarization (2 μM: +5ms, 4 μM: +6ms, p<ns). Again, no proarrhythmia was observed in this group.

Conclusion: In the present study, risperidone demonstrated a severe proarrhythmic potential. The occurrence of torsade de pointes was enhanced by an increase of spatial dispersion of repolarization and an increased occurrence of EAD. In contrast, quetiapine and cilazapram showed a safe electrophysiologic profile. In these groups, dispersion of repolarization remained stable although myocardial repolarization was significantly prolonged.

P1379 | BEDSIDE

Sudden death with structural normal heart: results from the West of Scotland Familial Arrhythmia Network (FANS) and Inherited Cardiac Conditions Clinic

R. McIntyre1, C. Brown2, D. Connelly3, A. Rankin2, A. Rhee2, D. Oxnard2, J. Anusis2, V. Murlad2, I. Findlay2. 1University of Dundee, Dundee, United Kingdom; 2NHS Greater Glasgow and Clyde, Glasgow, United Kingdom

Background: Our Inherited Cardiac Conditions Clinic (ICC) was established in 2007 to meet best practice guidelines for families with arrhythmias and sudden cardiac death, as outlined in the 2005 National Framework for CHD. The Familial Arrhythmia Network of Scotland (FANS) was launched in 2010 to provide familial arrhythmia patients and their families with expertise and knowledge from the relevant health professionals, and further assist with their care. Aims: We aimed to assess the efficiency of ICC/FANS in following up and screening of first degree relatives after a case of sudden death in the family. We also aimed to investigate: 1) the role of genetic testing in identifying the cause of death in cases with a structurally normal heart and 2) the prevalence of non-toxic alcohol intake in cases of sudden death.

Methods: We performed an audit of sudden death referrals to the ICC clinic following the establishment of the FANS network from 1st January 2011 to 31st January 2015. We focussed on cases of sudden death with structurally normal heart, classified as "SADS" or "unexplained" at post-mortem. We excluded cases of SIDS for the purposes of this study.

Results: Of the 27 cases of sudden death which fitted the above criteria, there were 125 first degree relatives. Of these 73 (58%) had an ECG and 53 (42%) alcohol intake at time of death, or non-toxic levels of alcohol found at post-mortem, in 15/27 (56%) cases. Mean age at death in those with a history of recent alcohol use was 30±10.2 years and 9/15 (60%) male.

We combined these findings with those obtained from the inception of the ICCC in 2007 and to date there have been a total of 56 cases of sudden death with structurally normal heart. Genetic testing was possible in 42/56 cases (75%) cases and pathogenic mutations were identified in a total of only 3/42 (7%) cases (2 SCNSA and 1 RYR2). History of alcohol intake/non-toxic levels of alcohol were present on post-mortem in 22/56 cases (39%), mean age 33±9.6 years and 15/22 (68%) male.

Conclusions: Family follow-up was less than ideal despite a formal mechanism to establish this. Yield of pathogenic mutations on genetic testing in this group of patients (7–10%) is lower than the literature reports (15–33%). This audit also highlights the high prevalence of recent exposure to alcohol/non-toxic levels of alcohol at time of death.

P1381 | BEDSIDE

Sudden cardiac death and mitral valve prolapse: a single center experience

A. Rafael1, P. Bartko2, R.A. Levine2, E.J. Starobinska3, S.A. Lubitz1, D.J. Milan1. 1Massachusetts General Hospital, Arrhythmia Service, Boston, United States of America; 2Massachusetts General Hospital, Cardiology Department, Boston, United States of America; 3University of Arizona, School of Medicine, Phoenix, United States of America

Introduction: Mitral valve prolapse (MVP) has been variably associated with a higher risk of mortality and appropriate ICD therapies in subjects with left ventricular dysfunction undergoing an electrophysiology study. Further studies are needed to confirm our results.

Background: To evaluate the risk of sudden death (SCD) in patients with left ventricular dysfunction undergoing an electrophysiology study. Further studies are needed to confirm our results.

Methods: We studied 131 consecutive outpatients with LVEF ≥ 40% who underwent a comprehensive clinical evaluation and a standard 12-lead ECG. Patients with structural heart disease, recent myocardial infarction, or a history of heart failure were excluded. We identified 12 cases of sudden death, with a mean age of 57±15 years, gender 75% male. The mean left ventricular ejection fraction (LVEF) was 34±17%.

Conclusions: The SCD rate in our population with LV dysfunction undergoing an electrophysiology study was 0.8%/year. Further studies are needed to confirm our results.
tricular arrhythmias and sudden cardiac death. A recent report identified a malignant form characterized by the triad of bileaflet MVP, multifocal PVCs and inferolateral T wave abnormalities. We sought to characterize patients seen at the MGH with MVP and sudden cardiac death.

**Methods:** Patients with MVP were identified from a search of the ECHO lab database. This dataset was crossed with an electronic medical record search for Sudden Cardiac Death in problem lists and billing codes from years 2000–2014. Patient histories were reviewed to verify the diagnoses. Patients with primary causes for ventricular arrhythmias were excluded.

**Results:** Our search yielded 32 subjects with MVP and cardiac arrest. 17 patients were excluded due to confounding etiologies including CAD, systolic dysfunction, or ruptured subvalvular apparatus. Mean age was 64±1.3 (53% male). MVP affected both leaflets in 11 patients (73%) and 7 (46%) underwent mitral valve repair or replacement (MVR). Mitral regurgitation was severe in 5 subjects (33%), moderate in 8 (53%) and mild in 2 (13%). The first documented cardiac arrest rhythm was ventricular fibrillation (VF) in 85.7%. All patients were treated with implantable cardiac defibrillators (ICDs) and 10 patients (67%) received appropriate ICD therapies in follow-up. Four of 7 patients treated with surgical valve repair (57.1%) received appropriate ICD therapy even after surgical repair. Three of the patients had prolonged QTc intervals. Frequent PVCs were noted in 9 of 14 subjects (64%) for whom data were available (multifocal in at least one case). Inferolateral T wave abnormalities were present in 26.7%. Only one patient had magnetic resonance imaging which showed no evidence of cardiac fibrosis by late gadolinium enhancement.

**Conclusion:** The majority of MVP and SCD subjects in this cohort had bileaflet MVP and frequent VPBs, consistent with findings of previously reported cohorts; however, gender was evenly distributed and a minority manifested T wave inversions. Ventricular arrhythmia persisted despite surgical correction of the valve in a majority of subjects.

### P1382 | BEDSIDE
**Initial prognosis and management of out-of-hospital cardiac arrest in women: the SDEC Paris study**

N. Karam, E. Marijon, F. Beganton, L. Lamhaut, F. Dumas, A. Cariou, C. Spaulding, X. Jouven. Inserm U970 - Paris Cardiovascular Research Center (PHRC), Cardiovascular Epidemiology-Sudden Death, Paris, France

**Background:** According to current guidelines on myocardial revascularization, immediate coronary angiography should be disregarded irrespective of ECG pattern in all survivors of out-of-hospital cardiac arrest (OHCA). However, little is known about the application of these guidelines in the real world, particularly in women.

**Purpose:** To assess the initial management and prognosis of OHCA among women

**Methods:** Data was gathered between May 2011 and 2014 in our Sudden Cardiac Death Expertise Center (SDEC) prospective registry that includes all patients who present OHCA in the Greater Paris Area.

**Results:** Among the 11420 OHCA, 4333 (38%) were women. Compared to men, their survival rate till hospital admission was lower (18% vs. 26%) and they had a lower rate of angiography procedures by OHCA (2% vs. 6%) and by survivor till hospital discharge rates and neurological outcomes with biphasic waveform defibrillation in patients who experienced out-of-hospital cardiac arrest (OHCA). Therefore, there is no clinical evidence for the superiority of biphasic waveform defibrillation over monophasic waveform defibrillation in OHCA patients.

**Conclusion:** The single-shock protocols using biphasic AEDs of the 2010 guidelines were superior to the others in patients with shockable, in terms of neurological benefits.

### P1384 | BEDSIDE
**Comparison of biphasic and monophasic waveform defibrillations in out-of-hospital cardiac arrest: an observational cohort study**

Y. Goto, T. Maeda, A. Funada, Y. Nakatsu-Goto. 1 Kanazawa University Hospital, Section of Emergency Medicine, Kanazawa, Japan; 2 Yamawata Medical Center, Department of Cardiology, Komatsu, Japan

**Background:** The 2010 cardiopulmonary resuscitation guidelines suggest that biphasic waveform defibrillation is associated with improved neurological outcomes in OHCA patients with an initial shockable rhythm compared to the outcomes with monophasic waveform defibrillation. Several randomised controlled trials and human studies failed to demonstrate better hospital discharge rates and neurological outcomes with biphasic waveform defibrillation in patients who experienced out-of-hospital cardiac arrest (OHCA). The primary endpoint was 1-month favourable neurological outcome after cardiac arrest. Study patients were divided into a monophasic (n=943) or biphasic (n=6,866) waveform defibrillator cohort. The secondary endpoint was 1-month survival after cardiac arrest.

**Methods:** We analysed the records of 7,809 patients (age, ≥ 18 years) with witnessed OHCA from presumed cardiac causes, having an initial shockable rhythm treated by emergency medical services personnel. Data were obtained from a prospectively recorded nationwide Utstein-style database from 2008 to 2010. Patients were divided into a monophasic (n=943) or biphasic (n=6,866) waveform defibrillator cohort. The primary endpoint was 1-month favourable neurological outcomes (cerebral performance category scale, category 1 or 2; CPC 1–2) and the secondary endpoint was 1-month survival after cardiac arrest.

**Results:** The rates of 1-month survival and 1-month CPC 1–2 were significantly higher in the biphasic waveform defibrillator cohort than in the monophasic waveform defibrillator cohort (29.9% vs. 24.9% and 20.2% vs. 15.7%, all P < 0.01, respectively). Multivariate logistic regression analysis using 10 prehospital confounding variables showed that biphasic waveform defibrillation was significantly associated with improved 1-month survival (adjusted odds ratio [aOR] 1.36; 95% confidence interval [CI] 1.15–1.61) and 1-month CPC 1–2 (aOR 1.43; 95% CI 1.09–1.81). In the multivariable logistic regression model for subgroup analyses, significant benefits of biphasic waveform defibrillator use for 1-month survival and 1-month CPC 1–2 were found with collapse-to-first-shock delivery time < 10 minutes (aOR 1.34; 95% CI 1.12–1.60, aOR 1.48; 95% CI 1.20–1.84, respectively).
Conclusions: In witnessed OHCA patients with an initial shockable rhythm, biphasic waveform defibrillation was significantly associated with improved 1-month survival and 1-month neurological outcomes compared to the outcomes with monophasic waveform defibrillation.

P1385 | BEDSIDE
ADRB2 Gln27Glu polymorphism impacts the timing of ventricular fibrillation during the acute phase of myocardial infarction
B. Ankou1, S. Chauveau1, E. Morei2, G. Morgan3, B. London2, P. Chevalier1.
1 Hospital Louis Pradel of Bron, Rhythmology Department, Lyon, France; 2 University of Iowa, Division of Cardiovascular Medicine, Iowa City, United States of America

Introduction: The genetic variant rs1042714 (Gln27Glu) in ADRB2 gene coding for the β2 adrenergic receptor is associated with sudden cardiac death (SCD) in heart failure.

Purpose: We investigated whether the same polymorphism is associated with ventricular fibrillation (VF) in ST elevation myocardial infarction (STEMI).

Methods: We recruited 349 patients between 2008 and 2013 during the prospective MAP-IDM study. 213 patients who experienced primary VF (cases) were compared to 181 patients with STEMI but without VF (controls). None of the patients had other cardiac history. Patients were genotyped for the ADRB2 Gln27Glu polymorphism by RT PCR.

Results: Cases and controls did not differ significantly in age, sex and smoker ratios and in troponin peak value. VF patients had a lower body mass index (BMI) and a lower left ventricular ejection fraction (LVEF) (25.6 vs. 26.7 kg/m² and 45.8% vs. 51.95%, respectively; both p < 0.05). The Gln27Glu polymorphism was in Hardy Weinberg Equilibrium (157Gln/Gln, 181 Gln/Glu, 56 Glu/Glu). The ADRB2 genotype repartition between cases and controls was similar. Genotypes were not associated with BMI, troponin, LVEF or smoking status in univariate analyses. The time to VF onset in Gln/Glu cases was twice faster than in the Gln/Gln and Gln/Glu cases (73±106 vs 162±256 and 163±315 min; both p < 0.05, figure.). There was a season-dependent time to VF onset only in the Gln/Gln cases (autumn/winter: 219±318 vs spring/summer: 87±110 min; p < 0.05).

Conclusion: The Gln27Glu variant is not associated with primary VF. However, the Gln27Glu polymorphism predisposes patients to a fast VF onset during acute ischemia. This might expose the Gln27Glu carrier to an increased risk of SCD by minimizing their chance of resuscitation.

P1386 | BEDSIDE
AKAP9 mutations identified in young patients with idiopathic ventricular fibrillation or polymorphic ventricular tachycardia
K. Sonoda1, S. Ohno2, M. Ichikawa2, Y. Fuji2, Q. Wang3, K. Kato3, M. Fukuyama2, H. Ito2, H. Hayashi2, M. Horie2,1 Niigata University Graduate School of Medical and Dental Sciences, Department of Cardiovascular Biology and Medicine, Niigata, Japan; 2 Shiga University of Medical Science, Department of Cardiovascular and Respiratory Medicine, Shiga, Japan

Background: A-kinase anchoring protein 9 (AKAP9) is a member of the large AKAP family, which recruits signaling molecules and presents them to downstream targets to achieve efficient spatial and temporal control of their phosphorylation state. In heart, AKAP9 is known to recruit protein kinases and protein phosphatase 1 in regulating IKs. AKAP9 mutations are causative for long QT syndrome. AKAP9 is also known as CG-NAP which was reported to interact with calmodulin. Recently, there is increasing evidence that calmodulin mutations are associated with various ventricular arrhythmias.

Purpose: To examine AKAP9 variants in patients with fatal arrhythmia.

Methods: The study included 41 (male = 29) Japanese patients who suffered idiopathic ventricular fibrillation (VF; n=34) or polymorphic ventricular tachycardia (PVT; n=7). Their mean age was 35±19 years. We performed DNA sequencing analysis of AKAP9.

Results: We identified 5 heterozygous AKAP9 variants in 5 patients. Three mutations were novel and others were reported as rare SNP with MAF <0.0015 in 1000 Genomes Project data. The first mutation (c.929T>C, M310T) was identified in a 19-year-old woman who suffered VF when she rushed into a train. Her father had a history of syncope. Second (c.3932T>A, p.I2287V) and third (c.6859A>C, M310T) was identified in a 19-year-old boy who suffered VF after running and was successfully resuscitated by AED. He had a syncopal episode at the age of 12 years. On 12-lead ECGs of the 5 patients with AKAP9 mutations, PR, QT and QTc intervals and QRS durations were within normal range. Among the VF and PVT patients, AKAP9 mutation carriers were significantly younger than non-carriers (mean age, 17±6 years vs. 38±19 years; P < 0.001).

Conclusion: We identified 5 AKAP9 mutations which might be associated with idiopathic VF and PVT, especially in the young, suggesting new insights on the mechanisms underlying juvenile fatal arrhythmia.

SUDEN CARDIAC DEATH AND CHANNELOPATHIES AND CARDIOMYOPATHIES

P1387 | BEDSIDE
Incidence and electrogram characteristic of non-sustained ventricular fibrillation in patients with primary electrical disorders

Background: Implantable cardioverter defibrillator (ICD) is frequently indicated in high risk patients with primary electrical disorders (Brugada syndrome [BrS], early repolarization syndrome [ERS], and idiopathic ventricular fibrillation [IVF]). Some patients present with ventricular fibrillation (VF) that terminates spontaneously. But limited information is available on non-sustained VF.

Objectives: The aim of the present study was to compare non-sustained VF and VF terminated by electrical shock and to investigate the difference in fluctuation in ventricular cycle length (CL) that could predict the self-termination of arrhythmia before electrical shock delivery.

Methods: We enrolled consecutive 27 patients (41.5±13.2 years; 22 males) with primary electrical disorders (BrS 16, ERS 7, IVF 4 patients) who experienced VF on ICD interrogation between April, 1996 and April, 2014. A total of 228 episodes were reviewed by two independent cardiac electrophysiologists.

Results: 1) Of 228 episodes, 193 (84.6%), 35 (15.4%) episodes were VF terminated by electrical shock and non-sustained VF, respectively. 2) Mean VFCL in non-sustained VF was longer than in VF terminated by electrical shock (193±35 vs. 179±28 ms) (P=0.036). 3) In each episode, VFCL became longer or did not change in non-sustained VF (187±31 vs. 196±38 ms) (first vs. last CL) (P=0.276) in contrast with progressively shorter VFCL in VF terminated by electrical shock (180±25 vs. 160±29) (first vs. last VFCL before electrical shock) (P < 0.001).

Conclusion: Non-sustained VF in primary electrical disorders was not infrequent. VFCL was longer and progressively increased or did not change in non-sustained VF compared with VF terminated by electrical shock. Whether ICD programming reflecting this characteristic shortening of VFCL could decrease frequency of ICD shock awaits further study.

P1388 | BEDSIDE
Right ventricular early ventricular ejection delay identifies high risk patients and gender differences in Brugada syndrome
S.C.H. Van Malderen1, D. Kerkhove2, D.A.M.J. Theuns3, C. Weyntjens2, S. Droogmans2, D. Daneels2, S. Van Dooren2, M. Meuwissen2, P. Brugada2, G. Van Camp2,1 Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands; 2 University Hospital (UZ) Brussels, Department of Cardiology, Brussels, Belgium; 3 University Hospital (UZ) Brussels, Centre for Medical Genetics, Reproduction Genetics and Regenerative Medicine, Brussels, Belgium

Background and purpose: Right ventricular (RV) conduction delay has been suggested as an underlying pathophysiological mechanism in Brugada syndrome (BS). In this cross-sectional study we non-invasively assessed the value of echocardiographic markers reflecting ventricular ejection delay in identifying BS patients at risk for life-threatening arrhythmic events. Furthermore, because male BS patients demonstrate a more malignant clinical phenotype, we sought to assess differences in ejection delays between both genders.

Methods: 124 BS patients (77 males and 47 males) and 62 control (CTR) (48.4% males) were included. Using Tissue Velocity Imaging, the ejection delay, determined as the time from QRS onset to the onset of the sustained systolic contraction, was measured for both RV free wall (RVWD) and lateral LV wall (LVED). From these parameters, the interventricular ejection delay between both walls (IVED) was calculated.

Results: BS patients had longer RVED and IVED compared to the CTR. BS patients with a previous history of syncope or spontaneous ventricular arrhythmia showed the longest RVEDs and IVEDs. Male BS patients demonstrated longer RVEDs and IVEDs than females. Male BS patients with malignant events had the longest delays. No significant differences regarding LVED were observed between BS patients and CTR.
Conclusions: We demonstrated that a previous history of malignant events was associated with longer RVEDI. Our findings supported the RV conduction delay mechanism behind BS and demonstrated for the first time that the predominant malignant male Brugada phenotype might also be the result of a more delayed RV conduction in males.

**P1389 | BEDSIDE**

Troponin T or I levels following ICD implantation with and without defibrillation testing and their predictive value for outcomes: Insights from the SIMPLE trial

M. Vamos1, S.H. Hohnloser 1, S.J. Connolly 2, G. Duray1, L. Vanerven1, X. Vinolas2, J. Neuzner3, M. Glikson2, J. Wang3, J.S. Healey2 on behalf of SIMPLE trial investigators. 1JW Goethe University, Dept. of Cardiology, Div. of Clinical Electrophysiology, Frankfurt am Main, Germany; 2McMaster University, Hamilton, Canada; 3Central Medical Centre, Hungarian Defence Forces, Budapest, Hungary; 4Leiden University Medical Center, Leiden, Netherlands; 5Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; 6Klinikum Kassel, Kassel, Germany; 7Chaim Sheba Medical Center, Tel Hashomer, Israel; 8Population Health Research Institute, Hamilton, Canada

SIMPLE randomized 2,500 patients receiving a first ICD to defibrillation testing (DT) or not. It demonstrated that DT did not improve shock efficacy or reduce mortality. This prospective sub-study sought to evaluate postoperative troponin (T) concentrations and their predictive value for total and arrhythmic mortality. Methods and results: A Trop measurement was taken between 6 and 24 hours following ICD implantation in 2201/2500 patients. A postoperative Trop above the upper limit of normal (ULN) was more common in patients undergoing DT (N=509, 46%) than in those not having DT (N=457, 41%; p<0.02). After excluding patients with known preoperative Trop > ULN, similar findings were observed (42% vs. 38%; p=0.04). During a mean follow-up of 3.1±1.0 years, the annual mortality rate was 7.3% in patients with a postoperative Trop > ULN compared to 4.2% in patients with Trop ≤ ULN (HR 1.73, 95% CI, 1.41–2.12; p<0.001). Similarly, patients with elevated Trop had a significantly higher risk of arrhythmic death (HR 3.20, 95% CI, 1.54–6.75; p<0.001). The rate of failed appropriate first shock (component of the primary outcome of the main trial) was similar in patients with or without Trop elevation (HR 1.13, 95% CI, 0.88–1.88; p=0.65).

Conclusion: DT at time of ICD implant is associated with increased Trop levels indicating some myocardial injury caused by the procedure. Trop appears to represent a valuable predictor or clinical outcomes in ICD recipients.

**P1390 | BENCH**

Increased myocardial expression of proapoptotic PERP, proadipogenic CPT1B and phospholamban in arrhythmogenic right ventricular cardiomyopathy/dysplasia compared to dilated cardiomyopathy and controls

D. Akdis1, A.M. Saguner1, J. Kast2, A. Medeiros-Domingo1, F. Enseel1, P. Braunschweig1, A. Pollak1, A. Schenkel1, F. Luescher1, C. University Heart Center, Cardiology, Zurich, Switzerland; 2Swiss Institute of Allergy and Asthma Research SIAF, Davos, Switzerland; 3University Hospital Zurich, Department of Pathology, Zurich, Switzerland

Introduction: Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is a mainly autosomal dominant heart muscle disorder. Mutations in desmosomal proteins can only be identified in 50% and the pathogenic mechanisms are not well understood.

Methods: mRNA levels of targeted molecules were measured in myocardial tissue. We screened for 64 junctional molecules, 4 apoptotic molecules, 6 adipogenic molecules, 5 ion channel molecules, and 7 structural molecules. The averaged expression of all candidate mRNAs (n=6 each) were compared. The ARVC/D samples were from patients with desmoplakin, desmoglein, plakophilin and titin mutations. We performed immunohistochemical staining and quantitative analysis to investigate protein expression of significantly increased mRNAs (n=5–4 in each group).

Results: In ARVC/D, compared to dilated cardiomyopathy (DCM) and controls, we found significantly increased mRNA levels of the desmosomal molecules desmoglein-2 (ARVC/D vs. DCM/control: p<0.001;0.004) and plakophilin-2 (ARVC/D vs. DCM/control: p<0.001) of the proapoptotic molecule PERP (ARVC/D vs. DCM/control: p<0.008) and calcium channel associated molecule phospholamban (ARVC/D vs. DCM/control: p<0.005). Immunohistochemistry revealed no significant difference in desmoglein-2 and plakophilin-2 expression. PERP, CPT1B and phospholamban protein expression was increased in ARVC/D samples compared to DCM and controls (p<0.01).

Conclusion: Changes in expression profiles of apoptotic and adipogenic molecules suggest that these cellular pathways may play a role in ARVC/D pathogenesis. Whether these molecules could be considered as specific markers needs further investigation.

**P1391 | BEDSIDE**

ABC1B gene variants, digoxin and risk of sudden cardiac death in a general population

M.N. Niemeijer1, M.E. Van Den Berg1, J.W. Deckers1, A.L.H.J. Aarnoudse2, A. Holman1, O.H. Franco1, A.G. Uitterlinden4, P.R. Rijnbreek1, M. Eijgelaar1, B.H. Stricker1, 1Erasmus Medical Center, Rotterdam, Netherlands; 2Catharina Hospital, Eindhoven, Netherlands

Background: The ATP-Binding Cassette B1 (ABC1B) gene encodes a transport protein, which plays an important role in the bioavailability of digoxin. Genetic polymorphisms within this gene might modulate the risk of sudden cardiac death (SCD).

Objectives: To investigate the interaction between variants within the ABC1B gene and digoxin on the risk of SCD.

Methods: Within a population-based cohort study in persons 45 years of age and older, we used Cox regression to analyze the effect of 3 frequently studied and relatively infrequent polymorphisms extracted from 1000 Genomes imputed ABC1B genotypes (C1236T, G2677T, C3435T) on the risk of SCD, stratified by digoxin use. We adjusted the analyses for age, sex, smoking, heart-rate corrected QT interval, and prevalent heart failure, coronary heart disease and atrial fibrillation.

Results: In a total study population of 10,932 persons, 419 SCDs occurred during a median follow-up of 9.8 years. At baseline, the mean age was 65.2±9.6 years and 42% was male. In nonusers of digoxin the risk of SCD was not different across genotypes. In digoxin users, homozygous T allele carriers of C1236T (HR 1.90; 95% CI 1.05, 3.30; allele frequency 0.43), G2677T (HR 1.89; 95% CI 1.10, 3.24; allele frequency 0.44) and C3435T (HR 1.72; 95% CI 1.03, 2.87; allele frequency 0.53) had a significantly increased risk of SCD in a recessive model. Interaction between the ABC1B polymorphisms and digoxin use was significant for C1236T (p=0.04) and G2677T (p=0.03) in the age and sex adjusted model.

Conclusions: In this study, we showed that in digoxin users, homozygous T allele carriers of the ABC1B gene had an increased risk of SCD compared to digoxin users with none or one T allele. This implies that the ABC1B genotype modifies the risk of cardiac digoxin toxicity. If these findings can be replicated in an independent cohort, testing ABC1B gene variants in new users of digoxin could enhance safe use of this drug if drug concentration monitoring alone is insufficient to reduce the associated risk in a specific group of patients.

**P1392 | BENCH**

A novel cardiac cytochrome P450 Reductase gene (RyR2) mutation as cause of sudden cardiac death by catecholaminergic polymorphic ventricular tachycardia

E. Diaz Pelayo1, E. Zatarain Nicolas1, J.M. Mena Latore2, E. Villacorta Arguelles1, I. Mendez-Fernandez2, M.A. Espinosa-Castro1, M. Centeno Jimenez1, R. Yotti Alvarez1, F. Fernandez-Aviles1, 1University Hospital Gregorio Maranon, Madrid, Spain; 2University Hospital Principe de Asturias, Alcalá de Henares, Spain

Introduction: Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a channelopathy due to abnormal intracellular calcium handling. Several mutations in RyR2 have been described, causing stress-induced ventricular tachycardia and sudden cardiac death (SCD) related to CPVT. Early diagnosis is mandatory to provide preventive treatment.

Purpose: To describe a genetically characterized family (Figure) with clinically suspected CPVT and a new variant in RyR2.

Methods: The proband (II:8) is a 17 y/o male survivor of SCD while swimming, recovered by external defibrillation. The ECG, echocardiography, Holter, flecainide test and exercise test were normal. He had family history of a 10 y/o half-brother suffered SCD, with inconclusive autopsy. His mother (I:2) and two half-sisters (II:2, II:7) reported history of stress-related syncopes (often watching scary films). No arrhythmias were noted in exercise test of any relative. Genetic screening was performed with a Next Generation Sequencing panel of 126 genes associated with SCD.
Results: Genetic analysis of the proband identified a heterozygous missense mutation in the C-terminal domain of the RyR2: exon 93, affecting the highly conserved residue in position 4495, changing Phenylalanine by Cysteine (F4495C). The variant identified clearly cosegregates with the clinical phenotype (I.2: II.2, II.7, II.8). In-silico analysis predicts a potential deleterious effect on RyR2. All carriers were treated with beta-blockers and remained asymptomatic for a follow-up of 24 months.

Conclusions: The missense variant in RYR2 F4495C cosegregates with symptoms and may cause CPVT. Within the same family, phenotype is worse in males. The sensitivity and specificity of exercise tests is limited, therefore genetic test may help in the diagnosis of suspected relatives.

P1393 | BEDSIDE
S-wave angle identifies ARVD with normal ECGs compared to healthy family members

D. Cortez1, S. Graw2, F. Brun3, A. Spezzacatena4, L. Mestroni2, 1University of Colorado, Pediatric Cardiology, Aurora, United States of America; 2University of Colorado, Aurora, United States of America; 3University of Trieste, Trieste, Italy

Introduction: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is associated with sudden death. Relatives of the proband are also at risk. Another inher-
teria (p-values 0.015). Utilizing a V2 S-wave angle of 11 degrees as the upper limit of normal cut-off value, the sensitivity and specificity for ARVC with normal
ECGs were measured in V1 and V2 (S-wave angle).

Methods: 12-lead resting ECGs from 54 patients meeting Task Force 2010 def-
inite ARVC criteria (age 41.1±14.8 years, 58.1% males) were assessed. 32 did not fulfill depolarization or repolarization criteria (including upslope of the S-wave <55ms) and were compared with 32 first degree relatives (age 36.7±13.4 years, 58.3% males). The angles encompassing the down-slope and up-slope of the S-wave were measured in V1 and V2 using a protractor.

Results: The S-wave angle in V2 significantly differentiated ARVD with normal variant ECG patients from family members who do not meet 2010 taskforce cri-
teria (p-values 0.015). Utilizing a V2 S-wave angle of 11 degrees as the upper limit of normal cut-off value, the sensitivity and specificity for ARVC with normal variant were 52% and 97%, respectively.

Conclusion: Discrimination of ARVC with normal variant ECG’s is improved with the S-wave angle, and in V2. This subtle change on the ECG may help to iden-
tify family members with normal variant ECG’s who meet 2010 Taskforce criteria otherwise. Larger studies are needed to validate this method.

P1394 | BEDSIDE
Prevalence of electrocardiographic findings associated to sudden cardiac death: spontaneous type 1 and type 2 Brugada patterns and QT disorders in Spanish population older than forty years


Introduction: There are different electrocardiographic (EKG) patterns associated with higher risk of sudden cardiac death (SCD) because of ventricular arrhythmias such as Brugada patterns, long QT and shortened QT. Data about the prevalence of these findings in general population are scant.

Objectives: To analyze the prevalence of spontaneous type 1 and type 2 Brugada patterns and QT disorders in Spanish population older than forty years.

Patients and methods: A cross-sectional study endorsed by the Spanish So-
ciety of Cardiology over the Spanish population ≥40 years was performed. Two-stage random sampling was used, where first stage units where primary care physicians randomly selected at every spanish province and second stage units were 20 randomly selected persons drawn from every participating physician’s assigned population. By this way we randomly selected a representative sample of Spanish population of 11,831 individuals which were invited to participate in the study. Finally, 8,343 consented to participate and completed the study pro-
tocol that included a 12-lead-EKG. There was centralized reading of the EKG recordings. EKGs were evaluated by a two trained cardiologists. In case of dis-
agreement in the diagnosis a third cardiologist was consulted and final diagnosis was reached by consensus. Type 1 and type 2 Brugada patterns were defined according to the 2002 Brugada Consensus Report. QT interval was measured from the start of the QRS complex until the end of the T-wave. The Bazett formula (QTc=QT/RR) was used to correct the interval for heart rate. Four categories were defined: normal QTc 340–439 milliseconds (ms), borderline 440–469 ms, prolonged QTc >470 ms, short QTc <340 ms.

Results: Overall, 8,343 randomized individuals were evaluated. Mean age was 59.2 years 95% CI: 58.6–59.8 (range, 40–104 years), 52.4% female. We identified 12 cases of type 1 and type 2 Brugada patterns (global prevalence 0.13%) with the following distributions:

- Type 1: two cases (0.02%), both were women, 55 and 54 years old.
- Type 2: ten cases (0.11%), nine of them were males, mean age 52.2 years old. For QTc analysis we excluded individuals with left bundle branch block and in-

inviduals without sinus rhythm. We analyzed data from 7,889 patients. 52.5% were women, mean age 58.3 years old. These are our findings: Borderline QTc: 763
cases, weighte prevalence 8.33%. Long QTc: 96 cases, weighted prevalence
1.01%. Short QTc: 18 cases, weighted prevalence 0.18%.

Conclusions: At least, 1.32% of Spanish population older than 40 years has an EKG pattern associated with higher risk of SCD.
Methods: Sixty-five patients with HCM were prospectively recruited and underwent routine clinical evaluation and cardiac MRI protocol including assessment of function and scar (1.5 Tesla scanner). Clinical evaluation and MRI study were performed within 2 months. The probability of SCD at 5 years was calculated for each patient using the proposed model. LGE imaging was acquired after the administration of 0.2 mmol/kg of gadobutrol. Quantification of LGE was performed using the gray-scale threshold method of >6 SDs. Extensive areas of LGE were defined by the presence of more than 15% of LGE of the total LV mass.

Results: 74% of the patients showed areas of LGE (n=48). The extension of LGE was positively correlated with the SCID risk prediction (r=0.68, p<0.0001). Low, intermediate and high-risk groups according to the model showed significantly different extent of LGE (6.1±7 vs. 15±10 vs. 22±4%, p<0.0001). 4 patients (7%) in low-risk group and 3 (50%) in the intermediate-risk showed extensive areas of LGE. All high-risk patients (n=5) showed extensive areas of LGE.

Conclusions: LGE extension is concordant with the model defining low and high-risk groups; in intermediate-risk patients it seems to provide additional information and may allow a better discrimination supporting ICD decision. LGE quantification holds promise for SCD stratification in HCM.

P1397 | BEDSIDE
Nadolol is superior to metoprolol SR in protection from exercise induced arrhythmias in patients with catecholaminergic polymorphic ventricular tachycardia (CPVT)
I.S. Lerén1, T.F. Haland1, J. Sabernjak1, E. Majid2, T. Edvardsen1, K.H. Haugaa1. 1. Oslo University Hospital, Dept of Cardiology and Center for Cardiological Innovation, Oslo, Norway; 2. University of Oslo, Oslo, Norway

Introduction: Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inheritable arrhythmogenic disease, predisposing to ventricular arrhythmias at exercise. Beta blockers are standard treatment, however not all beta blockers are equally effective.

Purpose: We aimed to serially investigate the incidence and severity of exercise induced arrhythmias in CPVT patients without medication, on metoprolol SR and on nadolol.

Methods: We included 34 CPVT patients (crossover study, 34±19 years, 56% male, 88% RYR2 mutations). In each patient, we performed 3 exercise stress tests to exhaustion: prior to beta blocker treatment, and after >6 weeks on maximum tolerated doses of metoprolol SR and nadolol, respectively. We recorded resting and maximum heart rate (HR) and the most severe arrhythmia during exercise. Severity of arrhythmias was scored as: no arrhythmias,0, single ventricular extra systoles,1, bigemini,2, couplets,3 and non-sustained VT,4. We performed 24 hour Holter recordings and scored arrhythmias similarly.

Results: HR at rest was similar on nadolol and metoprolol SR (53±10bpm vs. 56±14bpm, p=0.29), while maximum HR was lower on nadolol (120±20 bpm vs. 139±24 bpm, p<0.001). At exercise, incidence of arrhythmias was lower on nadolol (60%) than on metoprolol SR (96%) and no medication (92%) (both p<0.01). Also severity of arrhythmias was lower on nadolol than metoprolol SR and no medication (score 1.2±1.3 vs. 2.4±0.9, p<0.01) and no medication (1.2±1.3 vs. 2.5±1.2, p<0.01) (Figure). Arrhythmic score from Holter was lower on nadolol than no medication (0.8±1.0 vs. 1.2±1.0, p=0.03).

Conclusion: Incidence and severity of arrhythmias decreased on nadolol compared to metoprolol SR in patients with CPVT. Nadolol could be superior to metoprolol SR in arrhythmia control in CPVT patients.

P1398 | BEDSIDE
Deletion of SCN5A and SCN10A detected using NGS as a probable cause of Brugada syndrome. Results of a copy number variants cohort screening
A.J. Palomino Doza1, A. Garcia Fernandez2, J.G. Martinez Martinez3, M.L. Pena Pena1, J.P. Ochoa1, D. Garcia1, D. De Una1, C. Gayoso1, V. Climent Paya2, L. Monserat Iglesias1. 1. Instituto Investigacion Biomedica. A Coruña. Spain; 2. 2. Instituto de Órganos Cardíacos. Universidade de Santiago. Galicia. Spain; 3. Centro de Investigación en Salud. Hospital de lottery, Familial Cardiomyopathies Unit, Alicante, Spain

Background: Brugada syndrome (BS) is a genetic channelopathy associated with risk of sudden death, affecting predominantly young males and displaying autosomal dominant inheritance. SCN5A and SCN10A are the genes most commonly associated with BS in the literature. A responsible mutation is identified in only about 30% of BS patients with the rest remaining genetically undetermined. Copy number variants (CNVs) are the major type of structural variation in human genome and are important sources of human genetic and phenotypic variation. CNVs have been associated to predisposition to human diseases. Up to date there are no described associations between CNVs and BS. Next generation sequencing (NGS), unlike traditional Sanger sequencing, allows the detection of structural variants. Our aim was to explore the presence of CNVs in a cohort of BS patients who were sequenced using NGS.

Methods: Fifty nine patients with diagnosis of BS sent to our laboratory were sequenced using HiSeq NGS and a 214 gene panel. Analysis was focused on 17 previously associated genes. CNVs were explored using comparison of sequencing coverage after normalization for total coverage in each region. Each region was analyzed using absolute coverage and deviation from the median.

Results: Fifty nine patients were screened. An associated mutation was found in 25% of probands and 15% of the identified variants were located in SCN5A. One CNV was found in a proband (1.6% of the probands, 3% of those with definite diagnosis, 6.6% of the mutations found). The CNV found is a heterozygote deletion of the whole SCN5A and SCN10A genes.

Conclusion: This is the 13 years old male who was referred due to typical atrial flutter after exercise. He showed a Brugada type 1 pattern on the ECG. There is no family history of sudden death. Electrophysiological study (EPS) was performed without significant inducible arrhythmias. He underwent RFCA currently acutely analyzed on Holter monitoring signs of sinus node dysfunction have been documented. His father also showed a BS type 1 pattern.

Conclusion: This is the first report of a heterozygous deletion affecting both the whole SCN5A and the SCN10A genes associated with BS. NGS is a reliable method for detecting structural variants in BS genetic screening. CNVs could explain a relevant fraction of the genotype negative BS. CNV analysis should be performed routinely during genetic tests for BS.

Acknowledgement.Funding: Health in Code
P1400 | BEDSIDE
Early repolarization pattern: a marker of increased risk in patients with catecholaminergic polymorphic ventricular tachycardia
E. Tulumen1, E. Schulze-Bahr2, S. Zunnhagen2, B. Stallmeyer2, B.M. Beckmann3, S. Kaab1, C. Wolpert3, B. Rudic1, C. Veitmann4, M. Borggreve1,1, Medical Faculty Mannheim of the University of Heidelberg, 1st Department of Medicine, Mannheim, Germany;2 Institute for Genetics of Heart Diseases, Department of Cardiovascular Medicine, University Hospital Münster, Münster, Germany;3 Ludwig-Maximilians University, Department of Medicine I, University Hospital Munich, Munich, Germany;4 Klinikum Ludwigshafen, Department of Medicine-Cardiology, Nephrology and Internal Intensive Care Medicine, Ludwigshburg, Germany;5 Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany

Background: The early repolarization pattern (ERP) has been shown to be associated with arrhythmias in patients with short QT syndrome, Brugada syndrome and with ischemic heart disease. Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inherited arrhythmia syndrome and related to malignant ventricular tachyarrhythmias in a structurally normal heart.

Purpose: The aim of this study was to evaluate the prevalence of ERP and clinical events in patients with CPVT.

Methods: Digitalized resting 12-lead ECGs of patients were analyzed for ERP and for repolarization markers (QT and Tpeak-Tend interval). The ERP was diagnosed as “notching” or “slurring” at the terminal portion of QRS with >0.1 mV elevation in at least two consecutive inferior (II, III, aVF) and/or lateral leads (V4-V6, I, aVL).

Results: Among 51 CPVT patients [mean age 36±15 years, 11 males], the ERP was present in 23 (45%): strictly in the inferior leads in 9 (18%) patients, in the lateral leads in 9 (18%) patients and in interlateral leads in 5 (10%) patients. All patients with ERP were symptomatic at presentation (23 of 23 pts with ERP vs. 19 of 28 pts,without ERP, p<0.003). Syncope was also more frequent in patients with ERP (18 of 23 pts with ERP vs. 11 of 28 pts, without ERP, p=0.005).

Conclusions: A pathologic ERP is present in an unexpected large proportion (45%) of patients and is associated with an increased frequency of syncope. In patients with unexplained syncope and ERP at baseline, exercise testing should be performed to detect CPVT.

P1401 | BEDSIDE
Electroanatomical scar characteristics of patients presenting with fast ventricular tachycardia after myocardial infarction: the impact on substrate based ablation approaches
M. De Riva Silva, G.F.L. Kapel, J. Venlet, S.R.D. Piers, M. Watanabe, M.J. Schalij, K. Zeppenfeld, Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands

Introduction: Late potentials (LP) indicate slow conduction during sinus rhythm (SR) and are an accepted target for substrate based VT ablation post-myocardial infarction (MI). However, the substrate for fast VTs may not be detectable during SR.

Methods: Consecutive patients with prior MI referred for VT ablation underwent programmed electrical stimulation (PES: 3 cycle lengths (CL), 1–3 extra steps, 2 pacing sites) and LV endocardial electroanatomical mapping. Bipolar electrograms (EG) were displayed (0.13mV, 200mm/sec) and evaluated for voltage (BV), duration (EDG), earliest to latest sharp peak deflection and morphology. Late potentials (LP) were defined as EG with onset after QRS, separated from the far-field EG>20ms (very LP if >100ms). The entire scar area (SA, BV<1.5mV), deeper scar (DS, BV<0.5mV) and border zones (BZ, BV>0.5mV,<1.5mV) were measured. The density of LP was calculated as a percentage of the total EGs within the SA and DS.

Results: Eighty-three pts (77 men, 68±10 years, LVEF 33±11%, 33 on amiodarone) were included. In 80 (93%), a median of 3 VTs/pat (IQR 2–5) were induced. Mean SA was 71±39cm² (32±13% of total LV area), DS 22±29cm² (39±22% of SA), and BZ 38±21cm² (61±22% of SA). LP were present in 79% of the pts (12±15/pat, mean duration after offset QRS 57±27ms) and vLP in 33%. The presenting VT CL was >320ms in 56 pts (67%, mean CL 420±64ms) and ≤320ms in 27 pts (33%, mean CL 290±72ms). Pts with fast VTs had smaller SA (32±10% vs 38±12% of total LVA: P<0.0001), larger BZ areas (76±17% vs 53±20%; P<0.0001) and less evident slow conduction reflected by a lower density of LP within the SA and DS (3±4% vs 12±10%; 4±7% vs 17±16% respectively: all P<0.001). Of importance, in 27% of pts with fast VTs no LP were found compared to 9% in pts with VTCL>320ms (P=0.025; no vLP in 82% vs 58%; P=0.013).

Conclusions: Electroanatomical scar characteristics are significantly different in patients with fast and often poorly tolerated VTs. The scarcity of evident slow conduction during SR as target site for ablation may require additional strategies for substrate based ablation approach in these patients.

P1402 | BEDSIDE
Ventricular tacharyrhythmia during pregnancy in patients with structural heart disease: results from the ROPAC registry
E. Ertekin1, A.M.F. Salam2,1, M.V. Hanegan1, M.R. Johnson1, R. Hall1, J.W. Roos-Hesselink1 on behalf of Registry of Pregnancy and Cardiac disease (ROPAC), 1 Erasmus Medical Center, Cardiology, Rotterdam, Netherlands; 2 Hamad Medical Corporation, Doha, Qatar; 3 Chelsea and Westminster Hospital Trust, London, United Kingdom; 4 University of East Anglia, Norwich, United Kingdom

Background: The occurrence of ventricular tachyarrhythmia (VTA) during pregnancy may have devastating effects on both mother and baby, but literature is scarce. We investigated the incidence, onset, predictors and outcome of VTA in pregnant women with heart disease.

Methods and results: The Registry on Pregnancy and Cardiac disease (ROPAC) is a global, prospective observational registry of pregnant women with structural heart disease. Out of 2,966 pregnancies in ROPAC collected from 2007 to 2014, we identified 42 (1.4%) with VTA, which occurred mainly in the third trimester (53%). Multivariable analysis identified cardiomyopathy (OR 5.26, 95% CI 2.54–10.91) and NYHA class-1 (OR 2.64, 95% CI 1.42–4.91) as pre-pregnancy risk factors for VTA. Heart failure was more common during pregnancy in women with VTA compared to women without VTA (24% vs. 12%, p=0.03). More women with VTA delivered by cesarean section (68% vs. 47% in women without VTA, p<0.01). Preterm birth (<37 weeks) and low birthweight (<2500 gram) occurred more often in women with VTA compared to women without VTA (36% vs. 16%, p=0.001 and 33% vs. 15%, p=0.001, respectively). In the VTA group, one late foetal death occurred in a patient with hypertrophic CMF. VTA was not associated with a higher maternal mortality rate (2.4% vs. 0.3% in women without VTA).

Conclusions: VTA occurred in 1.4% of pregnant women with structural heart disease and presented mainly in the third trimester. Cardiomyopathy and NYHA class-1 were independent pre-pregnancy predictors. VTA during pregnancy has impact on preterm birth and low birth weight rates.

P1403 | BEDSIDE
Ventricular arrhythmias induced by sodium channel blocker is a risk stratification tool in patients with Brugada syndrome
A. Ueoka1, H. Morita2, M. Kubo1, K. Nakagawa1, N. Nishii1, S. Nagase1, H. Ito1, Okayama University Hospital, Department of Cardiovascular Medicine, Okayama, Japan;2Okayama University Hospital, Department of Cardiovascular Therapeutics, Okayama, Japan

Background: There is no evidence to detect high-risk patients with Brugada-type ECG in whom ST elevation was augmented by pilsicainide.

Objective: We intend to clarify whether piliscainide induced ventricular arrhythmias (VAs) and T-wave alternans (TWA) can identify high-risk patients.

Methods: We administered intravenous piliscainide (1mg/kg) to 273 patients (265 men, 47±13 years of mean age) with Brugada-type ECG (spontaneous type 1 ECG = 179 patients) and evaluated changes of ECG morphology and the occurrence of VA. Baseline characteristics of them included 13 patients with history of ventricular fibrillation (VF), 88 with history of syncpe.

Results: During 94±50.6 months of mean follow up, 4 patients died suddenly, 25 patients experienced VF events and 2 patients died from cancer. Intravenous piliscainide unmasked typical type 1 ST-segment elevation in 77 patients with non-spontaneous type 1 ECG. TWA induced by piliscainide was observed in 30 patients (11%) but it was not significant predictor for fatal arrhythmic events (sud-
den death (SD), VF, and ventricular tachycardia (VT)). Pilsicainide also induced VAs in 41 patients (15%; PIVA group) and did not induce in remaining patients (non-VA group): ventricular premature beats were provoked in 40 patients and VT/VF in 9 patients. Incidences of fatal cardiac events were significantly higher in PI-VA group than non-VA group (Hazard ratio: 4.08, 95% CI: 1.91–8.40, p < 0.001) (Figure A). Moreover, in patients without previous episodes of VF, drug-induced VA was strong predictor of fatal arrhythmic events (Hazard ratio: 5.61, 95% CI: 2.39–12.8, P < 0.001) (Figure B).

Conclusion: The occurrence of ventricular arrhythmia induced by pilsicainide can identify high-risk patients with Brugada-type ECG.

P1405 | BEDSIDE
Improvement in ventricular function and low incidence of ventricular arrhythmias in dilated cardiomyopathy
K. Broch, E. Kongsgaard, L. Gullestad, S. Aakhus. University of Oslo, Rikshospitalet University Hospital, Department of Cardiology, Oslo, Norway

Background: Current guidelines assign a IIB indication for implanting a cardioverter defibrillator (ICD) in patients with non-ischaemic dilated cardiomyopathy (DCM) who have an left ventricular (LV) ejection fraction (LVEF) < 40% and who are NYHA functional class II or III. However, studies have shown that LV function often improves in patients recently diagnosed with idiopathic DCM, and that the incidence of appropriate shocks in this population is low. Thus, the optimal timing of assessment for ICD implantation is uncertain.

Purpose: We aimed to assess whether the indication for ICD implantation changed over time in patients with recent-onset DCM, and the prevalence of serious arrhythmic events in this population.

Methods: 102 consecutive patients referred to our tertiary care hospital with idiopathic DCM, an LV EF <40% and no implantable devices were included in a prospective cohort study. Pharmacological treatment was adjusted according to current guidelines, and follow-up was performed after one year. Vital status, heart transplantations, device implantations and arrhythmic events were subsequently recorded.

Results: At baseline, 3.0 (0.6–6.4) months after the diagnosis had first been made, pharmacological treatment had been initiated in 101 (99%) of the patients. Over the first year of follow-up, three patients received cardiac alloplants. In transplant free survivors, LVEF increased from 26±10% to 41±11% (p < 0.001), and NYHA class improved by 0.6±0.8 units (p < 0.001). The number of patients with an indication for ICD implantation according to current guidelines fell from 71 (70%) to 26 (27%). After a median follow-up of 3.6 years, four patients were dead, and heart transplantations had been performed in nine patients. Only one patient, whose LVEF improved to 62%, died a sudden, unexplained death more than three years after inclusion. Two patients had been admitted due to syncope. Altogether 31 patients had received ICDs, but only five of these patients received appropriate shocks during follow-up. Overall survival at 5 years was 93%, and transplant-free survival was 84%.

Conclusion: In patients with recent-onset DCM treated according to current guidelines, we observed a substantial improvement in LVEF and functional status within the first year of follow-up. The proportion of patients with an indication for ICD implantation fell from 70% to 27% during follow-up. The number of serious arrhythmic events was low. Our results suggest that in stable patients with recent-onset DCM, one can safely await improvement before considering ICD implantation.

Acknowledgement/Funding: This work was supported by a grant from Iker and John Fredriksen to the Department of Cardiology, Oslo University Hospital, Rikshospitalet, and an un

P1405 | BEDSIDE
Scarc transmurality as a criterion for first-line endo-epicardial substrate-guided ventricular tachycardia ablation in ischemic cardiomyopathy
J. Acosta Martinez, J. Fernandez-Armenta, D. Penela, D. Andreu, R. Borras, F. Vassanelli, J. Brugada, L. Mont, A. Berruezo. Hospital Clinic de Barcelona, Arrhythmia Unit, Barcelona, Spain

Introduction: To date, there is no consensus on the appropriate indications for epicardial approach in substrate ablation of post-myocardial infarction (MI) ventricular tachycardia (VT). We hypothesized that scar transmurality (ST) could permit to identify patients that benefit from a combined first-line endo-epicardial approach.

Methods: ST was assessed before procedure by: contrast-enhanced-MRI (hyper-enhancement ≥75% of wall thickness), echocardiography (dyskinesia/akinesia + hyperrefrency + wall-thinning), CT (wall thinning), or scintigraphy (transmural necrosis). From January 2011, prospectively, patients with subendocardial scar underwent endocardial approach (group 1) and patients with transmural scar underwent endo-epicardial approach (group 2). Both groups were compared with patients with transmural scar and only endocardial approach due to prior cardiac surgery or procedure performed before January 2011 (group 3). Primary endpoint was survival free from VT recurrence.

Results: Seventy-seven patients (91% men, 65.7±9.9 years) undergoing VT substrate ablation were included: group 1, N=35; group 2, N=18; group 3, N=24. During a mean follow-up of 0.8±1.17 months, 4 patients in group 1 (11.4%), 3 patients in group 2 (16.7%) and 12 patients in group 3 (50%) had VT recurrences; p=0.002. Time to recurrence was shorter in group 3 (log-Rank p=0.019). Endocardial approach in patients with transmural scar was associated with an increased risk of recurrence (hazard ratio 2.78; IC 95% 1.01–7.6; p=0.04).

Conclusion: Endocardial approach in patients with transmural scar undergoing VT substrate ablation is associated with an increased risk of recurrence. ST may be a useful criterion in order to decide for a first-line combined endo-epicardial approach.

P1406 | BEDSIDE
Subjects with suspected Brugada pattern: best electrocardiographic parameters in predicting positive sodium channel blocker test
C. Giustetto1, N. Cerrato2, C. Rolando2, P. Carvalho2, D. Castagno3, M. Anselmino1, R. Pozzi2, L. Bergamasco1, F. Gaita1,1 University of Torino, Division of Cardiology, Department of Medical Sciences, Torino, Italy; 2San Luigi Gonzaga Hospital, Division of Cardiology, Orbassano, Italy

Background: Brugada syndrome is characterized by coved type ST segment elevation ≥0.1 mm in at least 1 right precordial lead, associated with increased risk of sudden death. Provocative test using Na-channel blockers is often required to unmask the diagnostic pattern (type-1).

 Aim: We retrospectively analysed pre-test ECGs of subjects who underwent drug challenge, to identify which ECG parameters could best predict the result of the test.

Methods: Baseline ECGs of consecutive patients who underwent a test with ajmaline (1 mg/kg) or flecainide (2 mg/kg), were analysed. A positive response was defined as the occurrence of type-1 ST-segment elevation ≥0.1 mm in right precordial leads, in standard or higher intercostal space. The following variables were evaluated at pre-test ECG: type 2 or 3 ST morphology according to the 2°Consensus Conference criteria: r wave duration ≥0.04 s in V1-V2; QRS duration in V1 ≥ 0.10 s; greater QRS duration in V1-V2 than in V5-V6; S wave duration ≥ 0.4 s in II, III and aVF; PR interval; fragmented QRS in V1-V3; ST-segment elevation ≥0.18 mV in V1-V2 at 0.08 s from J point; early repolarization.

Results: We evaluated 440 ECGs of 240 patients, 35% having a positive test. The parameters significantly different between positive and negative drug challenge at univariate analysis, with their sensitivity and specificity, are reported in Table 1. At multivariable analysis, greater QRS duration in V1-V2 than in V5-V6 (OR: 2.24, CI: 1.39–3.60) and S wave duration ≥0.04 s in II, III and aVF (OR: 2.81, CI: 1.80–4.40) were independent predictors of positive test, while the 2°Consensus Conference criteria were not (OR: 1.38, CI: 0.88–2.16).

Conclusion: All the significant variables at the univariate analysis show a good balance between sensitivity and specificity. The independent predictors of positive drug test were greater QRS duration in leads V1-V2 as compared to leads V5-V6.

Table 1. Significant ECG parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Odds ratio</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consensus Conference V1-V2</td>
<td>63%</td>
<td>55%</td>
<td>74%</td>
<td>71%</td>
</tr>
<tr>
<td>Consensus Conference V5-V6</td>
<td>71%</td>
<td>75%</td>
<td>56%</td>
<td>56%</td>
</tr>
<tr>
<td>r wave duration</td>
<td>&gt;0.04 s in V1-V2</td>
<td>&gt;0.10 s in V1</td>
<td>3.5</td>
<td>3.2</td>
</tr>
<tr>
<td>QRS duration</td>
<td>&gt;0.04 s in II, III, aVF</td>
<td>0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
V6 and S wave duration $\geq 0.04$ s in leads II, III and aVF, both expression of a conduc-
tion delay in the right ventricular outflow tract.

**P1407 | BENCH**


Sudden cardiac death (SCD) continues to be the most devastating complication of hypertrophic cardiomyopathy (HCM). The new guidelines of the European Society of Cardiology (ESC) define the current standard for estimation of SCD risk as an integral part of clinical management. The aim of this study was to compare the 2014 and 2011 implantable cardioverter-defibrillator (ICD) recommendations in HCM patients (pts), and correlate them with the presence of fibrosis.

**Methods:** We studied 80 HCM ambulatory pts, in our hospital. All of them had performed cardiac magnetic resonance for late gadolinium enhancement (LGE) evaluation. The recommendation for ICD was assessed using previous (ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy - 2011) and current guidelines (ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy - 2014). SCD risk was calculated by current guidelines. All statistics analyses were performed using SPSS 20.0 version.

**Results:** The mean age of our population was 50±18 years and 65% were male. The majority of pts were in NYHA class I (71%) or II (27%) and had sepal HCM (66%). LGE was present in 65 (82%) pts, mainly in the midventricle (51%) with a local distribution. A diffuse pattern was found in a minority of cases (26%). By 2011 guidelines, 51% of pts had a class IIa recommendation for ICD and 49% had no ICD indication (class III). In comparison, by 2014 guidelines, we found much more pts without ICD indication (82%; p < 0.001) and 10% of pts had a class IIb indication. HCM SCD risk by current guidelines did not correlate with the presence (p=0.063), extension (diffuse p=0.505; focal p=0.438) or location (septal p=0.366; apical p=0.796) of LGE.

**Conclusion:** In our population, we found several differences in regarding recommendation for prophylactic ICD between previous and current guidelines. Overall there were fewer pts with ICD indication than before and fibrosis did not correlate with calculated SCD risk.

**P1408 | BEDSIDE**

N-terminal pro-B-type natriuretic peptide is elevated and strongly associated with higher mortality in comatose out-of-hospital cardiac arrest patients - a TTM substudy

M. Fryland1, D. Erlinge2, Y. Devaux3, H. Friberg4, M. Kuiper5, N. Nielsen6, P. Stammert7, M.P. Wise8, J. Kaergaard1 on behalf of The Target Temperature Management Study Group. 1 Rigshospitalet - Copenhagen University Hospital, The Heart Centre, Department of Cardiology, Copenhagen, Denmark; 2 Lund University, Department of Cardiology, Lund, Sweden; 3 CRP-Sante, Laboratory of Cardiovascular Research, Luxembourg, Luxembourg; 4 Skane University Hospital, Department of Anesthesiology and Intensive Care, Lund, Sweden; 5 Medical Center Leuwarden, Department of Intensive Care, Leuwarden, Netherlands; 6 Hospital of Helsingborg, Department of Anaesthesia and Intensive Care, Helsingborg, Sweden; 7 Hospital Center of Luxembourg, Department of Anaesthesia and Intensive Care, Luxembourg, Luxembourg; 8 University Hospital of Wales, Department of Intensive Care, Cardiff, United Kingdom

**Background:** We hypothesized that elevated N-terminal pro-B-type natriuretic peptide (NT-proBNP), a biomarker of increased left ventricular strain, following out-of-hospital cardiac arrest (OHCA) was associated with higher cardiovascular and overall mortality.

**Purpose:** In this sub-study of the Target Temperature Management (TTM)-trial we assessed the association between NT-proBNP concentrations, all-cause mortality, and cause of death in patients comatose after OHCA. The TTM-trial reported similar mortality and neurological outcome with targeting either $33 \degree C$ or $36 \degree C$.

**Methods:** A total of 1234 pts were included in the biomarker substudy, of whom 700 patients included. 647 patients (92.4%) had NT-proBNP measured on day 1, 2, and 3 and was stratified into quartiles. Outcome was 180 days at-cause mortality and cause of death.

**Results:** Median NT-proBNP in the 4 strata was 466, 1140, 2296, and 6524 pg/ml.

**Figure 1**

A significant association with 180-day survival rates ($P < 0.0001$) was found (Figure). In a multivariate model adjusting for age, sex, time to ROSC, lactate on admission, bystander CPR, initial rhythm, creatinine, body mass index, ST-elevation myocardial infarction, and TTM allocation group, the lowest NT-proBNP levels (Q1) was associated with lower mortality (HR=0.53 (0.38–0.82) $p < 0.01$) compared to Q4. Increasing quartiles of NT-proBNP on day 1 was associated with cardiovascular (Q1: 3.1%, Q2: 8.0%, Q3: 12.4% Q4: 36.4%, $p = 0.0001$) and, to lesser degree, neurological death (Q1: 17.4%, Q2: 27.2%, Q3: 38.3% Q4: 30.3%, $p = 0.01$). Mortality ratio in NT-proBNP Q4/Q1: Neurological 1.7 vs. Cardiovascular 1.1. Similar findings were seen on day 2 and 3.

**Conclusion:** NT-proBNP is elevated and strongly associated with all-cause mortality and especially risk of cardiovascular death in comatose OHCA patients.

**P1409 | BEDSIDE**

Genetic screening identifies a high proportion of mutations in patients with idiopathic ventricular fibrillation and sudden cardiac death M. Frydland1, D. Erlinge2, Y. Devaux3, H. Friberg4, M. Kuiper5, N. Nielsen6, P. Stammert7, M.P. Wise8, J. Kjaergaard1 on behalf of The Target Temperature Management (TTM)-trial.

**Introduction:** Several gene defects are associated with idiopathic ventricular fibrillation (VF) and sudden cardiac death (SCD). The development of NGS-based mutation screening provides a unique opportunity to estimate extensively the spectrum and prevalence of rare variants in genes associated with cardiac diseases.

**Methods:** Cohort 1 was composed of 75 patients resuscitated from cardiac arrest related to IVF. All patients underwent a complete clinical cardiac examination including 12 lead-ECG, cardiac echography, coronaryography and exercise test. Cohort 2 was composed of 99 victims of SCD related to ventricular fibrillation younger than 45 years old and without explanation for the SCD at the time of the examination.

**Genetic screening:** Genetic screening was based on the use of the HaloPlex™ System (Agilent Technologies) prior to HiSeq sequencing (Illumina). The custom kit covers 163 genes newly implicated in cardiac arrhythmias, conduction defect and cardiomyopathies.

**Results:** In cohort 1, the mean age was 36±10 years with a male predominance (52 males, 69%). In cohort 2, the mean age was 37±7 years with a male predominance (76 males, 79%). In cohort 1, we identified 50 probable mutations in 35 patients (47%). In cohort 2, we identified 30 probable mutations in 24 patients (25%).

**Conclusion:** From our identified mutations in almost 50% of IVF patients after a cardiac arrest evaluation. These results suggest that molecular analysis must be part of the work up in this kind of patients. In young patients affected by unexplained SCD, the molecular analyses are less contributive probably because of a more important percentage of patients affected by ischemic cardiomyopathies.

**P1410 | BEDSIDE**


**Background:** Calsequestrin 1 (CALM1) mutations have been found to cause cardiac arrest in infants at very early age. Underlining etiology described is Long QT Syndrome (LQTS), Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) and Idiopathic Ventricular Fibrillation (VF). Data about CALM2 mutations are lacking. We present two unrelated children with sudden cardiac arrest and a novel camodulin 2 mutation (Asn89Ser) with a subtle phenotype of LQTS and CPVT respectively.

**Methods and results:** Two unrelated children aged 4 and 7, who were born to unrelated parents, were studied in a unique opportunity to analyze mutations in 24 infants. The first one correctly resuscitated after an IVF episode, and the second one died suddenly. In both cases basal QTc interval was within normal limits. Clinical study revealed a positive epinephrine test for LQTS in the surviving 4 year old girl, and polymorphic ventricular ectopics with bidirectional couplets in a 24 H Holter from the deceased 7 year old boy, strongly suggesting a CPVT phenotype (table 1).

Peripheral blood DNA was available to perform genetic exome sequencing. A novel Asn89Ser mutation in CALM2 was detected in the two cases. This affected
a highly conserved across the species residue, and the location in the protein was adjacent to critical calcium binding loops in the calmodulin carboxyl-terminal domain, predicting a high pathogenic effect. In the second case (non survivor, 7 years) it was a de novo mutation, but in the first one parents refused to be studied.

**Conclusions:** Human calmodulin 2 mutations are associated with a life-threatening condition in early infancy. Phenotype can be variable, with a low clinical penetrance. This is the first time for this gene to be associated with CPVT.

**ACKNOWLEDGEMENT/FUNDING:** This work was supported by grants from the National Natural Science Foundation of China (No. 8170162 and No. 81470457). Human calmodulin 2 mutations are associated with a life-threatening condition in early infancy. Phenotype can be variable, with a low clinical penetrance. This is the first time for this gene to be associated with CPVT.

**ACKNOWLEDGEMENT/FUNDING:** This work was supported by grants from the National Natural Science Foundation of China (No. 8170162 and No. 81470457). Human calmodulin 2 mutations are associated with a life-threatening condition in early infancy. Phenotype can be variable, with a low clinical penetrance. This is the first time for this gene to be associated with CPVT.

**ABSTRACT**

**P1410 | BENCH**

**Title:** Attenuation of normal quiescent Purkinje-myocardial junctions during acute myocardial ischaemia - an unexplored arrhythmogenic mechanism

**Authors:** F. Ng1, E. Behradfar2, M.T. Debney1, A. Nygren2, A. Hartley1, A.R. Lyon1, I.R. Ellison1, E. Vignod4, N.S. Peters1, 1Imperial College London, London, United Kingdom; 2University of Calgary, Calgary, Canada; 3Washington University in Saint Louis, Saint Louis, United States of America; 4University of Bordeaux, Bordeaux, France

**Introduction:** The conduction system activates ventricular myocardium through Purkinje-Myocardial Junctions (PMJs). Most PMJs are non-functional at baseline due to source-sink mismatches at these junctions. We hypothesised that gap junction uncoupling at the PMJs during acute ischaemia facilitates propagation across a greater number of functional PMJs, thereby leading to accelerated but more complex activation patterns.

**Methods:** In aortic-perfused rabbit hearts (n=12), the right ventricles (RV) were exposed, preserving the Purkinje system (Figure), and the endocardium optically mapped. Activation of the RV endocardium during atrial pacing was recorded during 40 minutes of global ischemia followed by 30 minutes reperfusion. A corresponding detailed 3D computer model of rabbit ventricles with PS was constructed to test the hypothesis.

**Results:** The percentage of RV activated within 5ms decreased from baseline 53±6% to 43±8% during early ischemia (<20 min), and paradoxically then increased to 59±8% (p<0.001), with more surface breakthroughs and complex activation during late ischaemia (Figure). This phenomenon was abolished if treated with the gap junction enhancer rotigaptide. In the computer model, a 6% reduction in conductivity was sufficient to render quiescent PMJs active. Increasing the fraction of functioning PMJs accelerated endocardial activation, increasing surface breakthroughs and the complexity of activation, matching the experiments.

**Conclusion:** At baseline, most PMJs are quiescent. Ischaemia-induced closure of gap junction channels causes more PMJs to become functional due to reduced source-sink mismatch. The resultant altered and more complex activation patterns may be pro-arrhythmogenic as they increase the pathways for meandering wavefronts and the likelihood of wave collision.

**Acknowledgement/Funding:** NIHR Clinical Lectureship (1716), Academy of Medical Sciences Starter Grant (AMS-SGCL8-Ng), BHF Travel Fellowship (FS/11/68/29017)

**P1412 | BEDSIDE**

**Title:** Attenuation of CLOCK-BMAL1 decreases the occurrence of ventricular arrhythmia in chronic heart failure

**Authors:** J. Zou, J. Yuan, Z. Qian, Y. Chen, Y. Wang, D. Zhu, P. Ge, X. Hou. Nanjing Medical University, Nanjing, China. People's Republic of

**Background:** Circadian rhythms influence the incidence of SCD in chronic heart failure (CHF), however, the underlying mechanisms are not well defined.

**Purpose:** We sought to investigate the role and mechanism of the CLOCK-BMAL1 in regulating the occurrence of ventricular arrhythmia (VA) in CHF.

**Methods:** Circadian variations of myocardial expressions of β1-AR and β2-AR and circadian gene CLOCK and BMAL1 were examined. Then, luciferase and ChIP assay were applied to determine whether CLOCK-BMAL1 transcriptionally regulate β1-AR expression.

**Results:** Adenovirus infections were applied to overexpress CLOCK and/or BMAL1 in the guinea pig ventricular cardiomyocytes and the action potential durations were measured. Electrocadiograms of Langendorff-perfused hearts with isoprenaline (ISO), ISO + CGP-20712A (β1-AR selective antagonist, CGP) and ISO + ICI118551 (β2-AR selective antagonist, ICI) at CT3 and CT15 were recorded and VA were induced by PES.

**Conclusions:** Sham operated animals showed circadian oscillations in the expression of β1-AR and CLOCK-BMAL1 (P<0.05), but not in β2-AR (P>0.05). Importantly, the expression of β1-AR in patients with CHF was attenuated in CHF at CT15 (P<0.05). Luciferase and ChIP-PCR analysis revealed that BMAL1 could bind to the enhancer of β1-AR to regulate arrhythmia severity after CHF (P<0.05).

**Conclusion:** CLOCK-BMAL1 affected repolarization of ventricular myocytes and regulated ISO-induced arrhythmogenesis through β1-AR.

**Acknowledgement/Funding:** This work was supported by grants from the National Natural Science Foundation of China (No. 81170162 and No. 81470457)

**P1413 | BENCH**

**Title:** Antipathogenic stress in atrial cardiomyocytes induces mitochondrial remodelling via mitofusin-2

**Authors:** L. Ishai1, M. Bou-Khalil1, H. McBride2, C. Redpath1. 1University of Ottawa Heart Institute, Ottawa, Canada; 2Mogill University, Montreal Neurological Institute, McGill University, Montreal, Canada

**Background:** Atrial Fibrillation (AF) is the most common sustained arrhythmia in humans. In normal atria, AF is initially paroxysmal and self terminating as ultra-rapid electrical activity cannot be maintained. However, atrial cardiomyocytes remodel and their response to repeated episodes of “fibrillatory stress”, becoming capable of sustaining ultra-rapid activation indefinitely, thus perpetuating AF. Purpose: AF creates a sudden increase in cellular metabolic workload demanding an immediate increase in calcium cycling and mitochondrial respiration if ultra-rapid activation is to continue. We observed the mitochondrial response to periods of high frequency activation in order to determine whether cardiomyocyte mitochondria remodel in response to fibrillatory stress.

**Methods:** Cultured atrial cardiomyocytes (HL-1 cells) were preconditioned at 1Hz (control) or 5 Hz (fibrillatory stress) for 24 hours (5% CO2, 37°C).

**Results:** Fibrillatory stress resulted in hyper-fused mitochondria, increased expression of mitofusin-2 (Mfn-2) on mitochondrial outer membrane and increased co-localization of mitochondria with sarcoplasmic reticulum (n=50, p<0.001 for all comparisons). Following fibrillatory stress, mitochondrial membrane potential (Δψm) became synchronized with calcium release events and prevented detection of both mitochondrial and cytoplasmic oxidative stress upon subsequent rapid activation (n=50, p=0.001 for all comparisons). These observations were reproducible when fibrillatory stress was performed in the presence of reducing agents or the L-type calcium antagonist Verapamil. Western blot analysis of whole-cell lysates and quantitative real-time PCR demonstrated no appreciable change in mitochondrial bioenergetic state.

**Conclusions:** Fibrillatory stress induced mitochondrial hyperfusion, increased expression of mitofusin-2 (Mfn-2) on mitochondrial outer membrane and increased co-localization of mitochondria with sarcoplasmic reticulum (50–500 for all comparisons). Following fibrillatory stress, mitochondrial membrane potential (Δψm) became synchronized with calcium release events and prevented detection of both mitochondrial and cytoplasmic oxidative stress upon subsequent rapid activation (n=50, p<0.001 for all comparisons). These observations were reproducible when fibrillatory stress was performed in the presence of reducing agents or the L-type calcium antagonist Verapamil. Western blot analysis of whole-cell lysates and quantitative real-time PCR demonstrated no appreciable change in mitochondrial bioenergetic state.

**Conclusion:** CLOCK-BMAL1 affects repolarization of ventricular myocytes and regulated ISO-induced arrhythmogenesis through β1-AR.

**Acknowledgement/Funding:** This work was supported by grants from the National Natural Science Foundation of China (No. 81170162 and No. 81470457)
Heterozygous plakoglobin deficiency results in increased biventricular beta-catenin expression

J.K.C. Mak1, F. Syeda1, T.Y. Yu1, E. Vloumidi 1, K. Gehmlich 2, P. Kirchhof1, L. Fabritz 1, 1University of Birmingham, Centre of Cardiovascular Sciences, School of Clinical and Experimental Medicine, Birmingham, United Kingdom; 2Univ. of Oxford, Department of Cardiovascular Medicine, Radcliffe Department of Medicine, Oxford, United Kingdom

Background: The cell-cell protein plakoglobin (γ-catenin, PG) is critical for Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) pathogenesis. Development of ARVC phenotype is accelerated by endurance training. In trained heterozygous PG-deficient (PG+/−) mice with RV dilation, gap junction protein connexin43 (Cx43) levels are downregulated. It is unclear if junctional protein changes besides PG exist before ARVC onset in PG deficiency.

Purpose: To investigate specific expression of PG, β-catenin (structural homologue of PG) and Cx43 in left and right ventricles (LV & RV) from young sedentary and paced plakoglobin-α− mice.

Methods: Echocardiography on 19-wk-old PG+/− and wildtype (WT) littermates (n=21–22) and SDS-PAGE-Western blotting (5 samples per genotype for each ventricle); all experiments blinded to genotype.

Results: No apparent ARVC phenotype detected as reflected by normal RV parameters (e.g. diastolic diameter PG+/− 1.60±0.33mm vs WT 1.65±0.33mm). Decreased PG in PG+/− LV (PG+/− 0.06±0.01 vs WT 0.08±0.01; p=0.05) and RV (PG+/− 0.06±0.04 vs WT 0.09±0.07; p=0.01) consistent with heterozygous PG deficiency. Increased γ-catenin in PG+/− LV (PG+/− 0.11±0.01 vs WT 0.07±0.01; p=0.01) and RV (PG+/− 0.22±0.02 vs WT 0.13±0.01; p<0.01). No significant downregulation in total (LV PG+/− 0.24±0.03 vs WT 0.27±0.04; RV PG+/− 0.82±0.11 vs WT 0.77±0.16) or non-phospho Cx43 (LV PG+/− 0.50±0.05 vs WT 0.55±0.07; RV PG+/− 0.09±0.02 vs WT 0.14±0.02) in PG+/− group. Figure: RV PG and γ-catenin expression normalised to loading control calnexin.

Conclusions: The increased γ-catenin expression in LV and RV of young sedentary PG+/− mice with confirmed PG protein deficiency might reflect a compensatory response to reduced PG. Our results suggest Cx43 is not critically downregulated before RV arrhythmogenesis onset.

Basic mechanisms of arrhythmias 215

P1414 | BENCH
The connexin40A96S mutation is arrhythmogenic in mice after transaortic constriction operation

J.W. Schrickel1, F. Stoeccklin1, R. Andrie1, G. Nickenig1, B. Tippaporn2, M. Linhart1, R. Meyer2, 1Dept. of Medicine–Cardiology, University of Bonn, Germany; 2University of Bonn, Dept. of Physiology, Bonn, Germany

Introduction: The Connexin (Cx)40A96S mutation leads to a severe impairment of the channel function in Cx40 containing gap junctions and is a known substrate factor for the perpetuation of atrial fibrillation (AF) in the mouse heart. We now investigated the role of the Cx40A96S mutation in AF associated to hypertensive heart disease and cardiac hypertrophy after transaortic constriction (TAC) operation in the murine heart.

Methods: Investigated groups consisted of mice with Cx40hetA96S/TAC (n=15); WT/TAC, n=11) and without TAC (Cx40hetA96S/TACsham, n=12; WT/TACsham, n=10). TAC was performed and resulted in relevant hypertension and hypertensive state. Whole body ECG was recorded during 60sec were not found significantly different among all groups. Significantly more episodes of VTs were inducible in Cx40hetA96S/TAC mice compared to all other groups (Cx40hetA96S/TAC group (69%) versus Cx40hetA96S/TACsham (33%); WT/TAC (29%) and WT/TACsham (9%), p<0.01). Epicardial mapping showed significantly reduced atrial conduction

P1414 | BENCH
Melatonin protects against low potassium induced ventricular fibrillation by preventing dephosphorylation and redistribution of ventricular connexin-43 in isolated rat hearts

1Dept. of Medicine-Cardiology, University of Bonn, Germany; 2University of Medicine, Bratislava, Slovak Republic; 3Univ. of Oxford, Department of Cardiovascular Medicine, Radcliffe Department of Medicine, Oxford, United Kingdom

Background:
Hypokalemia is the most common electrolyte abnormality encountered in clinical practice and enhances the propensity for ventricular fibrillation (VF). Melatonin up-regulates the gap junction channels connexin-43 (Cx43), restoring the heart more resistant to electrically-induced VF. We hypothesized that melatonin may protect against low potassium induced VF in part by affecting Cx43.

Methods: Isolated rat hearts underwent 10 min of Krebs-Henseleit perfusion (4.5 mEq/L K+) followed by K−-deficient (1 mEq/L) perfusion in the absence or presence of 100 μM melatonin. Low K+ perfusion was maintained 25 min until VF occurred earlier. Two min VF was followed by normokalemic perfusion aimed to restore sinus rhythm. Incidence of arrhythmias and heart function were registered and analyzed using Biolab software. Ventricular tissue analysis was performed for Cx43 expression and distribution.

Results: Melatonin reduced the incidence of low K−-induced VF from 100% in controls (13/13) (P=0.028), delayed the occurrence of VF from 7 min (5–12 IQR) to 12 min (9–25 IQR) (P=0.041) and resulted in a faster recovery of sinus rhythm (P=0.047). Melatonin did not affect heart rate, PR and QT intervals as well as the incidence of transient arrhythmias. The levels of total Cx43 were unaltered by melatonin, however, trended prevented dephosphorylation and abnormal topology (lateralization) of Cx43.

Conclusions: Our results suggest that acute treatment with melatonin protects against low potassium induced VF in part due to prevention of abnormal expression and distribution of myocardial Cx43.

Reduction activated of dorsal vagal preganglionic neurons associated with synuclein pathology predisposes the heart to ventricular arrhythmia

A. Machhada1, R. Ang1, G. Ackland2, N. Ninkina3, V. Buchman3, M.F. Lythe3, S. Trapp1, A. Tinker5, N. Marina2, A.V. Gourine1, 1Dept. of Medicine-Cardiology, University of Bonn, Germany; 2Univ. of Oxford, Department of Cardiovascular Medicine, Oxford, United Kingdom; 3Cardiff University, School of Biosciences, Cardiff, United Kingdom; 4University College London, UCL Centre for Advanced Biomedical Imaging, London, United Kingdom; 5Barts and The London School of Medicine and Dentistry, William Harvey Heart Centre, London, United Kingdom

Introduction: Vagus nerve stimulation has an anti-arrhythmic effect. It reduces the refractory period, shortens atrial and ventricular the ventricular effective refractory period (vERP). Despite this evidence, there has been no attempt to study the central nervous mechanisms underlying the anti-arrhythmic effect of cardiac vagal innervation. Since neurons of the dorsal vagal motor nucleus (DVMN) project to the brainstem and heart, Cx40 homomeric channels (Cx40hetA96S) were engineered, in which we hypothesised that these neurons may confer tonic electrical stability to the ventricle. The loss of DVMN activity has emerging clinical importance with respect to the pathogenesis of Parkinson’s disease (PD), the second most common neurodegenerative disorder characterized by profound motor impairment and DVMN dysfunction, resulting in a host of autonomic abnormalities. Using triple-synuclein null (GTKO), αβγ- (→−) mice we determine whether synuclein deficiency is associated with pro-arrhythmic features within the ventricle with age-dependent loss of DVMN activity as the aetiological basis.

Methods: Young (6 months) and ageing (12–18 months) TKO and age-matched wild type (WT) mice were anaesthetised with urethane (1.3 g kg−1, i.p.) and an octapolar 1.1 F miniature cardiac electrophysiology electrode was advanced into the right ventricle. For the assessment of vERP, 10 paced beats (10 x S1) were applied using a cycle length of 85 ms, followed by a gradually shortened extra single paced beat (S2) until failure of ventricular capture. The maximum S1-S2 coupling interval was measured as the vERP. Recordings of the activity of DVMN neurons were made using coronal (200 μm) brainstem slices, obtained from 12–14 month old TKO (n=5) and WT (n=6). Wildtype Rank-Sum test.

Results: Six months old TKO mice and their WT counterparts showed no significant differences in cardiac electrophysiology: both vERP (37.0±5.2 vs 37.0±3.0 ms) and ECG features including QTC were similar. In contrast, 12–18 months old TKO mice displayed a shorter vERP (30.6±0.8 vs 43.3±1.3 ms in the WT; P<0.002, Mann-Whitney-U) and a prolonged QTC (P=0.05). Electrophysiological recordings taken from the DVMN neurons in acute brainstem slices showed significantly reduced level of DVMN activity (∼80%) in older TKO mice (1.2±0.1 vs 2.1±0.2 Hz in the WT; P=0.04, Wilcoxon Rank-Sum test).

Discussion: These data suggest that synuclein pathology is associated with reduced activity of vagal preganglionic neurons in the dorsal vagal motor nucleus leading to manifestation of a clear pro-arrhythmic substrate in the ventricle.
velocities and more functional blocks in the mutants and in mutant animals after TAC.

**Conclusions:** The heterozygous Cx40A96S mutation results in elevated susceptibility to induction of long lasting AF-episodes TAC and sham operated mice compared to WT mice. More VTs were inducible in TAC operated mice with the Cx40A96S mutation. Dysfunctioning Cx40 and associated impaired conduction properties might therefore represent a factor contributing to structurally determined AF and VT in this hypertensive mouse model.

**P1418 | BENCH**

Orthogonal pacing reveals anisotropy in isolated rat atria and direction dependence of novel electrogram markers on a hitherto unprecedented scale.

J.A.B. Zaman1, S. Al-Aidarous1, S. Alayoubi2, P.M. Patel2, J.D. Simonato3, C.M. Terracciano1, N.S. Peters1.1 School of Medicine, Cardiovascular Medicine, Stanford, United States of America;2 Imperial College London, London, United Kingdom

**Introduction:** Despite the importance of anisotropic conduction in promoting arrhythmias, quantifying the impact of orthogonal pacing on electrogram (Eg) features remains challenging. We studied the relationships between direction of pacing & novel electrogram features, relating these to underlying fibrosis at the sub-millimetre scale in a novel isolated atrial model of AF

**Methods:** Superfused isolated rat atria (SHR, BN, WKY at 3, 12 and 20 months n=40) were placed on glass micro-electrode arrays (60 x 700 μm diameter electrodes), and paced horizontally (H) & vertically (V) (1–25Hz). For each pacing interval, 2s of unfiltered unipolar Eg (total number analysed 1.5 million) were characterized in time (duration, amplitude, line length, fractionation score) & frequency (dominant frequency (DF), DF dv/dt) domain and correlated to fibrosis using a 700 μm x 700 μm overlaid grid in Fiji (fig A). 20 month old atria underwent optical mapping using di-4-ANEPPS.

**Results:** Induced AF was rare in isolated atrial preparations. Eg features displayed anisotropy with only one pacing direction showing correlation with fibrosis (fig B). Overall Eg data from each grid confirmed Eg correlation with fibrosis (fig C). APD90 was inversely correlated to Eg duration and fractionation score (r=-0.63, r=-0.66, p<0.01 for both).

**Conclusions:** Unipolar Egs correlate with fibrosis in one direction demonstrating the importance of fibrosis in tissue anisotropy. Optical mapping reveals fractionated Eg are not summated individual action potential actions. Taken together these results confirm structure function relationships exist at a microscopic scale but depend on direction of pacing. These methods should be applied to attempts to prove voltage/fibrosis relationships in human atria.

**P1419 | BENCH**

Increased aldosterone-dependent Kv1.5 recycling causes atrial fibrillation in Kcne3−/− mice

T.K. Roepke1, C.K. Koehncke2, B. Spallek3, C. Gaertner3, N. Lange3, N. Wilck3, C.M. Terracciano1, N.S. Peters1.1 School of Medicine, Cardiovascular Medicine, Stanford, United States of America;2 Imperial College London, London, United Kingdom

**Background:** Mutations in human KCNE3 have been associated with AF. KCNEs are a group of K channel ancillary subunits that modulate K channel function. Mutations in human KCNE3 have been associated with AF.

**Objective:** We used mice with global Kcne3 deletion to study the molecular pathology of KCNE3-associated AF.

**Methods and results:** Holter ECG recordings revealed spontaneous episodes of paroxysmal AF in Kcne3−/− mice. Invasive electrophysiology studies demonstrated reduced atrial effective refractory period (AERP). Episodes of paroxysmal AF were also inducible by in vivo programmed electrical stimulation in Kcne3−/− mice. The cellular correlate for AF predisposition was a significant increase in K current densities in atrial cardiomyocytes with increased IKs. Kcne3 deletion also resulted in hyperaldosteronism with adrenal gland zona glomerulosa hyperplasia. Electrophysiological alterations in Kcne3−/− mice were aldosteronedefpendent and were caused by increased Rab4, Rab5, and Rab9-dependent recycling of Kv1.5 channels to the 2D-disc region and lateral plasma membrane via activation of Akt/AS160 pathway. Treatment with spironolactone inhibited Akt/AS160 phosphorylation, reduced Rab-dependent Kv1.5 recycling, normalized AERP and atrial K current densities to the level of Kcne3+/+ mice, and reduced spontaneous AF episodes and arrhythmia induction in Kcne3−/− animals.

**Conclusions:** Kcne3 gene disruption causes AF in mice. The underlying arrhythmogenic substrate for this phenotype is an increase in aldosterone-dependent recycling of Kv1.5 channels via activation of specific Rab GTPases downstream of the Akt/AS160 pathway. The findings uncover detailed molecular mechanisms underpinning a channelopathy-linked form of AF. Furthermore, they highlight the necessity of consideringextracardiac mechanisms even in monogenic arrhythmia syndromes.

**Acknowledgement/Funding:** DFG, Friede Springer Herzstiftung, Fritz-Thyssen-Stiftung

**P1420 | BENCH**

Mechanisms of fever-induced QT prolongation in patients with KCNH2 mutations in the SS-pore region

K. Hayashi1, T. Nakajima2, S. Tange2, T. Tsuda1, Y. Tanaka1, M. Kawashishi1, K. Ohta3, Y. Kaneko1, M. Kurabayashi1, M. Yamagishi1, Kanazawa University Graduate School of Medical Science, Division of Cardiovascular Medicine, Kanazawa, Japan;2 Gunma University School of Medicine, Department of Medicine and Biological Science, Maebashi, Japan;3 Maebashi Red Cross Hospital, Department of Cardiovascular Medicine, Maebashi, Japan; Kanazawa University, Department of Pediatrics, Kanazawa, Japan

**Background:** Patients with type-2 long QT syndrome (LQT2) caused by a KCNH2 mutation in the SS-pore region have an increased risk of arrhythmia during fever. However, few data exist regarding molecular basis of this phenotype.

**Purpose:** Since there were 2 patients with marked QT prolongation and torsades de points during fever and KCNH2 mutations G584S and D609G in the SS-pore region, we sought to characterize the temperature-dependent changes of electrophysiological properties of hERG channels.

**Methods:** CHO-K1 cells were transfected with hERG cDNA, and whole-cell potassium currents were recorded using patch-clamp techniques at 25°C, 35°C, and 40°C.

**Results:** At 25°C, G584S generated functional channels, whereas D609G did not. The tail current densities (TCDs) for two mutants were significantly smaller than that for wild-type (WT). G584S and D609G/WT showed a significant negative shift in steady-state inactivation curve (SSIC) compared to WT. To mimic physiological and febrile states, we next measured currents at 35°C and 40°C. While average TCDs for WT significantly increased with rising temperature, there was no statistical difference of TCDs for G584S alone and D609G/WT between these temperatures. When we evaluated steady-state inactivation, we found that G584S significantly shifted SSIC to negative potentials compared to WT at both temperatures. The difference in the potentials of half-maximum inactivation (Vh) between WT and G584S at 40°C was significantly larger than that at 35°C. The Vh of D609G/WT at 35°C was comparable to that of WT, whereas D609G/WT significantly shifted SSIC down in a temperature-dependent manner.

**Conclusions:** These results indicate that KCNH2 G584S and D609G reduce temperature-dependent increase in TCD through an enhanced inactivation, which may account for the development of QT prolongation and life-threatening arrhythmias at febrile state in this LQT2 patient.

**Acknowledgement/Funding:** The Ministry of Health, Labor and Welfare of Japan for Clinical Research on Intractable Diseases (H26-040, to H24-033)
A missense mutation of POPDC1 affecting cAMP-binding causes limb-girdle muscular dystrophy and cardiac arrhythmia

R.F. Schindler1, C. Scotton2, S.L. Smirnich1, C. Passarelli2, S. Rinne3, K.L. Poon1, V.O. Nikolaev4, N. Decher5, A. Ferlini1, T. Brand1,1 Imperial College London, Harefield Heart Science Centre, London, United Kingdom;2 University of Ferrara, Experimental and Diagnostic Medicine, Ferrara, Italy;3 Philips University of Marburg, Physiology and Pathophysiology, Marburg, Germany;4 University Medical Center Hamburg Eppendorf, Institute of Experimental Cardiovascular Research, Hamburg, Germany

Introduction: The Popeye domain containing 1 (POPD1) gene encodes a plasma membrane-localized cAMP-binding protein, which is abundantly present in striated muscle tissue. Functional analysis in mouse mutants and zebrafish morphants established an essential role of this gene and other members of the POPD family for the maintenance of structure and function of cardiac and skeletal muscle.

Results: Here we describe a homozygous missense mutation (c.602C>T, p.S201F) in POPD1, identified by whole exome sequencing in a family with severe cardiac arrhythmia (AV-block) and limb-girdle muscular dystrophy. Sanger sequencing validated the c.602C>T SNP and confirmed that it was present in homozygosity in the two patients and their grandmother, and in heterozygosity in both non-affected parents. This mutation affects a serine residue, which is part of the ultra-conserved DSPE motif directly involved in cyclic nucleotide binding. The S201F mutant protein displayed a 50% reduction in cAMP affinity, and affected the gating properties of the potassium channel TREK1. Membrane localization of mutant POPDC1 and POPDC2 was significantly reduced in patient’s skeletal muscle biopsies, suggesting that membrane trafficking of POPDC1 may require cAMP binding. The mutation was introduced into the homozygous gene in zebrafish (popdc1-S191F) by TALEN-based gene editing. Homozygotes revealed skeletal muscle biopsies, suggesting that membrane trafficking of POPDC1 may be impaired in zebrafish the mutant popdc1 protein displayed impaired membrane trafficking.

Conclusions: Our study identifies POPDC1 as a novel gene causing cardiac arrhythmia and muscular dystrophy. Moreover, this study is the first to demonstrate that high-affinity binding of cAMP is an essential property of POPDC1 to execute its biological functions.

P1424 | BENCH
Aliskiren suppresses extracellular matrix genes in atrial fibrillation - a global mRNA profiling in the canine experimental atrial fibrillation model


Introduction: We have previously reported atrial structural remodeling involving the extracellular matrix (ECM) synthesis in a canine model of atrial fibrillation (AF). Aliskiren, a direct renin inhibitor suppressed AF inducibility and atrial tissue fibrosis; however, the underlying molecular mechanisms remain unclear. In the present study, we analyzed the global responses in mRNA expressions in atria by using RNA microarrays to investigate the molecular mechanisms regulating the atrial remodeling in AF.

Methods: The stimulation device and pacing leads were implanted in 15 beagle dogs and paced into three groups as follows: 1) pacing control group (n=6); 2) continuous atrial rapid stimulation of 400 bpm was delivered for 3 or 6 weeks without any drug administration, 2) pacing + aliskiren group (n=6); aliskiren (30 mg/kg/day) was orally administered in similarly paced dogs as the control, and 3) sham group (n=3); no pacing and no drug administration. The total RNA was purified and the global mRNA expressions were profiled by Affymetric GeneChipR microarray with Canine Genome 2.0 Array in each group.

Results: Among the fibrosis related genes, mRNA expressions of thrombospondin-1 (TSP-1) and perisinus exhibited up-regulation in 3 week pacing control, but this change became insignificant in 6 week protocol. These up-regulations were suppressed in the pacing + aliskiren group. In contrast, collagen type 1, 3, 4 (COL1, COL3, COL4) exhibited significant up-regulation in 6 week pacing control but not in 3 week protocol. This up-regulation was suppressed in the pacing + aliskiren group. Rac1 and RhoA exhibited up-regulation in both 3 and 6 week pacing control, and this up-regulation was suppressed in the pacing + aliskiren group, while transforming growth factor-b (TGF-b) did not exhibit a significant difference.

Conclusions: Aliskiren suppressed the increase in AF inducibility in a canine AF model through suppression of atrial remodeling based on tissue fibrosis. In this model, appearance of tissue fibrosis was preceded by fibrotic gene up-regulations, such as TSP1 and perisinus via activation of Rac1 and RhoA, which were suppressed by aliskiren. Those changes were independent of TGF-b in relatively earlier phase of the atrial remodeling.

P1423 | BEDSIDE
Diagnosis of arrhythmias in patients with unexplained palpitations using long term continuous monitoring

T. Faber1, K. Rybak2, G. Rieger3, L. Mangoni4, S.H.K. The5, G. Tjeerdsma6, D. Lebedev7, N. Franco8, G. De Weerd9 on behalf of the INSIGHT investigators. 1 University Heart Center, Freiburg, Germany; 2Kardiologische Praxis, Dessau, Germany; 3Medtronic Bakken Research Center, Maastricht, Netherlands; 4Medtronic Clinical Research Institute, Rome, Italy; 5Bethesda Ziekenhuis, Hoogeveen, Netherlands; 6Tjingerschans Hospital, Heerenveen, Netherlands; 7Alzamov Federal Heart, Blood and Endocrinology Centre, St. Petersburg, Russian Federation; 8Medtronic, Inc, Minneapolis, United States of America; 9Orbis Medical Center, Sittard, Netherlands

Background: EHRA recommends the use of implantable loop recorders in patients with infrequent unexplained palpitations (UP). However, there is little published evidence about this topic.

Purpose: We investigated the clinical benefits of using an insertable cardiac monitor (ICM) in patients with UP.

Methods: The observational, multicenter, international INSIGHT XT study prospectively enrolled 1003 patients implanted with an ICM for arrhythmia diagnosis, irrespective of the clinical indication. Remote monitoring was not routinely used. This report focuses on 68 patients whose primary indication for an ICM was UP.

Results: The mean age was 59.6±15.6 years and 57.4% were female. The median follow-up time was 15 months (IQR: 12–24). At baseline, 65% had hypertension, 44% had hypercholesterolemia and 7.4% had diabetes. The stroke risk CHA2DS2VASC score was low to moderate (0–1) in 31%, and high (>2) in 69% of patients (means: SD: 2.4±1.6). Palpitations at baseline were associated with symptoms of presyncope/syncope (50%), chest pain (22.1%), dyspnea (32.4%) and fatigue (14.7%). The median time to first follow-up diagnosis was 4.4 months (Q1-Q3:1.8–6.5). Fifty-five patients (81%) had at least one arrhythmia detected, among which 91% had recurrent palpitations. Cardiac arrhythmias were ruled out in 13% (n=9) and palpitations remained unexplained in 6%. ICM guided clinical actions included pacemaker implantation (13.2%), ablation (2.9%), and initiation/continuation of AAD (63.2%), antiplatelets (38.2%) and OAC (14.7%) therapies.

Arrhythmias detected by ICM

% (number of diagnoses)

Atrial fibrillation/atrial flutter/bradycardy syndrome 36.8% (25)
Sinus arrest/bradycardia 26.5% (18)
Atrial tachycardia 23.5% (16)
Ventricular tachycardia 22.1% (15)
Sinus tachycardia 14.7% (10)
High degree atrioventricular block (2nd–3rd) 8.8% (6)
Other arrhythmias 28% (19)

Conclusion: The use of an ICM enabled physicians to rule out or identify arrhythmias in 9 out of 10 patients with unexplained palpitations. This resulted in therapeutic and clinical actions in many cases.

Acknowledgement/Funding: Medtronic, Inc

MECHANISMS OF ARRHYTHMIAS AND CHANNELOPATHIES

P1424 | BEDSIDE
Three-dimensional (3D) wavemapping of human persistent atrial fibrillation

B. Pathik, T. Walters, G. Morris, J. Kalman, G. Lee. Royal Melbourne Hospital, Melbourne, Australia

Background: The mechanism of persistent atrial fibrillation (AF) remains uncertain. We sought to determine the prevalence of focal drivers and rotors in persistent AF using a novel 3D Wavemapping technique that utilizes local activation timings during AF.

Methods: Global left atrial mapping was performed in 8 patients using the multi-electrode basket catheter and analyzed offline using novel 3D wavemapping soft-

Figure 1

A and B. Activation wavefront originates from the anterior wall. C Propagates posteriorly over the roof. D. Activates the posterior wall. t = time

Basic mechanisms of arrhythmias / Mechanisms of arrhythmias and channelopathies 217
ware. Continuous one-minute AF recordings were analyzed. Activation patterns were classified into i) Wavefronts (single or multiple) ii) Rotational circuits (≥2 rotations of 360°) or focal sources with radial spread.

**Results:** Over 3000 activation patterns were analyzed. Mean AF cycle length per AF segment analyzed was 185±107 ms. Activation patterns observed were highly dynamic and heterogeneous (figure 1). The most common patterns were the presence of i. single wavefronts (74.1%), ii. multiple simultaneous wave fronts 6.4%, iii. focal activations in 17.7%. No sustained focal activity or rotors were seen. In the majority of maps (54.2%), the wavefronts appeared to originate from the anterior wall of the left atrium. Focal activity most commonly arose from the posterior wall adjacent to the left superior pulmonary veins. No wavefronts or focal activity was seen to originate from the left atrial appendage.

**Conclusion:** Activation patterns in persistent atrial fibrillation are highly heterogeneous and fast rhythms representing to be dominant type. No rotors or sustained focal activity were observed.

**P1424 | BENCH**

The risk variant rs13143308T on 4q25 predisposes to increased spontaneous calcium release and hypertrophy in human atrial myocytes

A. Herrera1, A. Llach2, C. Tarifa1, S.A. Serra1, C. Munoz-Guijosa2, A. Aranega3, D. Franco1, J. Cinca4, L. Hove-Madsen5, 1 Cardiovascular Research Center (CCR-MCC), Barcelona; 2Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; 3University of Jaen, Jaen, Spain

**Background:** Human atrial fibrillation has been associated with altered right atrial myocyte properties such as increased size and disturbed calcium homeostasis. Recently, increased risk of atrial fibrillation has been associated to single nucleotide polymorphisms on chromosome 4q25.

**Purpose:** To test this hypothesis that risk variants on 4q25 predispose to alterations in myocyte size and calcium homeostasis before the onset of atrial fibrillation.

**Methods and results:** To test this hypothesis, myocytes isolated from the right atrial appendage of 45 patients without atrial fibrillation were genotyped for two risk variants on chromosome 4q25 and ionic currents were measured using perforated patch clamp technique. Comparison of the normal (CC) and the risk variant (CT) of the single nucleotide polymorphism at rs2200733 resulted as the GT and CT variants at rs13143308 revealed that the cell size, measured as the cell capacitance, was significantly larger in myocytes from 17 patients with the GT risk variant than in those from 28 patients with the normal GG variant (77±8 vs. 56±5 pF, p=0.02). By contrast, there was no difference between myocytes from patients with CT (n=7) and CC (n=38) variants (62±9 vs. 64±5 pF, p=0.88). Similarly, the frequency of transient inward currents activated by spontaneous calcium release from the sarcoplasmic reticulum was almost 4-fold higher in the GT risk variant than in the normal GG variant (1.41±0.33 vs. 0.37±0.10 events/min, p=0.05, n=25)

**Conclusion:** Presence of the risk variant rs13143308T on chromosome 4q25 predisposes human right atrial myocytes to present hypertrophy and increased spontaneous calcium release, which may contribute to increase the risk that persons with this variant develop atrial fibrillation.

**Acknowledgement/Funding:** Spanish Ministry of Science and Innovation [SAF2011-30312] and [CNIC-2009-08]

**P1425 | BENCH**

Stabilization of A78T-HERG that causes Long QT syndrome type 2 by heat shock protein family

T. Kondo1, J. Miale2, K. Ogura2, M. Kato3, K. Itskuda4, K. Yamamoto5, Y. Shirayoshi1, I. Hisatome1, 1Tottori University Hospital, Yonago, Japan; 2Tottori University, Department of Cardiovascular Medicine, Yonago, Japan; 3Tottori University, School of Medicine, Division of Regenerative Medicine and Therapeutics, Yonago, Japan

**Background:** The human ether-a-go-go-related gene (HERG) encodes the α subunit of the potassium current IKr. Its mutations destabilize the HERG protein and cause long QT syndrome type2 (LQT2). We studied the stability of a novel mutant A78T-HERG carrying the missense mutation in its intracellular loop and examined the effects of heat and heat shock protein (HSP) family on its stability.

**Aims and methods:** The aims of this study were to analyze the properties of A78T-HERG protein and investigate whether HSP family can improve the stability of A78T-HERG protein or not. To analyze the protein expression patterns of the wild type HERG (WT-HERG) channel and the A78T-HERG channel proteins, we conducted transfection of the WT flag-tagged-herg gene and the mutant flag-tagged herg gene into HEK293 cells and western-blotting for evaluation of the HERG protein expression levels and the ubiquitination levels. Immuno staining of the gene-transfected cells was also performed to evaluate the cellular localization of the HERG proteins. We conducted patch-clamp of the cells transfected with WT and A78T genes for the measurement of IKr. HEK293 cells were co-transfected with A78T mutant gene and either HSP70, 90, 40, and 27 to investigate whether these HSP family can improve the stability of A78T-HERG protein.

**Results:** In transfected HEK293 cells, the level of the mature form of A78T-HERG at 155kDa was remarkably lower than that of WT-HERG associated with significant increases in its ubiquitination. There were no changes in the levels in its immature form of A78T-HERG, whereas WT-HERG was predominantly localized on the plasma membrane. This localization was also supported by the small amplitude of IKr through A78T-HERG associated with small tail currents. Heat shock for 1 hour significantly increase of mature forms of A78T-HERG associated with increase of amplitude of IKr. It has been also tested whether HSP family could stabilize A78T-HERG. Hsp90, 70 and 27 but not HSP40 increased the mature form of the A78T-HERG proteins, indicating their stabilization.

**Conclusions:** A78T-HERG showed the impairment of trafficking to plasma membrane, and was degraded by the ubiquitin-proteasome pathway. Hsp70, 90, and 27 significantly increased the mature form of A78T HERG, and Hsp family might be a potential target in the treatment of LQT2 resulting from A78T HERG mutation.

**P1427 | BEDSIDE**

ST-segment elevation in Brugada syndrome patients is associated with activation and fractionated epicardial electrograms in the right ventricular outflow tract

J.N. Ten Sande1, R. Corone1, C.E. Corrath1, A.H.G. Diessen1, J.R. De Groot1, H.L. Tan2, K. Nademane2, A.A.M. Wilde1, J.M.T. De Bakker1, P.F.H.M. Veld1, 1Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands; 2Pacific Rim Electrophysiology Research Laboratory, Cedars-Sinai Medical Center, Los Angeles, United States of America

**Background:** Brugada syndrome (BrS) is characterized by a typical ECG pattern (coved-type ST-segment elevation and a negative T-wave in right precordial leads).

**Purpose:** We aimed to determine the pathophysiological basis of the ST-segment in the BrS-ECG with the use of data from various epicardial and endocardial right ventricular activation mapping procedures in 6 BrS patients and 6 non-BrS controls.

**Methods:** In 8 patients (2 BrS, 6 controls) with atrial fibrillation an epicardial 8x6 electrode grid electrode (interelectrode distance 1 mm) was placed epicardially on the RV outflow tract (RVOT) prior to Video Assisted Thoracic Surgical Pulmonary Vein Isolation (VATS-PVI). In two other BrS patients endocardial, epicardial RV (CARTO) and body surface mapping (BSM) was performed. In two additional BrS patients we performed decremental pre-excitation of the RVOT during endocardial RV mapping. During VATS-PVI and CARTO mapping.

**Results:** BrS patients (n=4) showed greater activation delay and more fractionated electrograms in the RVOT region than controls (n=6). The area with ST-segment elevation on the BSM-ECG was anatomically correlated with the area on the RVOT epicardium with fractionated electrograms and both regions expanded after infusion of Amjalone. The latter suggests that discontinuous conduction at the RVOT underlies electrogram fractionation. ST-segment elevation diminished after pre-excitation of the RVOT (n=2).

**Conclusions:** We conclude that the ST-segment elevation characteristic for BrS is caused by activation delay and is associated with discontinuous conduction in the epicardial RVOT.

**P1428 | BENCH**

Current and expression of HERG mutation L539fs/47-558W are regulated by chronic intracellular potassium concentration

Y. Lv1, Z. Liu1, C. Sun2, A. Zhang3, W. Han2, G. Li2, J. Wang4, S. Pan1, J. Pan1, 1Shanxi Provincial People's Hospital, Department of Cardiology, X'ian, China, People's Republic of; 2First Affiliated Hospital of Xian Jiaotong University, X'ian, China, People's Republic of

**Background:** Congenital or inherited long QT syndrome (cLQTS) often causes syncope and sudden cardiac death, especially in adolescents. LQT2 is the major
subtype in China. And LQT2 is highly related with mutations of human ether-a-go-go-related gene (HERG), which encoding a subunit activation of rapid delayed rectifier potassium channel (IKr). extracellular potassium ([K+]o) is known to facilitate LQTS by reduction in expression level and function of HERG.

**Purpose:** This study aimed to investigate the possible involvement of the rare large LQT2 patient cohort, L539fs/47-558W, in LQT2 and its regulation by chronic intracellular K+ concentration.

**Methods:** The wild-type HERG and its mutant L539fs/47-558W were transfected into HEK293 cells. After incubated with serial diluted K+ culturing medium 8h, chronic extracellular low K+ prompted the HERG currents in both wild-type and heterozygous mutant, especially in the latter.

**Conclusions:** Chronic K+ deprivation caused accelerated conduction with prolonged refractoriness and electrical instability. This study aimed to investigate the possible involvement of the rare large LQT2 patient cohort, L539fs/47-558W, in LQT2 and its regulation by chronic intracellular K+ concentration.

**Results:** Expression of HERG mutant gene L539fs/47 decreased which was not affected by extracellular K+ concentration. The mutant protein had partial retention in the cell membrane. The high extracellular K+ might enhance the stability of wild-type and this mutant channel protein in cell membrane. Chronic low K+ reduced their protein expressions.

**Methods:** The 135- and 155-kD two protein bands were found in wild-type HERG, while the 60-kD band was identified in mutant truncated L539fs/47. The 60-kD band was significantly less than 155-kD band. Mutant 60- kD and WT 155-kD bands up-regulated by high [K+]o.

**Conclusions:** Homozygotic hERG L539fs/47-558W. Homozygotic HERG L539fs/47-558W mutation function, indicated by no responses to chronic K+ fluctuation. Elevation of chronic [K+]o demonstrated cardio-protective effects by enhancing channel function of HERG mutant L539fs/47-558W in heterozygous state. In other words, persistent extracellular K+ concentration up-regulates heterozygous HERG and channel of HERG mutation L539fs/47 in HEK 293 cells.

**P1420 | BEDSIDE**

**Phase contrast MRI reveals impaired diastolic relaxation and prolonged contraction duration in LQTS patients**

- J. Brado1, M. Dechant2, M. Menza3, A. Komanscek2, J. Geiger4, B. Stiller2, C. Bode1, B.A. Jung2, K.E. Odening1.

- 1 University of Freiburg, Cardiology and Angiology I, Freiburg, Germany; 2 University of Freiburg, Pediatric Cardiology, Freiburg, Germany; 3 University of Freiburg, Medical Physics, Department of Radiology, Freiburg, Germany; 4 Children’s Hospital Zurich, Zurich, Switzerland.

**Background:** We have previously identified a regionally heterogeneous diastolic dysfunction with reduced diastolic myocardial peak velocities and prolonged contraction duration in transgenic LQT type 1 and type 2 rabbits. Moreover, the close link between regional electrical and mechanical dysfunction allows the differentiation between LQT2 rabbits with high and low arrhythmogenic risk solely based on MRI data.

**Purpose:** In this clinical pilot study, we aimed at investigating whether a similar pattern of regional electrical and mechanical dysfunction allows the differentiation between LQT2 rabbits with high and low arrhythmogenic risk solely based on MRI data.

**Methods:** Pediatric patients with genotyped LQTS and healthy age- and sex-matched controls underwent phase contrast MRI to analyze radial (VR) and longitudinal (Vz) myocardial velocities during systole and diastole in LV base, mid, apex, 12-lead and 24-h holter ECG were recorded to assess heart rate corrected QTc duration and arrhythmogenic risk.

**Results:** We included 9 LQTS patients (4 boys, 5 girls, average age 12.1±1.1 years) and 9 healthy controls (4 boys, 5 girls, average age 10.6±0.5 y, p<0.05). 7 patients had LQT1 (KCNQ1 mutation), one patient had LQT2 (KCN2 mutation) and one patient LQTS (KCN1 mutation). None of the patients has experienced ventricular tachycardia yet and all patients received anti-arrhythmic beta blocker therapy. QTc duration was significantly prolonged in LQTS patients compared to healthy controls. LQTS 472±15.9 ms vs. controls. 417±6.1 ms; p<0.001. Heart rate was slightly but not significantly slower in LQTS patients (LQTS, 69±1.5 min-1 vs. controls 82±3.9 min-1).

**Conclusion:** In the present pharmacologic model of early repolarization, administration of ranolazine led to a significant decrease of spatial dispersion of repolarization (+14ms, p<0.05) as compared with sole pinacidil treatment. Furthermore, administration of ranolazine led to a significant decrease of spatial dispersion of repolarization (+13ms, p<0.05).

Under baseline conditions, ventricular fibrillation (VF) was inducible by a standardized pacing protocol including programmed stimulation and aggressive burst stimulation in 4 of 12 hearts (16 episodes). After application of 1 μM pinacidil 8 of 12 hearts were inducible (248±54 ms, p<0.05) as compared with sole pinacidil treatment. Furthermore, administration of ranolazine led to a significant decrease of spatial dispersion of repolarization (+13ms, p<0.05).

**Methods and results:** 12 rabbit hearts were isolated and Langendorff-perfused. After obtaining baseline data, pinacidil, an IKAP+ channel opener, was infused in these preparations. The peak of an early repolarization (−13 ms, p<0.05) as compared with sole pinacidil treatment. Furthermore, administration of ranolazine led to a significant decrease of spatial dispersion of repolarization (+13 ms, p<0.05).
Background: Initiation of re-entry depends upon the time interval between the arrival of the premature wavefront distal to the initial region of block and regaining of excitability in tissue proximal to the initial region of block (Re-entry Vulnerability Index (RVI), ms). Locating critical regions susceptible to such unidirectional block has clinical relevance. Purpose: To develop a novel quantitative metric of the difference between activation and repolarization intervals measured from pairs of spatial locations during premature stimulation to accurately locate critical sites of re-entry formation.

Methods: Optical mapping was performed on sheep ventricular preparations along with computational simulations during S1-S2 arrhythmia-induction protocols. A spatial map of RVI was calculated based on matrix analysis of local activation and repolarization times between pairs of recording sites for the first premature beat following the S2.

Results: The calculated RVI in both cases successfully highlighted a distinct low region co-located with the site of initial block and re-entry (see Figure 1). Importantly, the simulations further showed that such a region of low RVI could also be identified with less-premature S2 where complete re-entry did not occur (bidirectional block). Simulations also showed that phase singularities associated with spiral waves were clustered in the vicinity of these regions of low RVI. Clinical applications were suggested for both computational and experimental studies.

Conclusions: We have developed an algorithm which spatially quantifies vulnerability to re-entry using intervals between local repolarization and activation times of a spatial map of RVI calculated based on matrix analysis of local activation and repolarization times between pairs of recording sites for the first premature beat following the S2. The calculated RVI in both cases successfully highlighted a distinct low region co-located with the site of initial block and re-entry (see Figure 1). Importantly, the simulations further showed that such a region of low RVI could also be identified with less-premature S2 where complete re-entry did not occur (bidirectional block). Simulations also showed that phase singularities associated with spiral waves were clustered in the vicinity of these regions of low RVI. Clinical applications were suggested for both computational and experimental studies.

Acknowledgement/Funding: The Centre of Excellence in Medical Engineering funded by the Wellcome Trust and EPSRC: WT088641/Z/09/Z

Figure 1

Conclusions: After its description, there was an better awareness of the BS, leading to a transient increase in the number of patients diagnosed per year. The inclusion of less severe forms of the disease and the better understanding of risk factors has lead to a significant decrease of the number of EPS and ICD implantations.

DEVICE THERAPY

P1435 | BEDSIDE
Preserved myocardial viability predicts response to cardiac resynchronization therapy better than targeted left ventricular placement

J. Ghouse, C. Theil Have, P. Weeke, J.B. Nielsen, S.P. Olesen, N. Grarup, A. Linneberg, O. Pedersen, J.K. Kanters, M.S. Olesen. Rigshospitalet - Copenhagen University Hospital, Laboratory of Molecular Cardiology; Department of Cardiology, The Heart Centre, Copenhagen, Denmark. 2University of Copenhagen, The Novo Nordisk Foundation Center for Basic Metabolic Research, Faculty of Health and Medical Sciences, Copenhagen, Denmark. 3University of Copenhagen, Copenhagen, Denmark

Background: We studied if variants previously reported to associate with congenital long QT syndrome have little or no effect on the QT interval

Methods and results: All genetic variants previously associated with cLQTS were surveyed using the Human Gene Mutation Database. We screened a Danish cohort of 1358 variants previously reported to associate with cLQTS. We screened a Danish cohort of 1358 variants previously reported to associate with cLQTS. Of these, 10 variants were found in 33 individuals. Electrocardiogram results showed that the cLQTS-associated genes, are more prone to experience syncope compared with non-carriers. The aim of the study was to echocardiographically investigate impact of myocardial viability and targeted LV lead placement on CRT efficacy.

Conclusions: Preserved myocardial viability was associated with better CRT efficacy.
Results: Responders (24 patients, 59%) showed a higher occurrence of preserved myocardial viability compared with non-responders (77% vs. 21%, P=0.0017). LV lead was targeted at the latest site of peak contraction in 25 patients (61%). A number of optimally targeted LV leads were not significantly different in responders and non-responders group (64% vs. 56%, P=0.7460).

Conclusion: Our findings demonstrate that preserved myocardial viability plays a more important role in predicting response to cardiac resynchronization therapy compared to targeted LV lead placement.

**P1436 | BEDSIDE**

**Electrical dyssynchrony in patients with left bundle branch block and factors related to its severity**

D. Duplyakov1, Z. Voitsekhova2, E. Sysyuenkova2, V. Golubova2, S. Kholdulin2,
1Samara Regional Cardiology Dispensary, Samara, Russian Federation; 2VAZ Medical Center, Togliatti, Russian Federation

Significant impact of left bundle branch block (LBBB) on heart failure (HF) development and progression has been demonstrated in many clinical studies. However, the true incidence of LBBB in a population, and factors related to its severity are not well established.

**Aim:** To evaluate the incidence of LBBB among patients <70 years of age, and to identify factors associated with the severity of electrical dyssynchrony.

**Methods:** 65,397 patients (35,585 male (59%) and 29,812 female (41%), mean age 52.7±12.5 yrs) underwent annual check-up with ECG screening between February 2008 and December 2012, followed by thorough examination. Congenital heart diseases, valvular diseases, cardiac tumors, and cardiomyopathies were exclusion criteria.

**Results:** During this period 104 (0.16%) patients with LBBB (51 male and 53 female, mean age 57.5±8.6 yrs) have been identified, and 11 of them met exclusion criteria. Among the remaining 93 patients: 35 (37.6%) had a history of coronary artery disease with 34 of them from MI. All of them underwent coronary angiography. Arterial hypertension has been diagnosed in 67 (72.0%) patients, and left ventricle hypertrophy was revealed in 32 (47.7%) of them. Signs of previous myocardial infarction were identified by coronary MRI with gadolinium in 22 patients (23.7%). Only 4 (4.3%) patients had no features of CVD after invasive angiography. Arterial hypertension has been diagnosed in 67 (72.0%) patients, and left ventricle hypertrophy was revealed in 32 (47.7%) of them. Signs of previous myocardial infarction were identified by coronary MRI with gadolinium in 22 patients (23.7%). Only 4 (4.3%) patients had no features of CVD after invasive angiography.

**Conclusion:** LBBB is not a rare finding in everyday clinical practice and is associated with a number of cardiovascular diseases.

**P1437 | BEDSIDE**

**Involvement of left anterior fascicular block and clinical impact of the intra-ventricular mechanical dyssynchrony caused by right ventricular pacing among the patients with normal ejection fraction**

M. Okada, K. Kashiwase, A. Hirata, K. Ueno, R. Amiya, Y. Ueda. Osaka Police Hospital, Osaka, Japan

**Background:** Right ventricular pacing (RVP) prolongs ventricular activation time and sometimes induces mechanical dyssynchrony among the patients with normal ejection fraction (EF). However, the clinical impact of the dyssynchrony motion is unknown.

**Objective:** To examine if the pacing-induced dyssynchrony motion is associated with the infranodal conduction abnormality before pacing, and if it has clinical impact on the patients’ prognosis.

**Methods:** and results: We retrospectively investigated consecutive 104 patients with complete atroventricular block and normal EF who received pacemaker implantation with the ventricular lead placed in the right ventricular septum. The relationship between the site of conduction disturbance at baseline and the occurrence of left ventricular dyssynchrony motion under RVP was analyzed. Forty-four patients (42%) had normal QRS duration (<120ms), while 60 patients (58%) had QRS duration >120ms. Among 60 patients with QRS duration >120ms, 28 patients had complete right bundle branch block (CRBBB) and 10 had left anterior fascicular block (LAFB) with left anterior fascicular block (CLBBB), and 2 patients had non-specific intraventricular conduction disturbance. Dyssynchrony motion was found in 10 (9.7%) patients at baseline without RVP and in 41 (39%) patients under RVP. Newly occurred dyssynchrony motion by RVP was strongly associated with CRBBB and LAFB and LFBB pattern (OR=3.9, p=0.009) at baseline. Dyssynchrony motion occurred more frequently in patients with LAFB at baseline than in those without LAFB regardless of the QRS duration.

During the follow-up period of 4.0±1.9 years, the dyssynchrony motion did not have clinical impact on the prognosis (new onset atrial fibrillation, heart failure hospitalization, and all cause death). However, it appeared to have non-significant correlation with device-detected atrial fibrillation (HR 1.81, p=0.08).

**Conclusion:** Among the patients with normal EF, the presence of LAFB at baseline was significantly associated with the occurrence of intra-ventricular mechanical dyssynchrony motion by RVP. The dyssynchrony motion did not have significant clinical impact on the patients’ prognosis.

**P1438 | BEDSIDE**

**Unexpected malfunctions and viability loss with current co-radial pacemaker leads: two-year follow up study**

M. Ishimura, M. Ueda, K. Miyazawa, T. Kajiyama, N. Hashiguchi, Y. Kobayashi, Chiba University Graduate School of Medicine, Cardiovascular Medicine, Chiba, Japan

**Introduction and purpose:** Lead fractures are one of the most important problems in patients after pacemaker implantations. The Petite™ S8ERB leads are manufactured using a hexafill coil consisting of two conductors connected to the anode and two conductors connected to the cathode, which were implanted for a pacing lead in our hospital from July 2010 and December 2012. The purpose of this retrospective study was to reveal the performance of the Petite™ S8ERB leads and to clarify the failure characteristics of pacing leads with a hexafill coil.

**Methods and results:** This study included 124 Petite™ S8ERB leads which were implanted for permanent ventricular pacing. The mean follow-up duration after the implantation was 38.5±14.5 months. Of the 124 Petite™ S8ERB leads, 10 lead failures occurred. In seven cases, the lead impedance leaped almost simultaneously in two years without any preceding decline. Noise oversensing with the normal impedance. Low impedance and the polarity switch were found in one case respectively. In three of ten cases, the fractured coils were found within the anchoring sleeve. In another seven cases, the fracture sites were unknown.

**Conclusion:** Hexafill coil pacing lead failures characteristically tend to exhibit a lead in the lead impedance without previous temporary decrease in the lead impedance. These findings clearly showed the Petite™ S8ERB leads have a certain reason for electrical dysfunction.
P1440 | BEDSIDE

Atrial lead characteristics, time from implantation and atrial high rate episodes compatible with silent atrial fibrillation: an unintentionally provoked situation?

J. Benezet Mazaruco1, J.A. Iglesias1, A. Del Rio Lechuga2, M. Cortes1, J.J. De La Vieja1, P.P. Perez1, J.M. Rubio1, M.A. Quinones1, P. Sanchez-Borque1, L. Checinski1, A. Slawuta2, J. Moszczynska-Stulin3, J. Gajek4.

Abstract P1439 – Figure 1. PETite overview of all detective

Introduction: Identification of atrial fibrillation (AF), even in the absence of symptoms, is crucial to permit an early intervention avoiding thromboembolic events as first symptom. Multiple studies have shown that atrial high rate episodes (AHREs) detected in cardiac implantable electronic devices (CIED) are related to an increased risk of stroke. Our group has also reported that AHREs are independently associated to a higher incidence of silent ischemic brain lesions (IBL) on CT-scan.

Purpose: To evaluate the relation between AHREs occurrence and time from atrial lead implantation and type of lead fixation used.

Methods: We analyzed prospectively the incidence of AHREs >5 min compatible AF and the presence of IBL on CT-scan in patients with dual-chamber CIED and no history of AF attending to time from implantation (<3 months vs. >3 months from implantation) and the type of atrial lead used (active vs. passive vs. VDD).

Results: We evaluated 124 consecutive patients (62% men, aged 74±10 years-old) during a mean follow-up of 25.6 months. Mean CHADS2 and CHA2DS2VASc scores were 2.0±1.1 and 3.6±1.5, respectively. CIED included 110 pacemakers, 91 DDD (73%) and 19 VDD (15%), and 14 CDI/CRT devices (12%). Time from implantation was >3 months in 89 patients (72%) and <3 months in 35 (28%). Patients with AHREs (52%), passive in 41 (33%) and VDD leads in 19 (15%). AHREs were detected in >1 VDD patient (5%) and in 13 atrial lead patients (12%) at 3 months of follow-up and in 6 (31%) and 34 patients (32%) respectively over the 3 first months; p=ns. The type of fixation used was active in 64 patients (52%), passive in 41 (33%) and VDD leads in 19 (15%). AHREs were detected in 1 VDD patient (5%) and in 13 atrial lead patients (12%) at 3 months of follow-up and in 6 (31%) and 34 patients (32%) respectively over the 3 first months; p=ns. AHREs were present in 5 passive fixation patients (12%) and 8 active fixation patients (12.5%) at 3 months and in 17 (41%) and 17 patients (28%) respectively after; p=ns. In this population, the presence of IBL on CT-scan was related with the presence of AHREs >5 min (OR 3.7 [1.5 - 9.1; p=0.05]) but not with the time from implantation, the CIED implanted or the atrial electrode used.

Conclusions: CIED can accurately detect AHREs compatible with silent AF. These AHREs are really prevalent in patients receiving CIED and has been associated to worse outcomes including a higher incidence of silent ischemic brain lesions on CT-scan. Our data show that these episodes are not related with the type of atrial lead used and time from implantation.

P1441 | BEDSIDE

Long lasting ventricular pacing in patients with SSS increases left ventricle diastolic dysfunction and myocardial fibrosis even after DDD pacing upgrade


1Wroclaw Medical University Hospital, Wroclaw, Poland; 2Klodzko County Hospital, Department of Cardiology, Klodzko, Poland; 3Wroclaw Medical University, Wroclaw, Poland

In patients with SSS, atrial or atrioventricular pacing is the therapy of choice. In some patients ventricular pacemakers were implanted in the past and these systems were upgraded to DDD pacing over time. VVI pacing can be deleterious in terms of symptoms in SSS patients but moreover it can be harmful to the heart muscle.

Abstract P1440 – Figure 1. PETite overview of all detective

There were no differences in basic echocardiographic parameters such as LVEDD, LVEDS, EF, LA. There was a trend towards greater percentage of paroxysmal atrial fibrillation in study group (35/61 vs 23/57, p=0.08).

Conclusions: Long lasting ventricular pacing in patients with SSS increases left ventricle diastolic dysfunction and myocardial fibrosis parameters. This could negatively influence the atrial arrhythmogenesis.

P1442 | BEDSIDE

Bachmann’s bundle pacing reduces the risk of chronic atrial fibrillation development

M. Kisi5, A. Slawuta2, P. Skoczynski3, J. Moszczynska-Stulin4, J. Gajek5.

5Wrocław Provincial Specialist Hospital, Wrocław, Poland; 4Klodzko County Hospital, Department of Cardiology, Klodzko, Poland; 2Wrocław Medical University Hospital, Wrocław, Poland; 3Wroclaw Medical University, Wroclaw, Poland

Background: Patients treated for sick sinus syndrome (SSS) have interventional conduction disorders which make them relatively often suffer from atrial fibrillation.

Purpose: To assess the hemodynamic and structural consequences of long term ventricular pacing in patients with SSS and primary VVI pacemaker implantation and afterwards pacing system upgrade to DDD.

Methods: The study group consisted of 61 patients (44 F, 17 M), aged now 77±8 years, implanted with VVI pacemaker for 10±54 months, and then upgraded to DDD pacing lasting 57±41 months. The control group included 57 patients (39 F, 22 M), aged now 79±6 years, implanted primarily with DDD pacemaker, with mean pacing time 96±38 months. Standard echocardiographic measurements were performed in both groups. Transmural diastolic flow parameters were assessed as indicators of left ventricle filling pattern. N-terminal procollagen-I-peptide measurements were used as markers of myocardial fibrosis.

Results: are shown in Table:

There were no differences in basic echocardiographic parameters such as LVEDD, LVEDS, EF, LA. There was a trend towards greater percentage of paroxysmal atrial fibrillation in study group (35/61 vs 23/57, p=0.08).

Conclusions: Long lasting ventricular pacing in patients with SSS increases left ventricle diastolic dysfunction and myocardial fibrosis parameters. This could negatively influence the atrial arrhythmogenesis.

P1443 | BEDSIDE

Puncture with care: as opposed to conventional wisdom, the course of the axillary vein’s course is too big to support such claims


Background: Lead implantation via the axillary vein provides quick access to cardiac implantable electronic devices (CIED) but the lead puncture site is reported to be inferior compared to the femoral approach. The placement of atrial leads is usually performed via the internal jugular vein (IJV) with no complications. Details on the course of the axillary vein and its complications are relatively small and have been summarized in separate studies.

Purpose: To assess the course of the axillary vein in a real-life population of...
PT. undergoing implantation of a pacemaker (PM) or implantable cardioverter-defibrillator (ICD) and calculate the likelihood of a successful venipuncture performed strictly according to the methods proposed by Burri et al. and Antonelli et al.

Methods: We reviewed all venography cine sequences acquired during implant procedures in the cath lab of our institution between November 2013 and November 2014. We only included studies performed before the first venous access attempt was made. 89 patients were included in the study (PM: 52 pts., ICD/ CRT-D: 37 pts.). Implants were performed on pts.' left side in 73 and the right side in 16 cases.

Using imaging software, the course of the vein was described by measuring the angulation of the axillary vein and the clavicle relative to the body’s longitudinal axis and the vein’s intersection with the rib cage margin. A virtual needle trajectory was drawn and its overlap with the axillary vein’s course assessed for both methods.

Results: Of the 89 patients analyzed, a fluoroscopy-only guided lateral puncture as described by Burri et al. would have been successful in 55 (62%) of patients, whereas the more medial first rib approach described by Antonelli et al. would have been successful in 64 (72%) of patients. Failure was neither predicted by patient demographics, nor the BMI nor by any signs apparent from the fluoroscopy without venous contrast.

Conclusion: If performed strictly as described, both the lateral and the first rib approach have a relatively high failure rate. Subsequent iterative changes of the needle position increase patient discomfort, the risk of patient injury and of long-term mechanical damage to the lead. On the other hand, venogram-guided puncture of the axillary vein was performed without any complications in all 89 pts. included in this study. Venography is a simple, quick, inexpensive and low-risk procedure. As the course of the axillary vein is highly variable and clinically unpredictable, contrast venography should always be performed before axillary vein puncture is attempted.

P1444 | BENCH
Effectiveness of closed loop stimulation pacing in preventing disabling cardioinhibitory vasovagal syncope. A single-center experience

I. Anguera Campos, F. Rodriguez, A. Di Marco, P. Dallaglio, X. Sabate, A. Cequier. Bellvitge University Hospital, Barcelona, Spain

Background: Vasovagal syncope (VVS) is a benign disease. However, in rare occasions, cardioinhibitory vasovagal syncope is recurrent and can produce severe physical injuries and psychological impairment, including a substantial limitation of social and working life. The Closed Loop Stimulation (CLS) algorithm is a form of rate-adaptive pacing, which responds to myocardial contraction dynamics, by measuring variations in right ventricular intracardiac impedance. During an incipient VVS it increases paced heart rate and avoids bradycardia, arterial hypotension and syncope.

Objectives: To determine whether dual-chamber rate-adaptive Closed Loop Stimulation pacing is effective in the prevention of recurrences of cardioinhibitory vasovagal syncope.

Methods: Patients with severe and recurrent vasovagal syncope and positive Head Up Tilt Test (HUTT) with significant cardioinhibition received a DDD-CLS pacemaker (VIVITRONIC®-VYLSYS DR, Biotronik GmbH Co.) and were reviewed. Severely cardioinhibited during HUTT was defined as bradycardia <40 bpm during >10 seconds or prolonged asystole (>3 seconds). Pacemakers (PM) were implanted if a minimum of 5 syncopal events had occurred.

Results: A total of 18 patients had a DDD-CLS PM implanted (10 males, mean age 49 years, range 27–76). Tilt test was positive in 17 patients and 4 patients had a subcutaneous holter recording implanted. Structural heart disease was present in 2 patients (aortic mechanical prostitution and ischemic heart disease in each patient). A total of 175 syncopal episodes had occurred before PM implantation (median of 8 syncope per patient, range 5–20). After a mean follow-up of 30±6 months during active CLS pacing, one a single syncopal episode was documented (median of 0 syncope per patient, which represents a 99% reduction in the risk of recurrence of syncope).

Conclusion: CLS pacing in patients with recurrent and severe VVS with significant cardioinhibition during HUTT contributes to a major reduction in the risk of subsequent syncope.

THROMBOSIS AND COAGULATION

P1445 | BENCH
Oxidative profile of intracoronary thrombi in STEMI patients increases with elapsed pain-to-PCI time

T. Pedro1, I. Ramaida1, J. Cubedo1, V. Martin-Yuste2, M. Sabate2, L. Badimon1.
1 Barcelona Cardiovascular Research Center (CSIC-ICC), IIB-Sant Pau, Hosp Sant Pau, UAB, Barcelona, Spain; 2Hospital Clinic de Barcelona, Department of Cardiology, Barcelona, Spain

Background: Distal embolization of intracoronary thrombi can be a complication in patients with ST-elevation myocardial infarction (STEMI), which is associated with impairment of myocardial perfusion and poor clinical outcome. Increasing evidence suggest thrombus composition as a key component for incidence of embolization during primary percutaneous coronary intervention (PCI). To this respect, we have recently reported that elapsed pain-to-PCI time and hence ischemic time has impact in the composition of STEMI thrombus.

Purpose: The present study was aimed to identify thrombus proteins related to oxidative stress, with a dynamic evolution in relation to pain-to-PCI elapsed time, and with potential relevance to the evolution of the ischemic process.

Methods: PEFs for STEMI-patients presenting for PCI were included in the study (n=28). Intracoronary thrombi obtained during PCI were analyzed by 2D-electrophoresis and MALDI-ToF mass spectrometry. Differential proteomic profiles were identified by comparing early thrombus (<3 hours pain-to-PCI) (T3) and aged thrombus with longer evolution (>4 hours) (T6) by using the PD-Quest analysis software. In silico analysis of protein function and networks was performed with the Ingenuity Pathway Analysis (IPA) software.

Results: Occulsive thrombus of longer evolution time (>6 hours) presented changes in proteins that are involved in the mitochondrial electron transport chain of the cell and therefore regulate the steady state concentrations of active species. Thus, T6 thrombi showed 4-fold increase in the complex II protein succinate dehydrogenase (p=0.002) and a 3-fold decrease in the mitochondrial membrane ATP synthase, which might turn in the impairment of ATP production and the increase of protons generated by electron transport complexes of the respiratory chain. Besides, thrombi with more than 6 hours evolution showed a significant decrease in proteins, as superoxide dismutase (2fold, p<0.01) and peroxiredoxin-2 (2fold, p<0.01), which are directly involved in eliminating anion free radicals. Antioxidant systems related to mitochondrial heat shock protein 70 and the peptide-yl cis-trans isomerase A, were 2-3fold decreased (p<0.01) in thromb of more than 6 hours from pain-to-PCI.

Conclusion: Occulsive thrombi of longer evolution creates an oxidative niche at culprit site that exacerbates vascular and ischemic damage worsening patient outcome.


P1446 | BENCH
In vitro generated high ploidy megakaryocytes show overexpression of genes involved in platelet activity and thrombosis

F.A. Chourdy1, S. Garcia1, K. Downes1, M. Kostadima1, J. Martin2, A. Mathur3, M. Frontini1, W.H. Ouwehand1.
1 University of Cambridge, Cambridge, United Kingdom; 2University College London, London, United Kingdom; 3Barts Health NHS Trust, London, United Kingdom

Introduction: Mean platelet volume is increased in the setting of acute myocardial infarction (AMI) and is a poor prognostic marker despite antplatelet use. The megakaryocyte (platelet precursor) that resides in the bone marrow has a mean physiological ploidy of 16n. Megakaryocyte size and DNA content are also shown to be increased in AMI. To investigate if megakaryocytes of higher ploidy are transcriptionally different from normal, we studied the ability to produce large and more active platelets we performed RNA sequencing in megakaryocytes cultured with or without dimethylsulfoxid (dMSF), an exogenous peptide that drives megakaryocyte ploidy further than previously documented by non-selective aurora kinase inhibition.

Methods: Human adult blood CD34+ derived megakaryocytes from 4 individuals underwent 3 days of culture with or without 5μM dMSF. RNA from untreated and treated cells was sequenced and used for differential gene and transcript expression analysis.

Results: Mean ploidy in the untreated megakaryocytes was 2n while dMSF treatment drove mean ploidy to approximately 8n associated with morphological increase in size and nuclear multilobulation. Differential gene expression analysis revealed that in megakaryocytes that had been driven to high ploidy levels, 33 genes were downregulated while 65 genes underwent significant upregulation when compared with untreated megakaryocytes. Gene ontology analysis demonstrated that the downregulated genes were significantly enriched for transcripts involved in the cell cycle including CCDC45, chromatin assembly factor 1β, and MCMs. In contrast, genes that were upregulated in higher ploidy megakaryocytes were significantly enriched for transcripts involved in haemostatic and coagulation pathways including VWF, coagulation factor XIII, thrombin receptor-like 2, PDGFα, thrombospondin 1 and plasminogen activator inhibitor type 1. Furthermore, glyco- protein IIIa (part of the fibrinogen/VWF receptor) and tubulin β1 (involved in microtubule changes in platelet release) were both significantly upregulated in higher ploidy megakaryocytes. Both of these genes are specific to megakaryocytes and platelets.

Conclusion: This is the first analysis of megakaryocytes driven to high ploidy level in vitro using RNA sequencing. Our results demonstrate that along with the anticipated modulation of cell cycle genetics with increasing ploidy, higher ploidy megakaryocytes significantly overexpress genes that are involved in platelet activation and thrombosis. These results therefore support a role for platelet production from megakaryocytes of higher ploidy in thrombotic disease.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475/75?guest=0 on 07 February 2019
P1447 | BEDSIDE
Altered fibrin clot properties affect the angiographic results of primary coronary intervention
M. Sadowski¹, M. Zabczyk², L. Zandezki², A. Undas², S. Swietokrzyski²
¹Swietokrzyskie Cardiology Center, Kielce, Poland; ²Jagiellonian University Medical College, Krakow, Poland

Background: Intracoronary thrombus architecture and its susceptibility to distal embolization during acute ST-segment elevation myocardial infarction (STEMI) are determined by circulating blood properties. In STEMI, pro-thrombotic and pro-inflammatory state results in the formation of denser fibrin network and impaired lysis.

Purpose: To investigate the impact of clinical characteristics, plasma fibrin clot properties and circulating fibrin clot modifiers on the immediate result of primary PCI in STEMI patients.

Methods: A total of 40 STEMI patients who underwent primary PCI were included. Plasma clot lysis time (CLT), platelet and endothelial activation, fibrinolysis and inflammation markers were measured in patients on admission and on the next morning. Thrombolysis in Myocardial Infarction (TIMI) grade, corrected TIMI flow grade (cTFC) and TIMI Myocardial Perfusion Grade (TMPG) were assessed.

Results: Final TIMI flow grade 3 was achieved in 31 patients (77.5%) and final TMPG 3 in 18 (45%) with median cTFC 8 (12–27.5). Final cTFC was positively correlated with body mass index (BMI) and CLT and negatively with anemia presence (decreased red blood cells count - RBC and haemoglobin concentration - HGB) and high density lipoprotein (HDL). Final TMPG was positively correlated with RBC, HGB and tissue plasminogen activator (t-PA).

Conclusion: Primary PCI success rate assessed by cTFC and TMPG is significantly determined by altered fibrin clot properties (prolonged clot lysis time, decreased tissue plasminogen activator) and unfavourable clinical characteristics (increased body mass index, decreased high density lipoprotein and the presence of anemia).

Acknowledgement/Funding: Jagiellonian University Medical College grant No. K/ZDS/202936

P1448 | BEDSIDE
Stent thrombosis in patients treated with bioresorbable vascular scaffolds: a meta-analysis of 7 studies and 2,568 patients
G. Quadrini¹, C. Moretti¹, F. D’Ascenzo¹, P. Omeda¹, A. Montefusco¹, E. Cerrato², F. Conrotto¹, C. Templini³, T.F. Luscher⁴, F. Gaita¹
¹University of Turin, A.O. Città della Salute e della Scienza, Division of Cardiology, Turin, Italy; ²Delegi Infermi Hospital, Rivoli, Italy; ³Ferrarotto Hospital, Catania, Italy; ⁴University Heart Center, Zürich, Switzerland

Introduction: Bioresorbable vascular scaffolds (BVSs) are an innovative technology for patients undergoing percutaneous coronary interventions. Controversial data regarding incidence of stent thrombosis (ST) following BVS implantation have been reported.

Methods: MEDLINE/PubMed were searched for studies evaluating BVSs with ≥50 patients and follow-up of ≥6 months. ST was the primary endpoint, and adverse cardiac events (death, myocardial infarction and target lesion revascularization) were the secondary endpoints.

Results: Seven studies with 2568 patients were included in the present analysis. Diabetes mellitus was present in 22% of the patients. The target vessel was the proximal left anterior descending coronary artery in 46%, with 15% of lesions involving a bifurcation. 25% of lesions were classified as type C, with moderate or severe calcification in 13% and thrombus in 15% of them.

After a mean follow-up of 6.5 months (range 6–12), the rates of any and definite/probable ST were 1.5% (0.7–2.3) and 1.4% (0.6–2.2) respectively, while subacute and late ST occurred in 0.9% (0.2–1.6) and 0.5% (0.2–0.9) of the patients, respectively.

Conclusion: ST in patients with ST-segment myocardial infarction and those with long coronary lesions shown an higher risk of BVS-ST. This can be reduced by post-dilatation and with the use of intravascular imaging technologies.

P1449 | BEDSIDE
Stenosis thrombosis reduces von Willebrand factor antigen levels: A systematic review and meta-analysis of randomized placebo-controlled trials
A. Sahebkar¹, C. Serban², S. Ursoniu², R. Mihaseu², D.P. Mikhailidis³, P. Munter⁴, J. Rysz⁵, A. Undas⁵, G.Y.H. Lip⁷, M. Banach⁵ on behalf of the Lipid and Blood Pressure Meta-analysis Collaboration (LBPMC Group).
¹Mashhad University of Medical Sciences, Mashhad, Iran (Islamic Republic of); ²University of Medicine Victor Babes, Timisoara, Romania; ³University College London, London, United Kingdom; ⁴University of Alabama Birmingham, Birmingham, United States of America; ⁵Medical University of Lodz, Department of Cardiology, Lodz, Poland; ⁶Jagiellonian University Medical College, Krakow, Poland; ⁷University Hospital Birmingham, Birmingham, United Kingdom

Background: Increased von Willebrand factor (vWF:Ag) levels are associated with a high risk of coronary artery disease (CAD). The effect of statin therapy on vWF:Ag has not been conclusively investigated.

Purpose: To investigate the effect of statin therapy on plasma vWF:Ag levels.

Methods: The search comprised PUBMED, Cochrane Library, Scopus, and EMBASE databases up to 31 January, 2015, to identify randomized controlled trials (RCTs) that investigate the effect of statin therapy on plasma vWF:Ag levels.

Results: Random-effect meta-analysis of 21 treatment arms with 1434 individual subjects revealed a significant decrease in plasma vWF:Ag levels following statin therapy (standardized mean difference [SMD]: –0.54 IU/dl, 95% confidence interval [CI]: –0.87, –0.21, p < 0.001). This effect size was robust and removing each of the included treatment arms from analysis did not change statistical significance of the pooled estimate. In subgroup analysis, the greatest effect was observed with simvastatin (SMD: –1.54 IU/dl, 95% CI: –2.92, –0.17, p = 0.028), followed by pravastatin (SMD: –0.61 IU/dl, 95% CI: –1.18, –0.04, p = 0.035), fluvastatin (SMD: –0.69 IU/dl, 95% CI: –1.12, –0.26, p = 0.002), atorvastatin (SMD: –0.73 IU/dl, 95% CI: –0.97, –0.50, p = 0.179), and the lowest effect for rosuvastatin (SMD: –0.20 IU/dl, 95% CI: –0.71, 0.30, p = 0.431). Overall, the effect size was calculated for lipophilic statins (atorvastatin, simvastatin and fluvastatin) (SMD: –0.56 IU/dl, 95% CI: –0.94, –0.19, p = 0.003) was greater than that of hydrophilic statins (pravastatin and rosuvastatin) (SMD: –0.38 IU/dl, 95% CI: –0.76, –0.01, p = 0.046). The lowering effect of statins on plasma vWF:Ag levels was greater in the subset of studies lasting ≥12 weeks (SMD: –0.70 IU/dl, 95% CI: –1.19, –0.22, p = 0.005) compared with the ones <12 weeks (SMD: –0.34 IU/dl, 95% CI: –0.59, 0.03, p = 0.052). Finally, low-intensity statin therapy was associated with a significant reduction in vWF:Ag levels (SMD: –0.66 IU/dl, 95% CI: –1.07, –0.24, p = 0.002) while the impact of high-intensity treatment was modest (SMD: –0.28 IU/dl, 95% CI: –0.82, 0.27, p = 0.320).

Conclusion: This meta-analysis showed a significant association between plasma vWF:Ag levels and statin therapy, with the largest effect for low-intensity, lipophilic statins administered for at least 12 weeks.
**P1451 | BENCH**

**The safety profile of new cationic dextran heparin antidotes**

E. Sokolowska1, B. Kalaska, K. Kaminski, A. Lewandowska, I. Kasacka, K. Szczubiakia, D. Pawlak, M. Nowakowska, A. Mogielnic1, 1Medical University in Bialystok, Department of Pharmacodynamics, Bialystok, Poland; 2Jagellonian University, Faculty of Chemistry, Krakow, Poland; 3Medical University in Bialystok, Department of Histology and Cytophysiology, Bialystok, Poland

**Background:** Prothrombin – a protein isolated from sperm of salmon fished around Japan is the only one registered antidote of unfractionated heparin (UHF). However, around one thousand deaths a year could be attributed to complications after prothrombin injection. We have already shown in vivo neutralization of UHF by FeCl3-induced venous thrombosis. The potential direct blood toxicity (osmotic resistance) of Dex40-GTMAC2 and prothrombin was measured in whole blood. Blood pressure, heart rate (HR), blood count and histopathology were estimated 1 hour after administration of tested antidotes (UHF). Blood count and blood chemistry were measured in 7, 14 and 28 days of observation, as well as we performed histological examination of main organs at the end of experiment (chronic toxicity).

**Results:** Dex40-GTMAC2 was more effective (0.21±0.03 mg; P<0.0001) than prothrombin (0.12±0.01 mg; P<0.0001) in reversing the effect of UHF (0.01±0.01 mg vs. 0.39±0.05 in the vehicle treated group; P<0.0001) on thrombus weight formed in vena cava. Dex40-GTMAC2 significantly reversed activated partial thromboplastin time (40.7±5.7 sec.; P<0.0001) prolonged by UHF (300.0±0.0 vs. 28.9±1.3 sec. in the vehicle treated group; P<0.0001), while platelet factor 4 did not. Dex40-GTMAC3 showed no significant acute and chronic toxicity, while Dex40-GTMAC2 decreased blood pressure, HR and changed blood morphology. Dex40-GTMAC3 did not induce hemolysis and did not cause any long-term changes in organs as examined in routine histology.

**Conclusion:** Dex40-GTMAC3 as a novel, easy to synthesize, potent and safe heparin antidote may become a potential marketable therapeutic.

**Acknowledgement/Funding:** Grants no. 2011/03/B/ZN7/00735 and UMO-2013/09/D/DTS/03864 National Science Center, Poland

---

**P1452 | BEDSIDE**

**Comparison of circadian laboratory measurements of coagulation assays between administrations of rivaroxaban and warfarin in patients with non-valvular atrial fibrillation**

Y. Hitaka1, M. Ogawa1, S. Goto, Y. Nagata, J. Morii1, S. Imai1, T. Yasuda1, N. Matsumoto, A. Matsunaga, K. Saku, 1Fukuoka University Hospital, Department of Cardiology, Fukuoka, Japan; 2Fukuoka University Hospital, Department of Laboratory Medicine, Fukuoka, Japan

**Background:** Although rivaroxaban (RB) has a relatively short half-life and peak concentration, and a trough blood concentration throughout the day in comparison with warfarin (WR), the ROCKET-AF study showed that RB was non-inferior to warfarin for preventing thromboembolic events in patients with non-valvular atrial fibrillation (NVAF).

**Objectives:** To clarify and compare the circadian laboratory measurements of coagulation assays in administrated patients with RB or WR.

**Methods and results:** We enrolled 28 consecutive NVAF patients administrated with RB (n=13) and WR (n=15) in this study. Blood samples were performed 4 times a day (6 AM, 11 AM, 3 PM, and 6 AM the next day) and the prothrombin time (PT), PT-INR, APTT, fragment 1+2, protein C and protein C activity were measured in each time for RB were significantly lower than those for WR. The APTTs measured at 6AM (34.6±8.4 vs. 41.1±8.4 sec, P<0.0001) measured at each time for RB were significantly lower than those for WR.

**Conclusion:** The protein C and its activity as physiological anticoagulant factor for RB were constantly and significantly kept higher than those for WR throughout the day as opposed to the coagulation assays. These findings may explain the specific lasting anticoagulant effect of RB, and not WR.

---

**P1483 | SPOTLIGHT**

**Potential clinical benefits and cost savings associated with inclusion of apixaban in the formulary for treatment of patients with venous thromboembolism**

M. Hamilton1, R. Leipold2, D. Rublee3, S. Sterri3, D. Gabrie4, T. Godes5, A. Cohen5, 1BMS, Princeton, New Jersey, United States of America; 2Evidera, Bethesda, Maryland, United States of America; 3Pfizer, New York, United States of America; 4Evidera, Lexington, Massachusetts, United States of America; 5Pfizer, Surrey, United Kingdom; 6Guy’s and St Thomas NHS Foundation Trust, London, United Kingdom

**Background:** Budget impact analysis estimates of the likely impact of a new drug on the healthcare decision maker’s annual budget and is generally required before national or local formulary approval or reimbursement.

**Purpose:** The goal of this study was to assess the impact of apixaban in patients with venous thromboembolism (VTE) on the NHS health care budget in the United Kingdom.

**Methods:** A model was developed to analyze the impact on 5-year total health care costs of introducing apixaban for acute treatment and secondary prevention in a representative VTE population. Market share projections were based on current market research data, with assumptions regarding future market shares. Clinical effects of apixaban and LMWH/VKA were derived from AMPLiFY, and effects of other NOACs were obtained from indirect treatment comparisons. Cost inputs measured in 2012 values were obtained from published data sources. Outcome measure was the percentage change in healthcare budget comprises pharmacy and medical costs in patients treated over several treatment durations.

**Results:** Use of apixaban instead of other treatments was predicted to lead to a reduction in recurrent VTEs, major and CRNM bleeds. Model projections if apixaban market share was drawn solely from rivaroxaban were that the total health care budget would be reduced by 0.3% to 0.9% in patients treated for 3 months to 5 years. Drawing market share from LMWH/VKA only, resulted in a change in budget savings of 0.7% and an increase of 4.0% in patients treated for 3 months to five years.

**Conclusions:** Apixaban is predicted to provide better clinical outcomes, with treatment acquisition costs largely offset by savings in the medical costs in most of the treatment pattern scenarios modeled. Improved clinical outcomes are predicted to be accompanied by small savings or modest increases in the healthcare budget over a 5-year period, depending upon the VTE treatment duration and market share.

**Acknowledgement/Funding:** This study was funded by Pfizer and BMS

---

**P1454 | BEDSIDE**

**TRAP induced platelet aggregation is enhanced in cardiovascular patients receiving dabigatran**

C.B. Olivier, P. Weik, M. Meyer, P. Diehl, Q. Zhou, U. Geisen, C. Bode, M. Moser, Albert-Ludwig University of Freiburg, Department of Cardiology and Angiology, Freiburg, Germany

**Background and objectives:** Novel (or non-vitamin K antagonist) oral anticoagulants (NOACs) are antagonists of coagulation factors, (F) Xa (rivaroxaban) or IIa (dabigatran) and have demonstrated a superior risk/benefit ratio compared with vitamin-K-antagonists in patients with non valvular atrial fibrillation (AF). However, it is still incompletely understood how dabigatran and rivaroxaban interact with platelet function. This observational trial aims to assess the platelet function in patients receiving dabigatran or rivaroxaban.

**Methods and results:** In a single centre observational study platelet aggregation was quantified in 80 patients treated with NOACs by multiple electrode aggregometry (MEA). Surprisingly, the thrombin receptor activating peptide (TRAP) induced platelet aggregation was significantly higher in 25 patients receiving dabigatran compared to control patients (dabigatran: 100±30 vs. control: 84±30 AU/min, p=0.0344). In intravascular time courses of 11 patients a significant higher MEA aggregation was observed after the administration of dabigatran compared to the measurement before the intake of dabigatran (before: 77±25 vs. on dabigatran: 90±28 AU/min, p=0.0327). Patients receiving rivaroxaban showed no differences compared to the control group (89±32 vs. 84±30 AU/min, p=0.4559).

**Conclusions:** Apixaban is predicted to provide better clinical outcomes, with treatment acquisition costs largely offset by savings in the medical costs in most of the treatment pattern scenarios modeled. Improved clinical outcomes are predicted to be accompanied by small savings or modest increases in the healthcare budget over a 5-year period, depending upon the VTE treatment duration and market share.
Conclusion: This data demonstrates that TRAP induced platelet aggregation is enhanced in cardiovascular patients taking dabigatran while this is not the case for rivaroxaban.

Acknowledgement/Funding: This work was supported by a grant from the Deutsche Forschungsgemeinschaft (OL 371/1-1 to Christoph B. Olivier).

P1455 | BENCH
Platelets are permanently activated after splenectomy
M. Gerges1, C. Gerges1, M.K. Frey1, S. Panzer1, I.M. Lang2, 1Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria; 2Medical University of Vienna, Department of Blood Group Serology and Transfusion Medicine, Vienna, Austria

Purpose: Patients after splenectomy are prone to complicated thrombosis. Recent data suggest that time to first thrombotic event or death (mainly due to "thrombotic" cardiovascular disease) may be shorter in patients after splenectomy than in matched controls. We tested the hypothesis that abnormal platelet function after splenectomy may contribute to thrombosis and delayed thrombosis resolution.

Methods: In this prospective case control study, we evaluated 144 outpatients after previous splenectomy referred from 1100 primary care practitioners. 91 (63.2%) splenectomies were due to trauma. Platelet function was measured in a subset of 36 splenectomized patients in whom splenectomy occurred after trauma, and in 7 matched non-splenectomized controls. The response to adenosine diphosphate (ADP), arachidonic acid (AA), prostacyclin-activated receptor (PAR-4), and thrombin receptor activating peptide 6 (TRAP-6) was tested by multiple electrode impedance aggregometry (Multiplate). Flow cytometry was used to detect circulating monocyte-platelet aggregates (MPA) in whole blood of both subgroups. We also compared agonist (TRAP-6, PAR-4, ADP and CRP)-induced P-selectin expression in whole blood of splenectomized versus non-splenectomized patients.

Results: During a median follow-up time of 7.9 years (25th and 75th percentile, 5.413 and 7.997 years), 10 patients (11%) died from various causes, mainly arterial and venous thrombotic events. According to the International Classification of Diseases (ICD) an increased incidence of non-fatal thrombotic events (n=28) was observed in patients after splenectomy, compared with controls (p<0.001). Multivariate analyses revealed increased platelet activity in splenectomized patients (97.0±6.22 area under the curve, AUAs, compared with controls (80.1±10.07 AUCs, p=0.04). Inducible P-selectin was higher in splenectomized patients (85.2±19.85%) compared with controls (62.5±21.52%, p=0.05). Levels of MPA (44.47%; 11–92%) were higher in MPAs: 31.59%; (13–70), P<0.001.

Conclusions: Platelets are activated after splenectomy, with increased concentrations of MPA, which may contribute to the high rate of vascular events in these patients.

P1456 | BENCH
Enhanced platelet aggregation is associated with plaque ruptures in patients with acute coronary syndrome
A.S.A. Autar1, M. De Maat1, H. Van Beusekom2 on behalf of CorTAsk Investigators, M. Kurata1, E. Regar1, M. Valgimigli1, F. Leebeek2, F. Zijlstra2, 1Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands; 2Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands

Purpose: We studied the associations between clinical data and the structure of coronary and peripheral arterial thrombus.

Methods: Patients of various age (36–98 years) and sex (40% female) were recruited over 22 months. Coronary thrombi were obtained by PCI-thrombus aspiration following AMI (n=100), peripheral clots were removed by embolectomy (n=50). Samples were processed by scanning electron microscopy for fibrin fiber diameter, relative occupancy by red and white blood cells, platelets, fibrin and by confocal microscopy with indirect immunostaining for fibrin and platelet receptor GpIIb/IIIa. Morphometric analysis was performed on 15 images/thrombus. Hypothesis tests and regression analysis were used to assess the correlation between structural features and selected clinical data, e.g. age, sex, antiplatelet therapy, ECG findings, ischaemic time, smoking, co-morbidities.

Results: Coronary clots contained less (mean 70.5% vs. 83.9%) and finer (mean fiber diameter 122 vs. 135 nm) fibrin than peripheral clots, while thrombi from smokers contained more fibrin than non-smokers (mean 78.1% vs. 62.2%) (P<0.05). In the first 24 h, fibrin content of coronary clots decreased with time, whereas in peripheral clots platelet content increased in the first 7 days. Higher clot platelet content was found in smaller vessels and at higher hematocrit values. A J-shaped dependence was found between systemic and intrathrombotic platelet count, which correlation was enhanced by aspirin and clopidogrel in peripheral thrombi and by smoking and dyslipidaemia in AMI patients.

Conclusion: Platelets are permanently activated after splenectomy, with abnormal platelet function, which may contribute to thrombosis and delayed thrombosis resolution.
determined by PCR and HPY CHIV restriction enzyme. The endothelial function was determined with flow mediated dilation (FMD). High sensitivity CRP (hsCRP) (mg/l) and D-dimers (μg/l) were determined with immunonephrometry, while fibrinogen (mg/dl) with the Clauss method. Interleukin-6 (IL-6) (pg/ml) and TNF-α (pg/ml) and sCD40L (pg/ml) were measured by ELISA.

Results: We found that the G allele carriers presented with significantly higher levels of all inflammatory markers compared to AA homozygotes both in CAD (IL-6: 3.10±1.36 vs. 2.27±1.17, TNF-α: 6.19±1.15 vs. 4.88±1.09, hsCRP: 2.31±0.69 vs. 1.92±0.92, p<0.002 for all) and in controls (IL-6: 1.52±0.56 vs. 1.28±0.58, TNF-α: 1.99±0.68 vs. 1.61±0.54, hsCRP: 1.10±1.39 vs. 0.89±0.95, p<0.018 for all). On the contrary, G carriers, compared to AA homozygotes, had not significant effect on any of the coagulation markers, both in CAD (fibrinogen: 444.4±132.9 vs. 483.0±142.6, sCD40L: 2.14±1.79 vs. 1.38±2.51, D-dimers: 456.4±51.7 vs. 486.4±51.7, p<0.05 in all) and in controls (fibrinogen: 385.0±103.9 vs 365.3±72.9, sCD40L: 0.73±1.93 vs. 1.31±1.67, D-dimers: 264.2±222.9 vs. 312.9±241.5, p=NS for all). Importantly, the AA homozygotes presented to have significantly higher FMD values compared to G carriers in both study groups (CAD: 4.15±2.09 vs 3.76±2.34, p=0.0118, controls: 6.89±2.9 vs 6.17±2.9, p<0.002). Moreover, the G allele was found to be associated significantly with the incidence of CAD (OR: 1.34, CI: 1.03–2.12, p=0.042), after adjustment for all major risk factors for CAD (age, diabetes, hypertension, dyslipidemia, BMI, smoking).

Conclusion: Our results show that the present genetic variant in CRP gene is an independent risk factor for CAD, while it modifies atherosclerotic process, mainly by inhibiting inflammatory mechanisms and endothelial dysfunction.

**P1459 | BEDSIDE**

**Plateletcrit and platelet distribution width as predictors of ST elevation myocardial infarction in young patients**

M.S. Celin, E.H. Ozcan Celin, S. Aydin, E. Kalender, S. Topaloglu, D. Aras, A. Turgut, E. Aydogdu, Ankara Turkey Yuksel Ihtisas Hospital, Department of Cardiology, Ankara, Turkey

**Introduction:** Platelets play a central role in atherosclerotic process and platelet activity can be assessed with mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW). We aimed to investigate these platelet indices as predictors of ST elevation myocardial infarction (STEMI) in young population.

**Material and methods:** Our study consisted of 453 patients. We classified the patients into 3 groups. Group 1: 168 young (age ≥45 for men and ≤55 for women) patients with STEMI (mean age 41.5±4.7, 72.8% male), Group 2: 173 non-young patients with STEMI (mean age 54.0±8.0, 78.0%) and Group 3 as the control group: 112 age-matched patients with normal coronary arteries (mean age 43.4±8.5, 65.0%).

**Results:** Compared with group 2, group 1 had significantly higher PCT (0.249±0.6 vs. 0.222±0.6 p=0.001), PDW (48.2±5.7 vs. 45.8±4.6 p=0.001) and MPV (8.8±1.0, 8.5±1.1, p=0.022). In comparison of group 1 and 3, in group 1, MPV (8.8±1.0, 8.5±1.1, p=0.022) was significantly higher than group 3. At multivariate logistic regression analysis of young STEMI and non-young STEMI patients MPV, PDW, PCT were still independent risk factors of STEMI in young patients. In comparison of young STEMI and age-matched control group with multivariate logistic regression analysis MPV, PDW, PCT were significantly independent predictors of myocardial infarction in young patients.

**Conclusions:** To our knowledge this is the first study to evaluate PDW, PCT in young patients with STEMI. In comparison to MPV, PDW and PD2, PCT levels seem to be independent predictors of STEMI in young patients and these simple, costless platelet activity indices can be used for risk stratification up on admission.

**P1460 | BEDSIDE**

**Usefulness of platelet indices as predictors of stent thrombosis in ST elevation myocardial infarction**

M.S. Celin, E.H. Ozcan Celin, S. Aydin, E. Kalender, O. Ozeke, H.L. Kisacik, S. Topaloglu, D. Aras, S. Aydogdu. Ankara Turkey Yuksel Ihtisas Hospital, Department of Cardiology, Ankara, Turkey

**Introduction:** Platelets especially larger and hyperreactive ones aggravate the formation of intracoronary thrombus leading stent thrombosis (ST). We aimed to investigate the usefulness of mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT) as predictors of ST after acute ST elevation myocardial infarction (STEMI).

**Materials and methods:** 925 patients who admitted with STEMI and under-went percutaneous coronary intervention between 01/2010—12/2014 were enrolled and followed up for median 2.9 years. During the follow-up, 91 patients were re-admitted to hospital with STEMI and diagnosed as “definite” ST with respect to ARC criteria. In statistical analysis patients were categroized into 3 groups according to MPV, PDW, PD2, PCT tertiles, respectively.

**Results:** The rates of ST were statistically higher in the highest tertiles for every platelet indices; MPV, PDW, PD2 (p<0.010, p<0.003, p<0.001 respectively). In ROC analysis, the cut-off values were MPV: 8.99 vs. 8.59, PDW: 48.0 vs. 45.3, PCT (OR: 1.117, 95% CI: 1.065–1.172; p<0.001) and PCT (OR: 1.25, 95% CI: 1.136–1.277; p<0.001) were independent predictors of ST after acute STEMI. In ROC analysis of platelet indices for prediction of ST, a cut-off value 45.75 for PDW has a 79.2% sensitivity and 65.5% specificity (AUC=0.705 p<0.001) and a cut-off value 0.2355 for PCT has a 77.1% sensitivity and 64.2% specificity (AUC=0.738 p<0.001) and a cut-off value 6.55 for MPV has a 62.5% sensitivity and 61.2% specificity (AUC=0.625 p=0.004).

**Discussion:** In addition to MPV, other platelet indices PDW and PCT seem to be independent predictors of ST in STEMI. These indicators may utilize risk stratification upon admission of acute STEMI patients.
Therefore we investigated the influence of morphine on platelet inhibition with clopidogrel and prasugrel in patients with primary PCI.

**Methods:** In the ETAMI trial patients with STEMI ≤12 hours scheduled for primary PCI were randomized to loading doses of either 600 mg clopidogrel or 60 mg prasugrel in the pre-hospital phase. The platelet reactivity index (PRI) was measured with the VASP assay at 2 and 4 hours after intake of the loading doses.

**Results:** A total of 62 patients were enrolled in the ETAMI trial, from these 32 (51%) received morphine in the acute phase. The PRI after 2 hours (50.4 ± 32.7% vs 66.3 ± 22.2%, p < 0.035) and after 4 hours (39.1 ± 27.5% vs 54.3 ± 49.3%, p < 0.005) was significantly lower with prasugrel compared to clopidogrel. The PRI values at baseline and after 2 and 4 hours according to he co-medication with morphine are given in the table.

<table>
<thead>
<tr>
<th></th>
<th>Clopidogrel</th>
<th>Prasugrel</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Morphine (n=13)</td>
<td>No morphine (n=14)</td>
</tr>
<tr>
<td>Baseline</td>
<td>80.2 ± 11.3</td>
<td>74.3 ± 23.7</td>
</tr>
<tr>
<td>2 hours</td>
<td>72.8 ± 15.3</td>
<td>60.6 ± 26.1</td>
</tr>
<tr>
<td>4 hours</td>
<td>59.1 ± 23.1</td>
<td>50.8 ± 24.9</td>
</tr>
</tbody>
</table>

Mean PRI values.

**Conclusion:** Both with clopidogrel and prasugrel inhibition of platelets is delayed by concomitant administration of morphine at 2 hours after the loading dose. However, after 4 hours the influence of morphine is observed only after clopidogrel.

**PI1465 | BEDSIDE**

Patients receiving dual antiplatelet therapy and concomitant oral anticoagulation with dabigatran show increased platelet reactivity


**Background:** Patients suffering from atrial fibrillation have an increased incidence of concomitant coronary artery disease (CAD). Following PCI a dual antiplatelet therapy (DAPT) is conducted to prevent in-stent restenosis and CAD progression. As a result of the RELY-trial the oral anticoagulation (OAC) with dabigatran during DAPT is safer than AOC with phenprocoumon. The current guidelines recommend dabigatran as the treatment for patients receiving DAPT with the need of OAC. However, a trend of elevated rates of myocardial infarction (MI) in the dabigatran treatment arm recently raised some concerns.

**Methods:** Using multiplate electrode aggregometry platelet reactivity of 30 patients on DAPT and dabigatran or phenprocoumon therapy was assessed.

**Results:** (platelet reactivity basal vs. 34mm and female as significant independent predictors of first ischemic events occurring during stent thrombosis, remains a major concern. We sought to determine whether thrombelastography was a good ex vivo platelet function measurement to facilitate risk stratification and personalized antiplatelet therapy.

**Methods:** We investigated the prognostic utility of the strength of adenosine diphosphate (ADP)-induced (MAADP) platelet-fibrin clots measured by thrombelastography in 759 East Asian patients undergoing elective PCI. A 600mg-dose clopidogrel loading was administered on the day before procedure (12h). High on-clopidogrel platelet reactivity (HPR) was defined by published consensus criteria. Ischemic and bleeding events were assessed over 2 years.

**Results:** The prevalence of HPR was 36% measured by TEG (n=273). Overall, 58 (7.6%) first ischemic events occurred. Patients with ischemic events had higher MA-ADP (P < 0.0001 for all comparisons). By receiver operating characteristic curve analysis, MA-ADP >34mm had the best predictive value of long-term ischemic events, with an area under the curve = 0.79 (95% CI 0.72–0.87, P < 0.0001). The univariate Cox proportional hazards model identified MA-ADP >34mm and female as significant independent predictors of first ischemic events at the 2-year time point (P < 0.0001). Eleven bleeding events occurred. Receiver

**Conclusion:** The observed trend towards increased rates of myocardial infarction in patients receiving dabigatran deduced from the RELY-trial could be due to elevated platelet reactivity. However, the effect of clopidogrel does not seem to be reduced by dabigatran co-medication.

**PI1464 | BEDSIDE**

Dual anti-platelet therapy after drug-eluting coronary stent implantation and risk of adverse cardiac events associated with surgery - a Danish registry study


**Background:** Surgery is a frequent reason for disruption of dual antiplatelet therapy (DAPT) within the first year after drug-eluting stent (DES) implantation. Disruption of antiplatelet therapy in relation to surgery has been associated with an increased risk of adverse cardiac events.

**Purpose:** To examine the risk of 30-day adverse cardiac events after cardiac and non-cardiac surgery after drug-eluting coronary stent implantation. Moreover, we evaluated the potential association between periprocedural DAPT and adverse cardiac events.

**Methods:** Patients with DES implantation were identified by use of the Western Denmark Heart Registry. Data on surgical procedures and adverse cardiac events defined as cardiac death, myocardial infarction, or definite stent thrombosis were obtained from population based Danish medical registries. In the nested-case control analysis, the Periprocedural DAPT was evaluated by explicit record review for patients with adverse cardiac events (cases) and for control patients matched by age, gender, oral anticoagulant medications, and type of surgery.

**Results:** In the cohort of 22,654 patients treated with DES, we identified 1944 patients (8.5%) who underwent surgery within 12 months. The most frequent types of surgery were cardiac and vascular (40%), abdominal (23%), and orthopedic (13%) procedures. Among surgical patients, 62 (3.2%) had an adverse cardiac event within the first 30 days after surgery. The nested case-control analysis included 62 cases with adverse cardiac events and 207 matched control patients. DAPT was prescribed periprocedurally for 69% of cases vs 76% of controls while 13% vs 15% received a single antiplatelet agent, and 18% vs 9% disrupted both antiplatelet agents periprocedurally. The risk of adverse cardiac events was not associated with the periprocedural DAPT strategy.

**Conclusions:** Cardiac and non-cardiac surgery were common within the first year of DES implantation. Surgery was associated with a relatively high risk of adverse cardiac events within 30 days. Periprocedural compliance to DAPT was much higher than previously reported, which may explain why the risk of adverse cardiac events was not associated with the periprocedural DAPT strategy.

**Acknowledgement/Funding:** TRYG, Knud and Edith Eriksen’sfond. Aarhus University Hospital, Department of Cardiology

**PLATELETS AND ANTIPLATELETS THERAPY I**

**PI1465 | BEDSIDE**

The relation between thrombelastography and long-term poststenting ischemic events: 2 years follow-up in East Asian patients after 600mg-dose clopidogrel loading

X. Hou, Shanghai Chest Hospital, Shanghai, China, People’s Republic of

**Background:** Recurrent ischemic event occurrence during dual antiplatelet therapy after drug-eluting stent thrombosis, remains a major concern. We sought to determine whether thrombelastography was a good ex vivo platelet function measurement to facilitate risk stratification and personalized antiplatelet therapy.

**Methods:** We investigated the prognostic utility of the strength of adenosine diphosphate (ADP)-induced (MAADP) platelet-fibrin clots measured by thrombelastography in 759 East Asian patients undergoing elective PCI. A 600mg-dose clopidogrel loading was administered on the day before procedure (12h). High on-clopidogrel platelet reactivity (HPR) was defined by published consensus criteria. Ischemic and bleeding events were assessed over 2 years.

**Results:** The prevalence of HPR was 36% measured by TEG (n=273). Overall, 58 (7.6%) first ischemic events occurred. Patients with ischemic events had higher MA-ADP (P < 0.0001 for all comparisons). By receiver operating characteristic curve analysis, MA-ADP >34mm had the best predictive value of long-term ischemic events, with an area under the curve = 0.79 (95% CI 0.72–0.87, P < 0.0001). The univariate Cox proportional hazards model identified MA-ADP >34mm and female as significant independent predictors of first ischemic events at the 2-year time point (P < 0.0001). Eleven bleeding events occurred. Receiver
operating characteristic curve and quartile analysis suggests MA-ADP ≤21 mm as a predictive value for bleeding.

Conclusions: The quantitative assessment of ADP-stimulated platelet-fibrin clot strength measured by thrombelastography can serve as a future tool in investigations of personalized antiplatelet treatment designed to reduce ischemic events and bleeding.

P1468 | BEDSIDE
The vasculo-angiogenic and vaso-protective effects of cilostazol in patients with high risk for cardiovascular disease
T.-H. Chao1, P.-Y. Liu1, W.-C. Tsai2, S.-Y. Tseng2, Y.-H. Lui1, 1National Cheng Kung University College of Medicine and Hospital, Tainan, Taiwan, ROC; 2National Sun Yat-Sen University, Kaohsung, Taiwan, ROC

Background: We have found that cilostazol may have beneficial effects on endothelial progenitor cells (EPCs) in vitro and can provide vasculo-angiogenic effects in vivo.

Purpose: This study, for the first time, investigated the vasculo-angiogenic effects of cilostazol on EPCs and flow-mediated dilatation (FMD) in patients with high risk for cardiovascular disease (CVD).

Methods: Seventy-one eligible patients (37 received 200 mg cilostazol and 34 took placebo per day for 12 weeks) who had high-risk profile for CVD but without pre-existing CVD were consecutively enrolled in this double-blind and placebo-controlled study. Circulating number and EPCs and in vitro functions were assessed, and plasma biomarkers were measured by enzyme-linked immunosorbent assay. Platelet response to reactive hyperemia was measured in the left brachial artery by using a high-resolution ultrasound machine equipped with a 7.5 Mhz linear array probe.

Results: The background characteristics and parameters in cilostazol treatment group and placebo group were similar and well matched. Cilostazol, but not placebo, significantly increased circulating EPCs (KDR+CD34+) count [percent-change: 149.0 (67.9–497.8) vs. 7.9 (-31.8–236.5%), P=0.024] without influence on apoptotic endothelial cells. Cilostazol also improved triglyceride and high density lipoprotein levels (−9.9±6.1 vs. 17.7±6.1%, P=0.002; 8.7±3.0 vs. −2.4±2.1%, P=0.003, respectively). Plasma levels of vascular endothelial growth factor (VEGF)-A165 and FMD were significantly increased [72.5 (32.9–120.4) vs. −5.8 (-46.0–57.6%), P=0.001; 232.8±83.1 vs. −46.9±21.5%, P=0.003, respectively], whereas stromal cell-derived factor-1a or adiponectin was not significantly affected. Changes of plasma triglyceride were -5.8 (−46.0–57.6)%, P=0.001; 232.8±83.1 vs. −46.9±21.5%, P=0.003, respectively). Plasma levels of vascular endothelial growth factor (VEGF)-A165 and FMD were significantly increased [72.5 (32.9–120.4) vs. −5.8 (-46.0–57.6%), P=0.001; 232.8±83.1 vs. −46.9±21.5%, P=0.003, respectively], whereas stromal cell-derived factor-1a or adiponectin was not significantly affected. Participants treated with cilostazol. Changes of plasma triglyceride were -5.8 (−46.0–57.6)%, P=0.001; 232.8±83.1 vs. −46.9±21.5%, P=0.003, respectively).

Conclusion: Cilostazol has significantly beneficial effects on mobilization of EPCs with better endothelium-dependent function partially modulated by modifying some metabolic and angiogenic markers in patients with high-risk profile for CVD.

Acknowledgement/Funding: NCKUH-10203022; DOH-102-TD-B-111-002; MOHW103-TDU-B-211-113002

P1467 | BEDSIDE
The effect of PEAR1 genetic variants on antiplatelet therapy among acute coronary syndrome patients after percutaneous coronary intervention
Y. Yao, X.F. Tang, J. Wang, J.H. Zhang, Y.L. Ma, C. He, J.Q. Yuan. Fujiw Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China, People's Republic of

Purpose: The platelet responses to antiplatelet drugs are wide inter-individual variability. Platelet endothelial aggregation receptor-1 (PEAR1) is a newly reported platelet transmembrane protein, preliminary researches indicate that PEAR1 may play an important role on platelet function. The aim of this study is to investigate the effect of PEAR1 genetic variants on antiplatelet therapy in patients with acute coronary syndrome after percutaneous coronary intervention. Method: 695 patients with acute coronary syndrome after percutaneous coronary intervention and under dual antiplatelet therapy with 100mg/d aspirin and 75mg/d clopidogrel were enrolled in the study. The effect of antiplatelet was assessed by thrombelastography platelet mapping assay (agonist: 20μmol/L ADP), results were recorded as the percentage inhibition of platelet aggregation (IPA). According to the results, patients with IPA less than 30% were included in the experimental group and patients with IPA greater than 70% were included in the control group. 16 candidate single nucleotide polymorphisms (SNPs) of PEAR1 were detected by the method of improved multiple ligase detection reaction in the two groups.

Results: 133 patients were included in the experimental group and 154 patients were included in the control group. Among 16 candidate SNPs of PEAR1, the minor alleles of 2 SNPs (T-allele at rs3773224, A-allele at rs11264581) displayed a significantly higher carrying frequency in the experimental group compared to the control group,showing a strongly associated with reduced platelet responsiveness to clopidogrel (P=0.0498 for rs3773224; P=0.0495 for rs11264581).

Conclusion: The genetic variants of PEAR1 may be related to insufficient antiplatelet effect in patients with acute coronary syndrome after percutaneous coronary intervention.

P1469 | BEDSIDE
Oral crushed and dispersed ticagrelor 180mg compared to whole tablets of equal dose in STEMI patients undergoing primary PCI: a pharmacokinetic/pharmacodynamic study (the LIQUID study)
Y. Xanthopoulou1, N. Barampoutis1, V. Gkizas1, C. Vogiatzi1, P. Davlouros1, G. Hahalis1, G. Tsigkas1, S. Nylander2, G. Parodi3, D. Alexopoulos1. 1Patras University Hospital, Cardiology Department, Patras, Greece; 2AstraZeneca R&D, Mölndal, Sweden; 3Careggi University Hospital (AOUC), Florence, Italy

Background: A delay in the onset of antiplatelet action of orally administered P2Y12-receptor antagonists is observed in ST-segment elevation myocardial infarction (STEMI) patients.

Purpose: We aimed to investigate the pharmacokinetic effect of Ticagrelor administered as crushed compared to integral tablets in STEMI patients undergoing primary percutaneous coronary intervention.

Methods: We randomized 20 patients to 180-mg ticagrelor loading either as 2 integral tablets administered in the supine position or crushed and dispersed, administered in semi-upright sitting position. Blood samples were drawn for pharmacokinetic and pharmacodynamic assessment at randomization (0 hour) and at 0.5, 1, 2 and 4 hours.

Results: At 1 hour, ticagrelor plasma exposure and area under the curve (AUC(0–1h), (primary and co-primary endpoints), were higher in the crushed vs integral tablets group (median 586 vs. 70.1 ng·mL⁻¹·h, and 234 vs. 24.4 ng·mL⁻¹·h), with a ratio of adjusted geometric means (95% confidence interval, CI) of 12.67 (2.34–68.51) (0.5), 18.93 (3.51–106.06), p=0.005 and p=0.002, respectively. Time to maximum plasma concentration was shorter in the crushed vs integral tablets group (median 2 vs. 4 h), with a ratio of adjusted geometric means (95% CI) of 0.69 (0.49–0.97), p=0.035. Similar findings were observed with AR-C124910XX (active metabolite). Platelet reactivity (VerifyNow) at 1 hour was lower with crushed vs. standard administration with least square estimates mean difference (95% CI) of 92.5 (−158.4 to 26.6) PRU, p=0.009.

Conclusions: In patients with STEMI undergoing primary PCI ticagrelor administered as crushed tablets leads in a faster - compared to standard administration – absorption, with stronger antiplatelet activity within the first hour.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475 by guest on 07 February 2019
A. Elsaesserr5, H. Schuehlen 6, U. Zeymer2 on behalf of ALKK-Study Group.

1 Klinikum Ludwigshafen, Ludwigshafen Am Rhein, Germany; 2 Institut für population in clinical practice. Results of the prospective ALKK-Regist

Background: Despite the new P2Y12-ADP receptor antagonists achieve faster, higher and less inter-individual variability platelet inhibition than clopidogrel, it is unknown the effect of intravenous lysine acetylsalicylate (LA) on cyclooxygenase platelet inhibition compared to oral aspirin on prasugrel inhibited platelets.

Purpose: The objective was to analyze the inter-individual variability effect of combined administration of oral prasugrel and intravenous LA versus prasugrel and aspirin orally on platelet aggregation.

Methods: A prospective, randomized, single-center, open, two-period crossover platelet function study conducted in 30 healthy volunteers. Subjects were randomly assigned to receive a loading dose (LD) of intravenous LA 450mg plus oral prasugrel 60mg, or LD of aspirin 300mg plus prasugrel 60mg orally in a crossover fashion after a 2-week washout period between treatments. Platelet function was evaluated at baseline, 30 min, 1h, 4h, and 24h using light transmission aggregometry.

Results: Figure 1 shows individual subject platelet response after AA 1.5 mM at baseline, 30 min, 1h, 4h and 24h. Subjects treated with oral aspirin presented higher inter-individual variability than intravenous LA (p < 0.05).

Conclusions: Compared with intravenous LA, oral aspirin showed significant higher inter-individual variability on cyclooxygenase platelet inhibition.

Acknowledgement/Funding: This study was supported by a grant from the Fundación Mutua Madrileña (FMM012).

P1470 | BEDSIDE
Comparative efficacy and safety of prasugrel and clopidogrel in patients with STEMI undergoing primary PCI in the prasugrel core population in clinical practice. Results of the prospective ALKK-Study Group.

1 Klinikum Ludwigshafen, Ludwigshafen Am Rhein, Germany; 2 Institut für population in clinical practice. Results of the prospective ALKK-Regist

Background: In the TRITON-TIMI 38 trial prasugrel reduced the combined endpoint of cardiovascular death, myocardial infarction in patients with STEMI without an increase in bleeding complications. Therefore we evaluated the impact of therapy with prasugrel on outcome in patients with primary PCI for STEMI in real life in a large number of patients in the so-called prasugrel core population.

Methods: We used the data of the ongoing prospective German ALKK-PCI registry and included patients with PCI for STEMI -24 h duration treated in 36 centres using both clopidogrel and prasugrel. We excluded patients with prior stroke, weight < 60 kg and age > 75 years.

Results: Between 2009 and 2012 a total of 6227 patients with PCI for STEMI were included. Of these 1921 (30.8%) were treated with prasugrel. Baseline characteristics, procedural features and in-hospital outcomes are given in the table. In a multivariate analysis prasugrel was associated with a reduced mortality (odds ratio 0.66, 95% CI 0.44–0.99).

Conclusion: In clinical practice prasugrel compared to clopidogrel in the so-called core population is associated with a lower use of GP IIb/IIIa inhibitors and a lower mortality in patients with STEMI undergoing primary PCI. These findings support the findings of the TRITON-TIMI 38 trial.

P1472 | BENCH
Associations of plasma microRNAs with platelet proteins and platelet function

K. Willeit2, P. Willeit3, T. Barwani1, A. Zampetaki1, A.C. Morton 4, S. Kiechl 2, R.F. Storey 4, M. Mayr1, 1King’s College London, Cardiovascular Division; King’s British Heart Foundation Centre, London, United Kingdom; 2Innsbruck Medical University, Department of Neurology, Innsbruck, Austria; 3University of Cambridge, Department of Public Health and Primary Care, Cambridge, United Kingdom; 4University of Sheffield, Department of Cardiovascular Science, Sheffield, United Kingdom

Objectives: Platelets shed microRNAs (miRNAs). Plasma miRNAs change upon platelet activation. It is currently unclear which plasma miRNAs are of platelet origin and best correlate with residual platelet reactivity in patients on dual anti-platelet therapy.

Methods and results: Next-generation sequencing of small RNAs was performed in platelet-poor and platelet-rich plasma. Selected platelet-related miRNAs were then measured in plasma samples from the population-based Bruneck cohort (year 2000 follow-up). Levels of miR-126, miR-223, miR-24, miR-191 and miR-21 strongly correlated with plasma concentrations of platelet proteins such as P-selectin, platelet factor 4 and platelet basic protein (r = 0.50–0.63, n = 390, p < 0.001). Next, platelet-related miRNAs were analysed in plasma of 125 patients with a history of ACS (STEMI, NSTEMI or unstable angina) who have undergone detailed assessment of platelet function 30 days after the acute event, including optical aggregometry using agonists arachidonic acid and ADP and flow cytometrically measured stimulated phosphoprotein (VASP) phosphorylation assay and VerifyNow P2Y12 assay. Significant positive associations were obtained for miR-126 with the VerifyNow (r = 0.347, n = 39, P = 0.033) and VASP assay (r = 0.224, n = 125, P = 0.013). MiR-23 (r = 0.231, P = 0.003) and other abundant platelet miRNAs also showed significant correlations with the VASP assay.

Conclusions: Platelets are a major determinant of plasma miRNAs as evidenced by the abundance of platelet miRNAs in plasma and their strong correlation to platelet proteins. Notably, levels of platelet-related plasma miRNAs correlate with platelet function tests in ACS patients on dual anti-platelet therapy.

Acknowledgement/Funding: British Heart Foundation; Fondation Leducq

P1473 | BEDSIDE
The role of CYP2C19 and ABCB1 polymorphisms on platelet reactivity during dual antiplatelet therapy

X. Hou. Shanghai Chest Hospital, Shanghai, China, People’s Republic of China

Background: Both high on-treatment platelet reactivity (HPR) and gene polymorphisms have been proposed to stratify cardiovascular event risk and to personalize maintenance dual antiplatelet therapy (DAPT) in stented patients. The current study sought to evaluate the clinical impact of newly reported genetic variations and their association with clopidogrel HPR in PCI patients with drug-eluting stent (DES) implantation.

Methods: The study enrolled 147 consecutive patients undergoing DES implantation. A total of 9 single nucleotide polymorphisms (SNPs) were selected from CYP2C19 loss-of-function (*2, *3) allele and ABCB1 C3435T variant. Thrombelastography (TEG) was performed to test the post-procedure maximum platelet agglutination (MA-ADP). The primary endpoint was a composite of cardiovascular death, non-fatal myocardial infarction (MI), stent thrombosis, and ischemic stroke at two-year follow-up after DES placement. The secondary endpoint was the incidence of bleeding events.

Results: The prevalence of post-procedure HPR was 36% measured by TEG (n = 53). Overall, 11 (7.5%) first ischemic events occurred. Patients with ischemic events had higher MA-ADP (P < 0.001 for all comparisons). Using multivariate logistic regression analysis, the carriage of CYP2C19*3 LOF alleles was an independent predictor of the post-procedure HPR (OR: 4.7, 95% CI: 1.70–17.23, p < 0.001). Through multivariate Cox regression analysis, the carriage of CYP2C19*3 LOF alleles and the post-procedure HPR were independent predictors of the primary endpoint (HR: 2.7, 95% CI: 1.60–5.97, p < 0.001; HR: 3.9, 95% CI: 1.42–8.57, p < 0.001, respectively). However, post-procedure MA-ADP did not predict a bleeding event (HR: 0.8, 95% CI: 0.34–1.49, p = 0.648).
Conclusions: This study indicates that CYP2C19*3 LoF allele carrier status is an important independent predictor of the pharmacodynamic response to clopidogrel. HPR and CYP2C19 LoF carriage are associated with clinical outcomes in high-risk clopidogrel-treated patients who have undergone PCI.

P1474 | BEDSIDE
Contemporary antithrombotic strategies in patients with acute coronary syndrome managed without revascularization: insights from the EYESHOT study.
L. De Luca1, S. Leonard2, I.M. Smeccas3, D. Formigli4, D. Luci5, B. Tuccillo6, Z. Oliwa7, M.M. Gulizia7, F.M. Bovenzi7, S. De Servi8 on behalf of EYESHOT Investigators. 1 European Hospital, Cardiovascular Sciences, Rome, Italy; 2 Policlinic Foundation San Matteo IRCCS, Pavia, Italy; 3 Ospedale Civico, Palermo, Italy; 4 G Rummo Hospital, Benevento, Italy; 5 Associazione Nazionale Medici Cardiologi Ospedalieri Research Center, Florence, Italy; 6 Santa Maria di Loreto Mare Hospital, Naples, Italy; 7 Hospital Santa Maria da Caroncella, Treviso, Italy; 8 Garbaldi Hospital, Catania, Italy; 9 Campo di Marte Hospital, Lucca, Italy

Background: Patients with acute coronary syndrome (ACS) who are managed without coronary revascularization represent a mixed and understudied population that seems to receive sub-optimal pharmacological treatment.

Methods and results: We assessed patterns of antithrombotic therapies employed during the hospitalization and in-hospital clinical events of medically managed patients with ACS enrolled in the prospective, multicenter, nationwide EYESHOT registry. Among the 2585 consecutive ACS patients enrolled in EYESHOT, 783 (30.3%) did not receive any revascularization during hospital admission. Of these, 478 (61.0%) underwent coronary angiography while 305 (39.0%) did not. The median GRACE and CRUSADE risk scores were significantly higher among patients who did not undergo coronary angiography compared to patients who did (180 vs 145, p < 0.0001, and 50 vs 33, p < 0.0001, respectively). Antithrombotic therapies employed during hospitalization significantly differ between patients who received coronary angiography compared to those who did not, with fractionated heparin and novel P2Y12 inhibitors more frequently used in the first group, and low-molecular weight heparins and clopidogrel in the latter group. During the index hospitalization, patients who did not receive coronary angiography presented a higher incidence of ischemic cerebrovascular events and of mortality compared to patients who underwent coronary angiography (1.6% vs 0.2%, p = 0.04 and 7.9% vs 2.7%, p = 0.0009, respectively).

Acknowledgement/Funding: Device support from ITC

P1475 | BEDSIDE
Determinants of post-discharge bleeding events in ACS patients during antplatelet therapy: insight from the A-MATCH trial.
Y.H. Jeong1, O.J.H. Oh1, S.E.S. Shin2, Y.H.J. Yoon3, S.J. Suh4, L.K.H. Lee5, L.S.H. Lee6, K.J.H. Kim7 on behalf of A-MATCH. 1 Gangneung National University Hospital, Jinju, Korea, Republic of; 2 Samsung Changwon Hospital, Internal medicine, Changwon, Korea, Republic of; 3 Ulsan University Hospital, Internal medicine, Ulsan, Korea, Republic of; 4 Keimyung University Hospital Dongsan Medical Center, Internal medicine, Daegu, Korea, Republic of; 5 Soonchunhyang University Hospital, Internal medicine, Bucheon, Korea, Republic of; 6 Gil Hospital, Internal medicine, Incheon, Korea, Republic of; 7 Soonchunhyang University Hospital, Internal medicine, Cheonan, Korea, Republic of; 8 Pusan National University, Internal medicine, Yangsan, Korea, Republic of

Background: During P2Y12 inhibitor therapy, determinants of post-discharge bleeding events have not been sufficiently understood.

Purpose: To evaluate the determinants related to bleeding episode in patients with ACS receiving dual antplatelet therapy.

Methods: After uneventful PCI, ACS patients on prasugrel (n=250) were followed with ACS or elective PCI were scheduled for platelet function assessment at 30–90 days post-discharge. Platelet function was assessed by whole blood impedance aggregometry, ADP test results and vitamin D levels (r=−0.11, p=0.028). Significant impact of ADP test values on platelet function in patients treated with dual antiplatelet therapy (DAPT) after a recent acute coronary syndrome or PCI.

Conclusion: Almost one-third of ACS patients are managed without revascularization during the index hospitalization. In this population, a lower use of recommended antiplatelet therapy and worse clinical outcome was observed in those who did not undergo coronary angiography as compared to those who did.

P1476 | BEDSIDE
Vitamin D levels and high-resolution platelet reactivity in patients receiving dual antiplatelet therapy with clopidogrel or ticagrelor.
M. Verdoia1, M. Nardin1, C. Sartori1, A. Schaffer1, G. Di Giovine1, P. Marino2, H. Suryapranata3, G. De Luca4, L. De Luca5, S. Leonardi2, I.M. Smecca3, D. Formigli4, D. Lucci5, B. Tuccillo6, M. Verdoia1, M. Nardin1, C. Sartori1, A. Schaffer1, G. Di Giovine1, P. Marino2, H. Suryapranata3, G. De Luca4, L. De Luca5, S. Leonardi2, I.M. Smecca3, D. Formigli4, D. Lucci5, B. Tuccillo6

Background: Suboptimal platelet inhibition still represents an important challenge, especially for patients undergoing percutaneous coronary interventions (PCI). However, very few is known so far on the predictors of high-resolution platelet reactivity (HRPR) despite antiplatelet strategies.

Purpose: Aim of our study, therefore, to evaluate the impact of vitamin D levels on platelet function in patients treated with dual antiplatelet therapy (DAPT) after a recent acute coronary syndrome or PCI.

Methods: Patients treated with DAPT (ASA + clopidogrel or ticagrelor) for an ACS or elective PCI were scheduled for platelet function assessment at 30–90 days post-discharge. Platelet function was assessed by whole blood impedance aggregometry. HRPR was considered for ASPI test > 862 AU*min (for ASA) and ADP-HPR > 258 BASE (for ADP-antagonists). Fasting samples were obtained for main chemistry parameters and vitamin D levels assessment.

Results: 432 patients were included, and divided according to vitamin D tertiles (11.3–20.5 ng/ml). Lower vitamin D levels related with diabetic status (p=0.007) and previous coronary surgery (p=0.02). Vitamin D inversely related with total and LDL cholesterol levels (p=0.003 and p=0.03, respectively), triglycerides (p=0.001), fibrinogen (p=0.001) and HbA1c values (p<0.001).

Conclusion: Lower vitamin D levels are associated with higher platelet reactivity and impaired effectiveness of ADP-antagonists, especially for ticagrelor, while not influencing the effectiveness of ASA. Future studies will tell whether vitamin D supplementation can reduce platelet reactivity, overcoming the phenomenon of resistance to antiplatelet agents.

P1477 | BEDSIDE
Real world evaluation of 1st and 2nd generation antiplatelet and anticoagulant therapy in patients following percutaneous coronary intervention (PCI).

Background: PCI with drug eluting stent (DES) necessitates dual antiplatelet therapy (DAPT). However, DAPT with requirement for anticoagulation remains problematic as duration of triple therapy is undetermined. Moreover, newer antiplatelet agents in conjunction with anticoagulants have not been tested in randomized trials.

Purpose: We present real world data on patients undergoing PCI and compare bleeding and MACCE (death, MI, stroke, target lesion or vessel revascularisation) on different antiplatelets and anticoagulants.

Methods: 424 consecutive patients underwent PCI through 2013. The indication for PCI was ACS (51%) or symptomatic angina. Male 71%, 8% <50yrs and 30% >75yrs. DAPT regimen with aspirin: clopidogrel 54%, prasugrel 23%, ticagrelor 10%. Other antiplatelet due to intoler-
Treated patients. By multivariate analysis, in prasugrel-treated patients insulin-treated DM (vs. prasugrel) and insulin-treated DM significantly affected PR in the overall population with a 58.4% decrease in PR compared to prasugrel or ticagrelor treated patients is not well studied.

Methods: We analyzed patient-level data from 5 studies of 207 P2Y12-receptor antagonist naïve patients with STEMI undergoing primary percutaneous coronary intervention (PCI). Patients were loaded with clopidogrel 600 mg, prasugrel 60 mg or ticagrelor 180 mg and had available platelet reactivity assessment with the VerifyNow assay (in PRU) prior to and 2 hours post loading. High platelet reactivity (HPR) was defined as >208 PRU.

Results: There was an incremental decrease in platelet reactivity at Hour 2 across quartiles of pain-to-antiplatelet loading time (Figure 1). Pain-to-antiplatelet loading time independently predicted platelet reactivity at 2 hours post loading: with a 7% decrease in platelet reactivity every 1-hour increase in pain-to-antiplatelet loading time, p=0.001. Pre-treatment platelet reactivity, body mass index, morphine and novel P2Y12 receptor antagonist also affected platelet reactivity 2 hours post loading. Per hour increase in pain-to-antiplatelet loading time and novel P2Y12 receptor antagonist use were independently associated with lower probability for HPR with a relative risk (95% confidence intervals, CI) of 0.87 (0.80 to 0.95) and 0.41 (0.31 to 0.55), p=0.002 and p<0.001, respectively. (C-statistic 0.75, 0.69 to 0.82 95% CI).

Conclusions: In STEMI patients undergoing primary PCI, a patient-level data meta-analysis revealed the pain-to-antiplatelet loading interval as a newly described factor affecting platelet reactivity shortly after P2Y12 receptor antagonist loading.

Conclusions: In patients on novel antiplatelet agents, apart from a lower PR provided by ticagrelor vs prasugrel, insulin-treated DM predicts higher levels of PR than non diabetic status. This detrimental effect of insulin-treated DM is confined in prasugrel-treated patients, while PR under ticagrelor is not affected by DM status or insulin/non-insulin treatment.

Conclusions: In patients on novel antiplatelet agents, apart from a lower PR provided by ticagrelor or prasugrel, insulin-treated DM predicts higher levels of PR than non diabetic status. This detrimental effect of insulin-treated DM is confined in prasugrel-treated patients, while PR under ticagrelor is not affected by DM status or insulin/non-insulin treatment.

P1480 | BEDSIDE
Diabetes mellitus, glucose control parameters and platelet reactivity in ticagrelor treated patients

M. Verdica, M. Nardinb, L. Barbieri1, A. Schaffer1, P. Marino1, H. Suryapranata2, G. De Luca1 on behalf of Novara Atherosclerosis Study Group. 1 Maggiore Della Carita Hospital, Department of Invasive Cardiology, Novara, Italy; 2 Radboud University Medical Centre, Nijmegen, Netherlands

Background: Advances in percutaneous coronary revascularization strategies and anti-thrombotic therapies have not filled the prognostic gap between diabetic and non diabetic patients after an acute cardiovascular event. In fact, diabetes mellitus and poor glycemic control represent well established pro-thrombotic conditions, that have been associated to a reduced effectiveness of antiplatelet therapies and an increased risk of high-residual platelet reactivity (HRPR) and recurrent ischemic events. New antiplatelet agents, as ticagrelor, have provided a more potent and predictable platelet inhibition, potentially offering larger benefits in those patients with enhanced thrombotic status.

Purpose: To investigate the relationship between diabetes mellitus and platelet reactivity in patients treated with ticagrelor for a recent acute coronary syndrome (ACS).

Methods: 224 post-ACS patients, treated with a dual antiplatelet therapy with ASA (100–160 mg) and ticagrelor (90 mg twice a day) were scheduled for platelet
reactivity assessment at 30–90 days post-discharge. Diabetic status was defined for an history of diabetes treated with or without drug therapies, fasting glucose >126 g/dl or HbA1c >6.5% at the moment of admission. Aggregation was assessed by multiple-electrode aggregometry. HRPR during ticagrelor treatment was defined as ADP test results >417 AU/min.

Results: 86 out of 224 patients (38.4%) were diabetic. Diabetic status related to older age (P < 0.05), higher BMI (P < 0.009), renal failure (P < 0.016), hypertension (P < 0.02), treatment with diuretics (P < 0.02), higher levels of WBC, glycemia, HbA1c, and lower levels of HDL-cholesterol (P < 0.01, respectively).

Platelet reactivity in diabetics is increased compared to non diabetics (p = 0.046 for ASPi for COL test, p = 0.03 for TRAP test and p = 0.002 for ADP test). 29 patients (12.9%) displayed HRPR with ticagrelor with an almost double ratio in diabetics as compared to non-diabetics (18.3% vs 9.4%, p = 0.06; adjusted OR 2.17, P = 0.021). Direct linear relationship was observed between ADP-mediated platelet reactivity and glycosylated hemoglobin, as a parameter of chronic glycomic control, (r = 0.15, p = 0.029), but not with fasting glycemia (r = 0.08, p = 0.20).

Conclusion: Present study shows among post-ACS patients, that diabetic status is associated with a higher platelet reactivity despite dual antiplatelet therapy with ASA and ticagrelor, and especially in those patients with poor chronic glycomic control. In fact, diabetes emerged as independent predictor of HRPR with ticagrelor.

bleeding cases

Backgrounds of bleeding cases

<table>
<thead>
<tr>
<th></th>
<th>DAPT group</th>
<th>N group</th>
<th>N2 group</th>
<th>N3 group</th>
<th>W2 group</th>
<th>W3 group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (n=104)</td>
<td>n (n=125)</td>
<td>n (n=30)</td>
<td>n (n=15)</td>
<td>n (n=30)</td>
<td>n (n=30)</td>
<td></td>
</tr>
</tbody>
</table>

Major bleeding events

<table>
<thead>
<tr>
<th></th>
<th>DAPT group</th>
<th>N group</th>
<th>N2 group</th>
<th>N3 group</th>
<th>W2 group</th>
<th>W3 group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>2 (2%)</td>
<td>2 (2%)</td>
<td>0 (1%)</td>
<td>2 (22%)</td>
<td>7 (23%)</td>
<td></td>
</tr>
</tbody>
</table>

Gastrointestinal

<table>
<thead>
<tr>
<th></th>
<th>DAPT group</th>
<th>N group</th>
<th>N2 group</th>
<th>N3 group</th>
<th>W2 group</th>
<th>W3 group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Intracranial

<table>
<thead>
<tr>
<th></th>
<th>DAPT group</th>
<th>N group</th>
<th>N2 group</th>
<th>N3 group</th>
<th>W2 group</th>
<th>W3 group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

P1484 | BENCH

CRTMP4 expression in platelet of patients under chronic aspirin treatment is influenced by microRNA modulation: a new mechanism for aspirin resistance?

L.M. Biasuccu1, C. Mandolini1, I. Massimi2, G. Coppolis3, F. Pulcinelli3, F. Crea1.

1 Catholic University of the Sacred Heart, Rome, Italy; 2Sapienza University of Rome, Rome, Italy

Background: MicroRNA are small molecule of non-coding RNA involved in the regulation of many physiological and pathophysiological pathway, including modulation of drug activity. microRNA are abundant also in platelets, where they might participate to the modulation of platelet reactivity.

Recently over-expression of the multidrug resistance protein-4 (MRP4), an ATP Binding Cassette membrane transporter, actively involved in the efflux of pharmacological and physiological compounds, has been suggested as a mechanism of platelet resistance.

Purpose: To establish whether microRNAs may induce MRP4 modulation in patients under aspirin treatment.

Methods: MRP4 mRNA expression was analyzed by RealTime PCR on 2 cohort of 25 platelet samples of patients under ASA treatment versus a control group. To test which microRNAs were present in platelets we run a microarray panel of 176 microRNA. We compared the pool of the cohorts under aspirin treatment, with a pool of the healthy volunteer. Different microRNAs were dys-regulated in presence of aspirin. We selected highly dys-regulated microRNAs, with a difference of the fold induction >2. A panel of 174 microRNA was run on the pool of each cohort. MicroRNA-26b was transfected in platelet with microRNA mimic technology and flow cytometry was performed to analyse MRP4 platelet expression.

Results: We found a higher MRP4 mRNA expression in platelets of patients under aspirin treatment versus control group. We measured in the two cohort of patients under aspirin treatment a significant up-regulation of microRNA-26b. Analysis revealed the absence of the two MRP4 targeting microRNA, mir-124a-3p and mir-506, in platelets. In the pool validation, microRNA 26b-5p, which targets MRP4, was found significantly down-regulated in the two cohort of patients under aspirin treatment, compared to control group (p < 0.005). Platelet transfusion with microRNA mimic 26b showed a significant down-regulation of MRP4 protein (p = 0.008).

Conclusion: Our study demonstrates that microRNA-26b-5p may down-regulate MRP4 in platelets. These evidences suggest that microRNAs are involved in MRP4 modulation in patients under ASA treatment, and suggest mir-26b-5p as putative therapeutic target in aspirin resistance.

Acknowledgement/Funding: grant from Catholic University 70112072

Platelets and antiplatelets therapy III

P1484 | BENCHMARK

Single nucleotide polymorphism in glycoprotein VI gene associated with platelet expression of the glycoprotein VI and risk of cardiovascular events

M. Dropra1, D. Rath1, K. Mueller1, F. Stemple1, A. Allobi2, E. Schaefeler2, M. Schwab2, M. Gawais2, T. Geiser1,1 University Hospital of Tubingen, Department of Cardiology and Cardiovascular Medicine, Germany; 2 Or Margarete Fischer-Bosch-Institute of Clinical Pharmacology, Stuttgart, Germany

Background: Platelet glycoprotein VI (GPVI) is an important receptor mediating platelet adhesion on collagen of extracellular matrix after vascular injury. It plays a crucial role in platelet activation and thrombus formation in patients with acute coronary syndromes and thrombosis. Genetic variants of GPVI have been related to adverse events in patients with coronary artery disease. We aimed to evaluate the influence of selected GPVI polymorphism on platelet expression of GPVI and adverse ischemic events in patients undergoing PCI.

Methods: 737 patients admitted with symptomatic coronary artery disease from Japan...
P1485 | BEDSIDE
The impact of therapeutic hypothermia on on-treatment platelet reactivity and clinical outcome in cardiogenic shock patients undergoing primary PCI for acute myocardial infarction
1Ludwig-Maximilians University, Department of Cardiology, Munich, Germany; 2German Heart Center, Clinic for Heart and Circulatory Diseases, Munich, Germany; 3Hospital Rechts der Isar, Medizinische Klinik I, Munich, Germany

Introduction: Mild therapeutic hypothermia (TH) is standard of care after cardiac arrest. Its impact on on-treatment platelet reactivity and clinical outcome in patients with acute myocardial infarction (AMI) complicated by cardiogenic shock and undergoing primary PCI with P2Y12 receptor inhibitor treatment is largely unknown.

Methods and results: 145 patients with AMI complicated by cardiogenic shock and undergoing primary PCI in two centers between January 2009-May 2012 were analysed. Of these, 64 (44%) patients received TH treatment. The median (IQR) ADP-induced platelet aggregation following thienopyridine loading dose administration (clopidogrel in 95 and prasugrel in 50 patients) did not differ between the two groups (419 [283 - 684] for TH vs. 355 [207–710] AU x min for non-TH patients, P=0.22). After 30 days follow-up, no significant differences were observed between both groups for mortality (42 vs. 44%, HR: 0.93, 95% CI [0.56–1.53], P=0.22), MI (8 vs. 7%, HR: 0.99 95% CI [0.27–3.7], p=0.99) and TIMI minor bleedings (22 vs. 21%, HR: 0.99 95% CI [0.45–2.18], p=0.98). TIMI major bleedings were numerically higher in the TH vs. non-TH cohort (31% vs. 15%, HR: 2.1 95% CI [0.95–4.63], p=0.07). Three definite stent thrombosis (ST) were observed in patients in the TH group compared to none in the non-TH cohort.

Conclusion: Results of this registry suggest that TH does not negatively impact on platelet reactivity in shock patients receiving either clopidogrel or prasugrel. The numerically higher rate of major bleedings and the clustering of STs in the TH cohort warrant further investigation.

P1486 | BEDSIDE
Short versus prolonged dual antiplatelet therapy (DAPT) duration after coronary stent implantation: a comparison between the DAPT trial and 9 other trials evaluating DAPT duration
T. Toyota1, H. Shiomii1, T. Morimoto2, M. Natsukai3, T. Kimura1.
1Kyoto University Graduate School of Medicine, Department of Cardiovascular Medicine, Kyoto, Japan; 2Hyogo College of Medicine, Department of Clinical Epidemiology, Nishinomiya, Japan; 3Saiseikai Fukuoka General Hospital, Division of Cardiology, Fukuoka, Japan

Aims: The Dual Antiplatelet Therapy (DAPT) trial demonstrated that DAPT beyond 1-year after drug-eluting stent (DES) implantation, as compared with aspirin therapy alone, significantly reduced the risk of major cardiovascular and cerebrovascular events, by which stent thrombosis and myocardial infarction were included. However, the optimal duration of DAPT remains unclear.

Methods and results: By a systematic literature search, we identified 9 trials comparing prolonged- versus short-DAPT in addition to the DAPT trial. The result from the DAPT trial (N=9961) with public–private collaboration was discordant with the pooled result from the 9 other investigator-driven trials (N=22174) in terms of the effect of prolonged-DAPT on MI (odds ratio [OR] 0.48 [95% CI 0.38–0.62] versus pooled OR 0.88 [95% CI 0.67–1.15], P=0.01 for difference), strokes (145 patients with AMI complicated by cardiogenic shock) and other trials evaluating DAPT durations after DES implantation.

Conclusion: Given the discrepancy between the DAPT trial and other trials, further studies may be mandatory to define the optimal DAPT duration after coronary stent implantation.

Acknowledgement/Funding: This project was supported in part by the DFG-Klinische Forschergruppe (KFO) 274 “Platelets and Molecular Mechanisms”
P1489 | BEDSIDE
Use of oral antiocoagulants in combination with antiplatelet therapy: insights from the GLORIA-AF registry

G.Y.H. Lip1, J. Halperin2, H.C. Diener3, S.J. Dubreuil4, C.S. Ma5, K.J. Rothman6, K. Zinn7, A. Elsasser8, C. Teutsch9, M.V. Huissman10, 1University of Birmingham, Centre for Cardiovascular Sciences, Birmingham, United Kingdom; 2Mount Sinai School of Medicine, New York, United States of America; 3University of Essen (Ruhr), Department of Neurology and Stroke Center, Essen, Germany; 4Cleveland Clinic Foudnation, Cleveland, Ohio, United States of America; 5University of Chile, Santiago, Chile; 6University of Buenos Aires, Buenos Aires, Argentina; 7University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin, United States of America; 8University of Leipzig, Leipzig, Germany; 9Boehringer Ingelheim GmbH, Corporate Department Global Epidemiology, Ingleheim, Germany; 10Boehringer Ingelheim Corporation, Clinical Trial Portfolio, Burlington, Canada; 11Boehringer Ingelheim GmbH, Cardiology, Ingleheim, Germany; 12Leiden University Medical Center, Department of General Internal Medicine, Leiden, the Netherlands.

Background: Antiplatelet drugs (AP) are often co-prescribed with oral anticoagulants (OAC) in patients with atrial fibrillation (AF) and associated vascular disease, or if the patient is at high vascular risk, even though there is little evidence of added efficacy and there is potential for excess harmful bleeding, especially intracranial haemorrhage. For patients with vascular disease, there has also been the perception that AP should be added to non-vitamin K antagonist OACs (NOACs).

Methods: We examined concomitant use of AP in GLORIA-AF (a prospective, global, observational study program of patients with newly diagnosed non-valvular AF), in relation to vascular and non-vascular AF.

Results: Of 10675 patients in Phase II (median age 71 years, 54.5% male; median CHA2DS2-VASc score 3), 20.6% had coronary artery disease (CAD), 10.5% had a prior myocardial infarction and 3.3% had peripheral artery disease (PAD). The majority were on OAC (n=8539, 80.0%), with only 12.3% on AP alone and 7.6% on an antithrombotic therapy. AP was co-prescribed with VKA in 5.4%, and with NOACs in 6.6% of patients. Amongst males with a CHA2DS2-VASc=1 (moderate risk), AP was co-prescribed with VKA in 4.4% and with NOACs in 5.1%. In male AP patients with CHA2DS2-VASc=2, AP was co-prescribed with VKA in 6.8% and with NOACs in 8.5%. In females with CHA2DS2-VASc=1 (low risk), AP was co-prescribed with VKA in 2% and with NOAC in 1.2%. In females with CHA2DS2-VASc=2, AP was co-prescribed with VKA in 4.5%, and with NOAC in 5.4%. Regional variation was evident, with VKA+AP most common in North America (6.6%) and Asia (6.7%), vs Europe, 4.2% and Latin America, 2.3%. NOAC+AP was more common in North America (11.4%) and Latin America (11.1%), compared with Europe (4.0%) and Asia (3.1%). AP patients with PAD had higher use of VKA+AP (10.1% vs no PAD, 5.1%) and NOAC+AP (14.6% vs no PAD, 6.2%). As did AF patients with coronary artery disease (CAD), with VKA+AP (11.4% vs no CAD, 3.8%) and NOAC+AP (15.2% vs 4.3%).

Conclusion: These observational data show that a minority of AF patients are prescribed AP in combination with OAC, with co-prescription being similar between NOACs and VKAs. Combination therapy with AP in patients taking OAC was 2–3 fold more common where PAD or CAD was present.

Acknowledgement/Funding: This study was funded by Boehringer Ingelheim.

P1490 | BEDSIDE
Short versus long term dual antiplatelet therapy after drug eluting stent implantation: systematic review and meta-analysis of randomized controlled trials

P. Villablancas Spinetti1, 2, P. Christia2, 3, D. Briceno1, 3, M. Salih4, 5, W. Gonzalez1, 5
1Montefiore Medical Center (Bronx), New York; 2Jacobi Medical Center/ Albert Einstein College of Medicine, New York, 3St. Luke's Hospital, Cardiology, Chesterfield, United States of America

Background: The benefit of 1-year dual antiplatelet therapy (DAPT) as compared to short-term (<6 months) treatment, in patients undergoing percutaneous coronary intervention (PCI) after drug-eluting stent (DES) implantation remains controversial.

Purpose: Goal of the current meta-analysis was to compare the efficacy and safety of short (<6 months) versus long (≥12 months) duration of DAPT after DES implantation.

Methods: Medical literature databases were scrutinized to identify randomized controlled trials fulfilling inclusion criteria between January 1990 and December 2014. Efficacy endpoints were all-cause and cardiovascular mortality, stroke and major bleeding, myocardial infarction at 12 months. Safety endpoints were the incidence of all and major bleeding, definite or probable stent thrombosis and target vessel revascularization. Data were compared by OR and 95% CI using the Mantel-Haenszel (MH) method. Fixed-effect model was used; if heterogeneity was (I2) >50%, effects were obtained with random model.

Results: Seven randomized controlled trials met inclusion criteria, enrolling a total of 16,017 patients. No statistically significant benefit was found in terms of efficacy endpoints when 12 months of DAPT was compared with short term treatment (Figure 1). In particular, no statistically significant fewer events were observed in the long term treatment group compared with the short term treatment group. No difference was identified in terms of stent thrombosis between short and long term treatment group.

Conclusion: Our data suggest no benefit of one year versus short term therapy in patients undergoing DES implantation. There is a significant harm with regards to bleeding episodes associated with long term DAPT therapy.

P1491 | BEDSIDE
Genome-wide and candidate gene approaches of clopidogrel efficacy using pharmacodynamic and clinical end points - International Clopidogrel Pharmacogenomics Consortium (ICPC) study design

T.O. Bergmeijer - For The International Clopidogrel Pharmacogenomics Consortium Investigators on behalf of International Clopidogrel Pharmacogenomics Consortium (ICPC) Investigators. St Antonius Hospital, Department of Cardiology, Nieuwegein, Netherlands.

Background: The P2Y12 inhibitor clopidogrel is widely used in patients with coronary artery disease and other atherosclerosis related conditions. An important limitation of clopidogrel is the wide inter-patient variability of platelet inhibition observed with pharmacokinetic and pharmacodynamic testing, in which high platelet reactivity is a strong predictor of atherothrombotic events. The CYPC2192*2 polymorphism is the strongest genetic predictor of clopidogrel response known today; however, this variant only explains a small minority of the variability in platelet inhibition with clopidogrel, while heritability studies suggest that other important genetic determinants may exist. The aim of the International Clopidogrel Pharmacogenomics Consortium (ICPC) is to identify novel genetic determinants of clopidogrel response and correlate them with platelet function data and clinical outcomes by using GWAS and candidate gene approaches in a large dataset from independent patient cohorts.

Methods: Based on the available data published on www.clinicaltrials.gov, clopidogrel intervention studies containing genetic and platelet function data were selected. Lead investigators were invited to share DNA samples, platelet function test results, clinical baseline characteristics and cardiovascular outcome data to perform GWAS and candidate gene analyses. For the primary GWAS analysis a combined thrombotic end point consisting of cardiovascular death, spontaneous myocardial infarction, ischemic stroke and definite stent thrombosis was used. Results: In total, 18 study centers from 13 countries are participating in the ICPC, providing individual data from 8,829 patients. A first GWAS analysis of over 2,600 patients has been performed; the remaining patients serve as a replication cohort. In the GWAS group – 76% male, average age 64 years – 1 year follow-up is available for the majority of patients. The primary end point occurred in 5.8% of patients. Platelet function tests were performed in all patients, predominantly Vasodilator-Stimulated Phosphoprotein assay (VASP), adenosine diphosphate stimulated Light Transmittance Aggregometry (LTA) and VerifyNow P2Y12. A QC analysis using the individual genotypes reported in each cohort showed a strong correlation between CYP2192*2 and thrombotic outcome (p<0.01). Specific pre-specified sub analyses are planned.

Conclusion: The ICPC aims to identify new genes influencing clopidogrel efficacy by using state of the art genetic techniques in a large cohort of clopidogrel treated patients. Our findings may further facilitate the development of personalized medicine programs.

Acknowledgement/Funding: National Institutes of Health (NIH) grant (L01HL091918). SNP genotyping is supported by the PharmacoGenomics Research Network & CGM Global Alliance.
P1491 | BEDSIDE
A systematic review and meta-analysis of optimal antiplatelet therapy for diabetic patients with acute coronary syndrome
J. Rossington, O.I. Brown, A. Hoye, Hull York Medical School, Academic Cardiology, Hull, United Kingdom

Introduction and aims: Diabetic patients are at increased risk of Acute Coronary Syndromes (ACS), with relatively higher rates of mortality and morbidity. This systematic review sought to establish the optimum P2Y12 receptor antagonist therapy for this high risk population.

Methods: We searched databases (Medline and Embase) and conference abstracts to 8th June 2014; for randomised control trials with clinical outcomes for P2Y12 inhibitors in adult diabetic patients with ACS. 2 authors independently evaluated the quality of studies and extracted data. Meta-analysis was performed with statistical direct and indirect comparison. Studies were evaluated for the primary composite end point of cardiovascular death, non-fatal myocardial infarction and non-fatal stroke.

Results: 1162 studies were reviewed and 17 articles (7 studies) satisfied protocol criteria. 4 compared clopidogrel to placebo in diabetic patients of which 2 had the required primary outcome (n=3122). Results showed superiority of clopidogrel (relative risk (RR) 0.84 (95% confidence interval (CI) 0.72–0.99)). Irrespective of management strategy, the newer agents prasugrel (2 studies) and ticagrelor (1 study) had a lower primary event rate compared to clopidogrel; RR 0.80 (95% CI 0.66–0.97) and RR 0.89 (95% CI 0.77–1.02) respectively. Ticagrelor was indirectly compared to prasugrel showing a trend to an improved primary outcome with prasugrel (fig 1) particularly in those managed with percutaneous coronary intervention (PCI).

Conclusions: This meta-analysis shows that the addition of a P2Y12 Inhibitor is superior to placebo, with a trend favouring the use of prasugrel in diabetic patients with ACS. This supports the 2011 ESC guidance for the preferential use of prasugrel in the diabetic population due PCI for ACS.

Acknowledgement/Funding: Nil

P1492 | BEDSIDE
High on-treatment platelet reactivity (HTPR) with Ticagrelor versus Prasugrel: a comprehensive metaanalysis
G. Lemesle1, G. Schurz1, C. Bauters2, M. Hamon3, 1Cardiology Hospital of Lille, Intensive Care Unit, Lille, France; 2Cardiology Hospital of Lille, Lille, France; 3Centre Hospitalier Universitaire de Caen, Service de Cardiologie, Caen, France

Background: Ticagrelor and prasugrel have shown superiority as compared to clopidogrel. It remains however unclear if one is superior to another regarding on-treatment platelet reactivity.

Objectives: To compare the impact of ticagrelor and prasugrel on high on-treatment platelet reactivity (HTPR).

Methods: The PubMed and Cochrane database were searched for eligible studies in December 2014. Studies were eligible if they compared ticagrelor and prasugrel on HTPR. Pooled estimates were calculated by using a random-effects model with 95% confidence intervals.

Results: We included 14 studies and 1822 patients: 805 and 1017 in the ticagrelor and prasugrel groups, respectively. Altogether, 7 studies used the VerifyNow-P2Y12 assay and 6 used the vasodilator stimulated phosphoprotein test, 1 used both. The rate of HTPR was significantly lower in the ticagrelor group: 1.5% versus 9.8% (RR=0.27 [0.14–0.50]). The pre-specified analysis focusing on randomized trials (n=10) showed consistent results (RR=0.27 [0.12–0.60]).

Conclusion: Our results suggest that ticagrelor allows a higher platelet reactivity inhibition as compared to prasugrel and leads to further decrease the rate of HTPR.

P1493 | BEDSIDE
Antiplaque effect of clopidogrel monotherapy in patients with oral anticoagulation with phenprocoumon undergoing coronary stent implantation

Background: The WOEST trial showed that in patients on oral anticoagulation with a vitamin K antagonist (VKA) undergoing coronary stent implantation, antiplatelet monotherapy with clopidogrel as compared to clopidogrel and aspirin is associated with less bleeding without increase in ischaemic events. However, retrospective data suggested a potential interaction of clopidogrel and the VKA phenprocoumon leading to a decreased antiplatelet effect. This would patients treated with the WOEST approach put on a particular high risk since no additional antiplatelet agent is used.

Purpose: This prospective controlled trial investigated the antiplatelet effect of clopidogrel in patients on phenprocoumon undergoing coronary stenting.

Methods: From 2013 to 2014, 100 patients on dual antiplatelet therapy (DAPT - aspirin and clopidogrel, but no VKA) and 100 patients on clopidogrel monotherapy and phenprocoumon (WOEST-cohort) were enrolled. ADP-induced platelet reactivity was assessed on day 1 following coronary stenting by impedance aggregometry (Multiplate Assay). High on-treatment platelet reactivity (HTPR) was defined according current consensus recommendations (≥468 AU*min).

Results: The WOEST- and DAPT-cohorts were, apart from mean age (75 vs 66 yrs), comparable with respect to variables impacting on antiplatelet effect of clopidogrel (male: 76 vs 77%; BMI: 27.4 vs 27.2; diabetes: 32 vs 27%). Mean ADP-induced platelet reactivity was similar in both cohorts (Figure). The incidence of HTPR was comparable low in both cohorts (4 vs 3%; p=0.70).

Conclusion: Following coronary stent implantation, the extent of ADP-induced platelet reactivity is similar in patients on clopidogrel monotherapy and phenprocoumon as compared to patients on dual antiplatelet therapy and no oral anticoagulation.

PLATELETS AND ANTIPLATELETS THERAPY IV

P1494 | BEDSIDE
Platelet surface expression of TGF-beta 1 is associated with platelet surface expression of SDF-1, CXCR4 and CXCR7

Background: TGF-β1, SDF-1 and the two SDF-1 receptors CXCR4 and CXCR7 are expressed on the surface of human platelets. Similar to SDF-1, platelet surface expression of CXCR7 is elevated in ACS (acute coronary syndrome) patients. High platelet surface expression of CXCR7 is associated with myocardial regeneration after ACS. Low CXCR4 levels are associated with increased rate of death and re-infarction in patients with symptomatic coronary artery disease (CAD). In addition, low platelet TGF-β1 is associated with mortality and re-infarction in CAD patients. Recently, few studies have suggested, that there might be a crosstalk between TGF-β1 and SDF-1 and that TGF-β1 might upregulate CXCR4 and CXCR7. We therefore investigated associations of TGF-β1, SDF-1, CXCR4 and CXCR7 in a clinical cohort of patients with symptomatic CAD.

Subjects and methods: Blood samples were collected during percutaneous coronary intervention (PCI) and immediately analysed for platelet surface expression of TGF-β1, SDF-1, CXCR4, CXCR7 by flow cytometry. We included 284 consecutive patients with symptomatic CAD (stable CAD n=143, ACS n=141).

Correlations were assessed by Spearman’s rank correlation coefficient (ρ).

Results: We found a strong correlation between TGF-β1 and CXCR7 (ρ=0.572, p<0.001). Platelet-TGF-β1 correlated significantly with platelet-CXCR4 (ρ=0.330, p<0.001) and platelet-SDF-1 (ρ=0.229, p=0.009).

Conclusion: Following coronary stent implantation, the extent of ADP-induced platelet reactivity is similar in patients on clopidogrel monotherapy and phenprocoumon as compared to patients on dual antiplatelet therapy and no oral anticoagulation.
P1494 | BEDSIDE
Comparison of short-term clinical outcomes between new p2y12 receptor inhibitors and clopidogrel in patients with acute myocardial infarction: from the core cohort in Korea


Background and objects: It has been well known that new P2Y12 receptor inhibitors (Ri: prasugrel or ticagrelor) could improve clinical outcomes in patients with acute myocardial infarction (AMI). However, there were little data about the impact of new P2Y12 Ri in Korean patients with AMI. Therefore, we compared the short-term clinical outcomes between new P2Y12 Ri and clopidogrel in patients with AMI undergoing successful percutaneous coronary intervention (PCI).

Methods: Between November 2011 and August 2014, a total of 4,029 patients (3,186 patients were prescribed clopidogrel and 843 patients new P2Y12 Ri [474 patients prasugrel and 369 patients ticagrelor]) with AMI undergoing successful PCI were included from Korea Acute Myocardial Infarction Registry-National Institute of Health. The patients older than 75 years, weight >60 kg, or with a history of stroke and with in-hospital switching among 3 antiplatelet agents were excluded. The propensity score matching (802 pairs) were performed in order to compare the in-hospital clinical outcomes between new P2Y12 Ri and clopidogrel after adjusting for baseline clinical and procedural confounders.

Results: P2Y12 reactivity unit by the VerifyNow P2Y12 test was 77.5±74.50 in new P2Y12 Ri and 92.5±87.72 in clopidogrel. The incidences of Thrombolysis In Myocardial Infarction (TIMI) major bleeding and minor bleeding were significantly higher in new P2Y12 Ri than clopidogrel (3.1% vs. 1.1%, p=0.006; 4.1% vs. 1.9%, p=0.006). However, there were no significant differences in in-hospital mortality and the composite of cardiac death, MI or stroke during hospital stay between new P2Y12 Ri and clopidogrel (1.0% vs. 0.7%, p=0.591; 1.0% vs. 1.1%, p=0.807). Also, no difference in the composite of cardiac death, MI, stent thrombosis, target vessel revascularization or stroke at 6 months was observed in both group (1.0% vs. 2.3%, p=0.114). On multivariate analysis, use of statin, TFM vs. TRU and use of glycoprotein IIb/IIIa inhibitors were independent predictors of the composite of cardiac death, MI, stent thrombosis, stroke or TIMI major bleeding (odd ratio [OR]=0.187; 95% confidence interval [CI]=0.083–0.422, OR=10.811; 95% CI: 2.560–45.652, OR=2.174; 95% CI: 1.103–4.284).

Conclusions: Our study showed that new P2Y12 Ri had similar efficacy for preventing ischemic events compared with clopidogrel, but an increased bleeding complications. The large scale, long-term, randomized trials should be needed to assess the safety of P2Y12 Ri for Korean AMI patients undergoing successful PCI.

P1495 | BEDSIDE
High on aspirin platelet reactivity predicts cardiac death in acute coronary syndrome patients undergoing PCI (RECLOSE2-ACS study)


High on clopidogrel platelet reactivity (HCPR) is associated with a higher risk for MACCE in patients with acute coronary syndromes (ACS) undergoing PCI; on the contrary, fewer and conflicting data are available on high on aspirin platelet reactivity (HAPR) and clinical outcome.

We performed a prospective study of 1789 consecutive patients with ACS undergoing PCI in whom platelet reactivity after clopidogrel loading was assessed by high-throughput aggregometry (APACT4, Helena Laboratories, Milan, Italy) using arachidonic acid (AA) as an agonist. HAPR was found in 20.3% of patients (364/1789). Patients with HAPR were significantly older, and with a higher prevalence of hypertension, diabetes and reduced ejection fraction. Patients with three-vessel disease and multivessel PCI had a significantly higher prevalence of HAPR. In addition, total stent length, number of stents per patient and use of DES were significantly higher in HAPR patients. At a 24 month-follow-up, in 89 patients we registered a cardiac death; in 41 a myocardial infarction was documented, in 22 an ischemic stroke, in 59 a stent thrombosis. Sixteen patients underwent a urgent revascularization.

The prevalence of cardiac death was 9.7% in HAPR (35/362) and 3.8% in no-HAPR (54/1410) [HR 2.63 (1.72–4.24) p<0.0001]; stent thrombosis 6.1% in HAPR (22/362) vs 2.6% in no-HAPR (37/1410) [HR 2.4 (1.42–4.07) p<0.001], whereas there were no significant differences in the other clinical end-points. The prevalence of cardiac death and stent thrombosis was 9% and 34.7%, respectively. HAPR was found to be an independent risk factor for cardiac death and stent thrombosis in ACS patients undergoing PCI.

P1497 | BEDSIDE
Characteristics of dyspnoea and associated clinical outcomes in the CHAMPION PHOENIX study

R.F. Storey1, D.L. Bhatt2, P.G. Steg3, H.D. White4, C.M. Gibson5, C. Linares6, J. Prats7, K.W. Mahaffey8, R.A. Harrington9 on behalf of The CHAMPION PHOENIX investigators. 1Department of Cardiovascular Science, University of Sheffield, Sheffield, United Kingdom; 2Brigham and Women’s Hospital, Department of Medicine, Cardiovascular Division, TIMI Study Group, Boston, United States of America; 3University of Paris Diderot, Paris, France; 4Columbia University Medical Center, New York, United States of America; 5Auckland City Hospital, Auckland, New Zealand; 6Harvard Medical School, Boston, United States of America; 7Kerckhoff Heart and Thorax Center, Bad Nauheim, Germany; 8The Medicines Company, Parsippany, United States of America; 9Stanford University Medical Center, Stanford, United States of America; 10School of Medicine, Stanford, United States of America;

Background: Dyspnoea may be induced by some reversibly-binding P2Y12 inhibitors, including cangrelor and ticagrelor. The CHAMPION PHOENIX study compared initial treatment with cangrelor versus clopidogrel in patients undergoing PCI.

Purpose: To investigate the incidence, characteristics, and associated clinical outcomes in patients with dyspnoea in CHAMPION PHOENIX.

Methods: Adverse events (AEs) of dyspnoea were recorded in patients randomized to cangrelor or clopidogrel. The composite primary endpoint of death, MI, ischaemia-driven revascularization (IDR), or stent thrombosis (ST), as well as its individual components, were assessed in patients who did or did not report dyspnoea.

Results: 68 (1.2%) cangrelor-treated and 18 (0.3%) clopidogrel-treated patients reported dyspnoea (P<0.001). Most dyspnoea events in cangrelor-treated patients were transient (median 1.6 hours) and were considered mild (71%) or moderate (28%); 1 event was considered severe. No patient in either group discontinued treatment due to dyspnoea. Rates of the primary outcome and its individual components in the modified intention-to-treat population are shown (Table 1).

<table>
<thead>
<tr>
<th>Clinical outcomes with dyspnoea status</th>
<th>Cangrelor</th>
<th>Clopidogrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>With dyspnoea</td>
<td>N=68</td>
<td>N=17</td>
</tr>
<tr>
<td>Death</td>
<td>6 (8.8%)</td>
<td>2 (11.8%)</td>
</tr>
<tr>
<td>ST</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>IDR</td>
<td>2 (3.0%)</td>
<td>1 (5.9%)</td>
</tr>
<tr>
<td>ST</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

Conclusion: Cangrelor-related dyspnoea appears transient, is usually mild or moderate but does not seem to lead to therapy discontinuation. The occurrence of dyspnoea does not seem to be associated with any reduction in the efficacy of cangrelor compared with clopidogrel as initial therapy in PCI patients.

Acknowledgement/Funding: The Medicines Company

P1498 | BEDSIDE
Dual anti-platelet therapy after drug-eluting coronary stent implantation and risks associated with gastroscopy - a Danish registry study

G. Egholm1, T. Thim1, M. Madsen2, H.T. Soerensen2, S.E. Jensen2, L.O. Jensen3, S.D. Kristensen4, H.E. Boekler1, M. Maeng1, 1Aarhus University Hospital, Department of cardiology, Aarhus, Denmark; 2Aarhus University Hospital, Department of Clinical Epidemiology, Aarhus, Denmark; 3Aalborg University Hospital, Department of cardiology, Aalborg, Denmark; 4Odense University Hospital, Department of cardiology, Odense, Denmark;

Background: Dual antiplatelet therapy (DAPT) is recommended for up to 12 months following percutaneous coronary intervention (PCI) with drug-eluting stent...
implantation (DES) and increases the risk of upper gastrointestinal bleeding and need for gastroscopy. Real-life handling of DAPT in relation to gastroscopy varies and the associated risk of adverse cardiac events and bleeding complications is largely unknown.

**Purpose:** To quantify 1) the frequency of gastroscopy 2) the incidence of bleeding and cardiac events in relation to gastroscopy and 3) the association between DAPT discontinuation, cardiac events and bleeding within the first 12 months after DES implantation.

**Methods:** We studied the frequency of gastroscopy within 12 months and numbers of adverse cardiac events and hemostatic intervention in relation to gastroscopy among all-comers treated with DES by cross-linkage of Danish registries. In two nested case-control studies we evaluated hospital charts for the exposure to DAPT. In the adverse cardiac events nested case-control study, patients with cardiac death, myocardial infarction, or stent thrombosis were cases. In the hemostatic intervention study, patients with hemostatic intervention were cases, and patients with gastroscopy including biopsy were controls.

**Results:** In a cohort of 22,654 patients treated with DES, we identified 1497 patients (6.6%), who underwent gastroscopy within 12 month. Among these, 22 patients (1.5%) suffered from an adverse cardiac event within the first 30 days after the gastroscopy and 93 patients (6.2%) had hemostatic intervention during gastroscopy. The nested case-control studies showed heterogeneity in DAPT prescription; 74% received DAPT during gastroscopy. Discontinuation of dual antiplatelet therapy (DAPT) was not associated with an increased risk of hemostatic intervention compared to no antiplatelet treatment (odds ratio 1.31, 95% confidence interval 0.37–4.70). No patients experienced bleeding complications as a consequence of gastroscopy with hemostatic intervention or biopsy.

**Conclusion:** Gastroscopy is a frequent procedure within the first year of stent implantation. While adverse cardiac events were increased with discontinuation of DAPT, the risk of bleeding did not increase. Discontinuation of antiplatelet drug with or without biopsy can be performed despite ongoing treatment with DAPT.

**Acknowledgement/Funding:** TRYG. Knud and Edith Eriksens mindefond.

**Aarhus University Hospital, Department of Cardiology**

**P1490 | BEDSIDE**

Effect on clinical outcomes of short or long duration of dual antiplatelet therapy after drug-eluting stents: a meta-analysis of randomized trials

G. Ferrante 1, P. Pagnotta 1, S. Arioti 2, P. Calabro 3, E. Moscarella 3, P. Presbitero 1, E. Corrada 1, M. Valgimigli 2.

**Purpose:** The aim of this study was to assess benefits and risks of shorter (i.e., < 12 months) DAPT vs. at least 12 months DAPT duration.

**Methods:** PubMed, EMBASE, the Cochrane Central Register of Controlled Trials, ClinicalTrials.gov databases were searched for randomized trials comparing 1) shorter than 12-month DAPT vs. at least 12-month DAPT; 2) longer than 12-month DAPT vs. shorter than 12-month DAPT after drug-eluting stent implantation, with concomitant use of oral anticoagulation.

**Conclusion:** Shorter than 12-month DAPT improves safety with reductions in major bleeding, and is associated with comparable cardiovascular outcomes and mortality. Conversely, a higher efficacy of DAPT continuation beyond 12 months on cardiovascular outcomes is achieved at the expense of higher major bleeding and all-cause mortality.

**Acknowledgement/Funding:** This work was supported by the Italian Association for the Study of the Heart (AISI).
an increased risk of bleedings (12.3% versus 9.9%) (OR [95% CI] = 1.37 [1.16–
1.62], p=0.0002; pefet = 0.20), while we did not find any significant difference in
term of recurrence of myocardial infarction (p=0.39), stent thrombosis (p=0.46) or
stroke (p=0.15).
Conclusion: This meta-analysis showed that among patients undergoing coro-
nary artery stent implantation, requiring chronic oral anticoagulation, the use of a triple
antithrombotic therapy is associated with a significant reduction in mortality that
largely outweighed the risk of major bleeding complications associated with
triple therapy.

P1502 | BEDSIDE
Comparison of in-hospital clinical outcomes between ticagrelor versus clopidogrel in patients with acute myocardial infarction undergoing successful revascularization
K.-H. Park1, M.-H. Jeong1, H.-K. Kim1, D.-S. Sim1, Y.-J. Hong1, Y.-K. Ahn1,
S.-H. Kim2, T.-A. Hahn3, D.-J. Oh4, Y.-J. Kim1
1 The Heart Center of Chonnam National University Hospital, Gwangju, Korea, Republic of; 2 Saint Carollo Hospital, Suncheon, Korea, Republic of; 3 Aarhus University Hospital, Department of Surgical Gastroenterology, Aarhus, Denmark; 4 Aarhus University Hospital, Department of Anesthesiology, Aarhus, Denmark.

Objectives: This study sought to determine the efficacy and safety of ticagrelor compared to clopidogrel in patients with acute myocardial infarction (AMI).

Background: It has been well known that ticagrelor could improve clinical outcomes in patients with AMI without increasing bleeding risk. However, the clinical impacts of ticagrelor in Korean patients with AMI have not been well established.

Methods: Between November 2011 and August 2014, a total of 4,029 patients (3,186 patients were prescribed clopidogrel and 843 patients ticagrelor) with AMI undergoing successful percutaneous coronary intervention were analyzed from Korea Acute Myocardial Infarction Registry-National Institute of Health registry. The patients with in-hospital switching between two antiplatelet agents were excluded. The propensity score matching (802 pairs) were performed in order to compare the in-hospital clinical outcomes between ticagrelor and clopidogrel after adjusting for baseline clinical and procedural confounders.

Results: PY2Y12 reactivity unit by the VerifyNow PY2Y12 test was 68.6±66.82 in ticagrelor and 237.9±99.57 in clopidogrel. There were no significant differences in a composite of cardiac death, MI or stroke during hospital stay between ticagrelor and clopidogrel (1.1% vs. 1.3%, p=0.780). However, the incidences of Thrombolysis In Myocardial Infarction (TIMI) major bleeding and minor bleeding were significantly higher in ticagrelor than clopidogrel (4.6% vs. 1.5%, p=0.003; 5.8% vs. 2.4%, p=0.006). No difference in the composite of cardiac death, MI, stent thrombosis, target vessel revascularization or stroke at 6 months was observed in both group (1.8% vs. 2.9%, p=0.444). On multivariate analysis, use of ticagrelor, ≥75 years old or body weight <60 kg, TFI vs. TR and non ST elevation MI were independent predictors of TIMI major bleeding (odd ratio [OR]=3.94, 95% confidence interval [CI]=1.589–9.120, OR=3.105; 95% CI: 1.240–7.771, OR=7.675; 95% CI: 2.144–27.471, OR=2.720; 95% CI: 1.236–5.985).

Conclusions: Our study shows that ticagrelor might have an increasing bleeding complications compared with clopidogrel, without preventing ischemic events. The large scale, long-term, randomized trials should be needed to assess the efficacy and safety of ticagrelor for Korean AMI patients undergoing successful PCI.

P1504 | BEDSIDE
Stent thrombosis after second generation drug-eluting stent implantation and duration of dual antiplatelet therapy
H. Amano1, K. Kadota1, S. Otsuru1, D. Hasegawa1, S. Habara1, T. Tada1, H. Hanaka1, Y. Fuku1, T. Goto1, M. Mitsudo1, T. Kurashiki Central Hospital, Kurashiki, Japan

Background: Stent thrombosis (ST) is one of the main concerns after drug-eluting stent (DES) implantation, but its incidence has declined in an era of second generation DES. Dual antiplatelet therapy (DAPT) is still a controversial issue despite some reports on shortening of its duration.

Methods: From January 2010 to August 2014, 5022 consecutive patients were treated with second generation DES (cobalt chromium everolimus-eluting stent, platinum chromium everolimus-eluting stent, biolimus-eluting stent, and Resolute zotarolimus-eluting stent). We investigated the timing and incidence of ST within one year, and evaluated the risk factors of ST. ST was defined as definite stent thrombosis by the Academic Research Consortium definition.

Results: ST occurred in 18 patients within one year. The timing and cumulative incidence of ST are shown in the figures. Diabetes mellitus (odds ratio [OR]: 3.94, 95% confidence interval [CI]: 1.20 to 12.8, p=0.02), hemodialysis (OR: 7.75, 95% CI: 2.25 to 26.3, p<0.01), acute coronary syndrome (OR: 5.78, 95% CI: 1.71 to 19.6, p<0.01), and bifurcation two-stenting (OR: 4.90, 95% CI: 1.48 to 16.1, p<0.01) were independent predictors of ST.

Conclusions: All ST occurred within 3 months, except for one which was an antiplatelet therapy cessation case; therefore, DAPT duration may be 3 months. Some reports suggested even shorter durations, but in our experience, ST can occur within 3 months despite DAPT. DAPT duration shorter than 3 months requires a risk-benefit consideration.
**P1505 | BEDSIDE**

**Access site versus non-access site bleeding in primary PCI: Incidence, impact on mortality and risk reduction according to antithrombin treatment. The EUROMAX trial**

S. Klicic, 1 A.W.J. Van 't Hof, 1 J.M. Ten Berg, 2 A. Ayesta Lopez, 2 U. Zeymer, 3 M. Harnon, 4 L. Souta, 5 D. Bernstein, 6 E.N. Deliargyris, 7 P.G. Steg, 8 Isala Hospital, Zwolle, Netherlands; 9 St Antonius Hospital, Nieuwegein, Netherlands; 2 University Hospital Gregorio Maranon, Madrid, Spain; 3 Klinikum Ludwigshafen, Ludwigshafen Am Rhein, Germany; 4 University Hospital of Caen, Caen, France; 5 Hospital Center of Chateauroux, Chateauroux, France; 6 Medicines Company, Parsippany, United States of America; 7 Hospital Bichat-Claude Bernard, Paris, France

**Purpose:** Impact of post-PCI bleeding on prognosis after STEMI may differ according to the site of bleeding. We determined the frequency and origin of bleeding, the associated risk for 30 day death and the impact of antithrombin choice in PCI.

**Methods:** We blindly reviewed all case records of TIMI major or minor bleeds and assigned them in 4 groups: access only, non-access only, both locations and no location. Mortality at 30 days and impact of randomized treatment were assessed for each group.

**Results:** A total of 231 out of 2198 ITT patients suffered a TIMI major or minor bleed (50/1967, 2.5%; p<0.001). There was no difference in mortality for patients with an access site related bleed (3/112, 2.7%; p=0.76) compared to non-access site-related bleed (13/119, 10.9%) compared to patients who did not suffer a bleed (50/1967, 2.5%; p<0.0001). There was no difference in mortality for patients with an access site related bleed (3/112, 2.7%; p=0.76) compared with non-bleeders. Bivalirudin reduced both access site only and non-access site related bleeds with relative risk reductions of 34% and 46% respectively.

**Conclusion:** In PPCI, bleeding is equally distributed between access and non-access related locations with a higher risk for 30 day death associated with non-access site bleeds. Bivalirudin reduces the risk of bleeding irrespective of origin.

**Acknowledgement/Funding:** Medicines Company

---

**P1506 | BEDSIDE**

**Coronary index of microcirculatory resistance and echocardiographic parameters evolution in patients with ST-elevation acute myocardial infarction treated with primary angioplasty**

M. Faustino, S. Bravo Baptista, A. Freitas, C. Monteiro, P. Leal, M. Nedio, C. Antunes, P. Farto E Abreu, V.M. Gil, C. Morais. Hospital Prot. Dr. Fernando Fonseca, EPE, Amadora, Portugal

**Purpose:** The coronary index of microcirculatory resistance (IMR) is an indicator of coronary microvascular dysfunction (MD) and has demonstrated prognostic value in patients with ST-elevation myocardial infarction (STEMI), treated with primary angioplasty (P-PCI). IMR showed to be correlated with infarct size and subsequent recovery of left ventricular function, as assessed by various imaging techniques. This study aims to evaluate the relationship between IMR and echocardiographic parameters evolution in STEMI patients, treated with P-PCI.

**Methods:** IMR was evaluated at the end of angioplasty; under adenosine-infusion. Echocardiograms were performed in the first 24 hours (Echo1) and after about 3 months (Echo2).

**Results:** 40 STEMI patients (mean age 59.3±12.7 years, 34 males) were included. IMR median was 25.9 (interquartile range 32.5) and patients were divided in two groups: Group1 (IMR ≥26, without MD) and Group2 (IMR ≥26, with MD). In Echo1 there were no significant differences between the groups in TsV, LVF, WMSI and E/E' ratio (table). However GLS was significantly better in Group1 patients (−4.8 vs. −12.7, p<0.005). IMR correlated positively and significantly with the GLS (R=0.6, p<0.001). Between Echo1 and Echo2, there were significant improvements in LVF, SLG and ratio E/E' in Group 1, but these improvements were not observed in Group 2. The WMSI improved in both groups, although significantly more in Group 1 (reduction of −17.1% vs. −6.8% in Group 2, p=0.015).

**Conclusion:** IMR evaluated immediately after P-PCI in STEMI patients correlates with GLS. Absence of MD as evaluated invasively (IMR ≥26) is associated with a significantly higher recovery of the LVF, WMSI, E/E' ratio and GLS, suggesting that IMR is an early marker of cardiac remodelling after acute myocardial infarction.

---

**Abstract P1506 | Table 1**

<table>
<thead>
<tr>
<th>Echocardiographic parameters</th>
<th>Group 1 (IMR ≥26)</th>
<th>Group 2 (IMR &lt;26)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Echo1</td>
<td>Echo2</td>
</tr>
<tr>
<td>Left ventricle telesistolic volume (TsV) (mL)</td>
<td>53.8±12.3</td>
<td>48.2±12.2</td>
</tr>
<tr>
<td>Left ventricle ejection fraction (LVEF) (%)</td>
<td>60.8±6.06</td>
<td>55.5±6.06</td>
</tr>
<tr>
<td>Wall motion score index (WMSI)</td>
<td>1.4±0.24</td>
<td>1.19±1.33</td>
</tr>
<tr>
<td>Left ventricle global longitudinal strain (GLS) %</td>
<td>−14.9±3.3</td>
<td>−17.3±7.6</td>
</tr>
<tr>
<td>E/E' ratio</td>
<td>9.3±3.4</td>
<td>8.2±1.02</td>
</tr>
</tbody>
</table>

<sup>1</sup>*T*-Test Student, P<0.005 vs Eco 1 in Group 2;  <sup>2</sup>*T*-Test for paired samples.

**Conclusion:** Microvascular dysfunction post-STEMI is associated with worse short and long term LVF. In patients with impaired baseline CFVR, recovery of the microcirculation function is associated with improvement of LVF at 4 months, underlying its clinical significance.

---

**P1507 | BEDSIDE**

**Microvascular dysfunction following ST-segment elevation myocardial infarction is associated with short and long term cardiac function assessed by cardiac magnetic resonance imaging**


**Background:** Despite restoration of epicardial blood flow, compromised myocardial tissue perfusion due to microvascular dysfunction has been described in 30–40% of reperfused ST-segment elevation myocardial infarction (STEMI) patients. Analysis of the time course of microvascular dysfunction and its implications on long term left ventricular function is lacking.

**Purpose:** We investigated the relationship of microvascular dysfunction following STEMI on long term left ventricular function (LVF) as assessed by cardiac magnetic resonance imaging (CMR).

**Methods:** In 62 patients, Coronary Flow Velocity Reserve (CFVR) in the infarct related artery (IRA) was assessed with intracoronary Doppler flow measurements within 1 week and 4 months after STEMI. CMR was performed within one week, at 4 months and 2 years.

**Results:** CFVR at baseline in the IRA is associated with left ventricular ejection fraction (LVF) and wall thickening in the affected segments at both 4 months (β = 4.66, SE = 2.10; P = 0.03 and β = 9.37, SE = 4.42; P = 0.04) and 2 year follow-up (β = 5.84, SE = 2.45; P = 0.02 and β = 12.36, SE = 5.88; P = 0.04). In patients with an initial CFVR <2, the absolute increase in CFVR was the only variable associated with LVF improvement in the first 4 months (β = 3.43, SE = 1.65, P = 0.045). The difference in infarct size and extent transmurality and MVO at baseline were not. As shown in figure 1, patients that experienced an increased improvement in CFVR (median ± 3 CFVR) had an increased LVF 4 months compared to baseline.

**Conclusion:** Microvascular dysfunction post-STEMI is associated with worse short and long term LVF. In patients with impaired baseline CFVR, recovery of the microcirculation function is associated with improvement of LVF at 4 months, underlying its clinical significance.
Methods and results: In a cohort study, platelet surface expression of CXCR4, CXCR7 and SDF-1 was measured by flow cytometry in 30 patients with symptomatic coronary artery disease (CAD) at the time of percutaneous coronary intervention (PCI). SDF-1 single-nucleotide polymorphism analysis was performed with MALDI-TOF mass spectrometry. Platelet CXCR4 levels were significantly elevated in the SDF polymorphisms rs266085 and rs266087 (CXCR4 median MFI 31.18; 25th/75th percentile 24.09/57.45 vs. 22.44; 25th/75th percentile 17.24/26.28, p<0.019) and median MFI 31.18; 25th/75th percentile 24.09/57.45 vs. 22.44; 25th/75th percentile 17.24/26.28, p<0.019) as compared to the wild type. Platelet CXCR4 levels were significantly decreased in the SDF polymorphism rs1065297 as compared to the wild type (median CXCR4 MFI 20.88; 25th/75th percentile 17.78/24.47 vs. 30.10; 25th/75th percentile 23.27/51.59, p<0.032). We could not find any significant associations between any of these SDF-1 polymorphisms and platelet CXCR7 and SDF-1 expression.

Conclusions: These findings highlight a possible influence of distinct SDF-1 polymorphisms on the platelet SDF-1/CXCR4/CXCR7 axis. Large scale studies are warranted to validate these results.

P1509 | BEDSIDE
Predictive factors of left ventricular thrombus after myocardial infarction using cardiovascular magnetic imaging
M. Audonnet, University Hospital of Angers, Maine et loire, Angers, France

Background and introduction: Left ventricular (LV) thrombus is a current and potentially dangerous complication of myocardial infarction. Prior studies highlighted cardiovascular magnetic resonance imaging (CMR) to detect LV thrombus, but none of them evaluated the interest for a combined reading of the various CMR sequences that are available.

Purpose: This study sought to assess 1) the predictive factors of LV thrombus after myocardial infarction and 2) whether the first pass perfusion sequence improved the detection of LV thrombus.

Methods: Between January 2006 and June 2014, 331 patients with myocardial infarction underwent CMR at baseline and at 3 months follow-up. Patients were seen at 3, 6, 12 months for assessment of clinical status and adverse events. CMR were analyzed twice by three blinded examiners (2 CMR experts and 1 novice). On the first hand, an analysis was performed on cine MR and late gadolinium enhancement. On the second hand another analysis was performed following initial protocol combined to first pass perfusion sequences.

Results: On CMR at baseline, a thrombus was found in 29 of 331 (8.7%) patients. Thrombus formation was independently associated with lower LV ejection fraction (40.3±7.9% vs. 48.0±9.7%; p<0.001), peak creatinine kinase (4076±2402 UI/L vs. 2873±2122 UI/L; p=0.004), and infarct size (33.6±19.6 g vs. 22.4±17.1 g; p=0.004). For a composite of all-cause death, recurrent myocardial infarction, cerebrovascular accident, and any revascularization and stent thrombosis during 717 days of follow-up. We compared the outcomes between groups both in the propensity adjusted and matched cohorts.

Results: Mean difference of PRU values was not significant in the CYP 3A4-metabolized statin and its association with clinical outcomes during dual antiplatelet therapy following percutaneous coronary intervention (PCI).

Conclusion: Among 3,755 patients enrolled the HOST-ASSURE trial, 1,187 patients were assigned to the CYP 3A4-metabolized statin group (n=725) or non-CYP 3A4-metabolized statin group (n=462) according to type of used statins. The primary outcome was the difference of PRU values both in the baseline and follow-up PRU values. The secondary outcomes included the composite of all-cause death, recurrent myocardial infarction, cerebrovascular accident, and any revascularization and stent thrombosis during median 717 days of follow-up. We compared the outcomes between groups both in the propensity adjusted and matched cohorts.

Results: Mean difference of PRU values was not significant in the CYP 3A4-metabolized statin group (mean difference: −43.84, p=0.367) and was significant in the non-CYP 3A4-metabolized statin group (mean difference: −12±69, p=0.006) both in the propensity score adjusted and matched cohorts. Patients with high PRU value at baseline, irrespective of the type of used statins, were associated with a significant reduction in mean difference of PRU values both in the propensity score adjusted (mean difference: −53.35, p<0.001) and matched cohort (mean difference: −41.57, p<0.001). The composite of clinical events did not differ between groups both in the propensity score adjusted (hazard ratio [HR] 0.962, 95% confidence interval [CI] 0.621–1.498, p=0.861) and matched (HR 0.902, 95% CI 0.554–1.468, p=0.678) cohorts.

Conclusion: This study showed that a CYP 3A4-metabolized statin slightly reduces antiplatelet activity of clopidogrel during dual antiplatelet therapy but did not increase clinical events in patients following PCI.
P1512 | BEDSIDE
Discontinuation rates in patients with non-valvular atrial fibrillation treated with non-vitamin K antagonist oral anticoagulants are mainly related to drug specific side effects and bleeding

F. Al-Khalil1, C. Lindstrom2, A. Majeed3, 1Karolinska Institute, Dept. of Clinical Sciences, Danderyd Hospital, Stockholm, Sweden; 2Stockholm Heart Center, Stockholm, Sweden; 3Karolinska Institute, Department of Medicine, Stockholm, Sweden

Background: The non-vitamin K antagonist oral anticoagulants (NOACs) have similar efficacy as warfarin in terms of stroke prevention in patients with non-valvular atrial fibrillation (NVAF). The aim of the study is to assess the drug tolerability and discontinuation rates in NVAF patients treated long-term with dabigatran (D), rivaroxaban (R) or apixaban (A) in a well-structured atrial fibrillation clinic.

Methods: Treatment with different NOACs in NVAF patients was initiated and followed for 1–2 years in the same clinic. Data on side effects, bleeding events, cardiovascular events and drug discontinuation were obtained during patient visits, telephone calls and from the patient data registry.

Results: NVAF patients treated with D (n=233), R (n=282) and A (n=251) were followed. There was no significant difference between the three NOAC groups in age, sex, renal function, HAS-BLED or CHADS-VASC Score. Discontinuation rates (DR) were lower for A (10%) than for D (30%), or R (24%; p < 0.001 for both). DR in D were mostly due to side effects (70% of all DR) mainly gastrointestinal symptoms, while bleeding events accounted for 17% (major and clinically relevant). DR for R were mostly due to bleeding (43%) and side effects (37%), mainly itching, tiredness and headache. DR for A were mostly due to diverse side effects (48%) and bleeding (19%).

Conclusion: Long-term follow-up of the different NOACs in clinical practice showed marked differences in the discontinuation rates mainly due to different rates of drug specific side effects and bleeding when used for treatment of patients with NVAF.

P1513 | BEDSIDE
Patterns of uptake of non-vitamin K antagonist oral anticoagulants in Europe: an analysis from the GARFIELD-AF registry

A.J. Camm1, G. Ambrosio2, D. Atar3, J.-P. Bassand4, F. Cools5, K.A.A. Fox6, P. Jansky7, M. Kettal8, J.-Y. Le Heuzey9, A.K. Kakkar10, on behalf of GARFIELD-AF Investigators. 1St George’s University of London, London, United Kingdom; 2University of Perugia School of Medicine, Perugia, Italy; 3Oulu University Hospital, Oulu, Finland; 4University of Oslo, Oslo, Norway; 5University of Franche-Comté, Besançon, France; 6AZ Klinia, Brusschaela, Belgium; 7University of Edinburgh, Edinburgh, United Kingdom; 8Motol University Hospital, Prague, Czech Republic; 9Hungarian Institute of Cardiology, Budapest, Hungary; 10Georges Pompeiu Hospital, René Descartes University, Paris, France; 11Thrombosis Research Institute, London, United Kingdom

Purpose: To compare non-vitamin K antagonist oral anticoagulant (NOAC) uptake in different European populations of atrial fibrillation (AF) patients.

Methods: 27,106 patients with newly diagnosed non-valvular AF and ≥ 1 additional stroke risk factor were enrolled in GARFIELD-AF in 2010–14. 16,805 in Europe. NOAC uptake was evaluated by country at 2-y follow-up. The date the first patient on a NOAC was enrolled in the registry was taken as the start of NOAC therapy in each country. The proportion of patients on NOACs is the number on NOACs at enrolment over the total number enrolled after the start date.

Results: 2819 (16.8%) European patients used NOACs at enrolment. Their mean age was 71.0 y; 46.6% were female. The date of first NOAC use was from Mar 2010 (Austria) to Oct 2012 (the Netherlands and Russia). At 8 mo from first NOAC use, the proportion of patients on NOACs varied from 1.4% (UK) to 50.0% (Belgium). At 12 mo, it ranged from 1.5% (France, Italy) to 52.8% (Belgium). At 24 mo, it varied from 1.1% (Italy) to 56.9% (Belgium). The greatest increase was seen in Sweden and France. At the end of the enrolment period there were still marked differences in NOAC uptake, ranging from 3.0% (Finland) to 57.0% (Belgium).

Conclusion: Large variations in NOAC uptake were observed between European countries, which may be due to differences in availability and reimbursement.

Acknowledgement/Funding: The GARFIELD-AF registry is funded by an unrestricted research grant from Bayer Pharma AG.

P1514 | BEDSIDE
Risk factors for major bleeding and efficacy of modified HAS-BLED score in patients on oral anticoagulation after coronary artery stenting


Background: Dual antiplatelet therapy is required for a long time after coronary artery stenting, and oral anticoagulation (OAC) is necessary for the prevention and treatment of thromboembolic events; however, increased risk of bleeding events needs to be considered when deciding the initiation of triple oral antithrombotic therapy. The HAS-BLED score could be recommended to assess bleeding risk, but clinical usefulness of the score remains unclear.

Purpose: To compare the clinical implication of HAS-BLED score and modified HAS-BLED score.

Methods: Between January 2010 and December 2011, 1507 patients required dual antiplatelet therapy after coronary artery stenting. Until January 2015, 200 of them required OAC, and their backgrounds and major bleeding events (Bleeding Academic Research Consortium criteria ≥ 3) were analyzed. A modified HAS-BLED score comprised the following points: 2 points for bleeding/gastric ulcer and oldest old (≥ 80 years); 1 point for a past history of hypertension, abnormal renal function (estimated glomerular filtration rate ≤ 30), stroke, labile international normalized ratio (INR), elderly (66 to 79 years), and drug/alcohol consumption. Results: At baseline, the mean age was 71.8 years, 75.5% were men. OAC was taken in 107 patients (54%) for atrial fibrillation/flutter, 53 (27%) for low cardiac output syndrome/intraventricular thrombus, 31 (16%) for postoperative cardiovascular surgery, and 6% for pulmonary embolism/deep vein thrombosis. During the follow-up period, 31 patients suffered from major bleeding, 130 survived without major bleeding, 36 died without major bleeding, and 3 dropped out. We show the distribution and the rate of major bleeding in patients classified into scores by HAS-BLED score or modified HAS-BLED score in the table.

Abstract P1513 – Table 1

<table>
<thead>
<tr>
<th>Score</th>
<th>Patients on NOACs, % (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>HAS-BLED N (%)</td>
</tr>
<tr>
<td>1</td>
<td>BARC ≥ 3</td>
</tr>
<tr>
<td>2</td>
<td>Modified HAS-BLED N (%)</td>
</tr>
<tr>
<td>3</td>
<td>BARC ≥ 3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>&lt;5</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>20</th>
<th>25</th>
<th>30</th>
<th>40</th>
<th>50</th>
<th>60</th>
<th>70</th>
<th>80</th>
<th>90</th>
<th>100</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>3</td>
<td>20</td>
<td>46</td>
<td>26</td>
<td>6</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>44</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>16</td>
<td>36</td>
<td>22</td>
<td>63</td>
<td>39</td>
<td>31</td>
<td>19</td>
<td>6</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>44</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>44</td>
<td>30</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: A modified HAS-BLED score could be more effective to assess and classify bleeding risk in patients taking triple oral antithrombotic therapy.

P1515 | BEDSIDE
D-dimer levels in patients with acute chest pain

Y. Kotani, M. Toyofuku, T. Tamata, T. Hamasaki, T. Tsujimoto, T. Chishiro. Japan Red Cross Society Wakayama Medical Center, Cardiology, Wakayama, Japan

Current guideline of European Society of Cardiology recommended the measurement of d-dimers to rule out acute aortic dissection in patients presenting acute chest pain, however, the distribution of d-dimer levels in various diseases presenting acute chest pain is not sufficiently assessed. We retrospectively reviewed 953 consecutive patients who admitted to the hospital due to acute chest pain between January 2011 and April 2014. D-dimer levels were measured in 887 patients (acute aortic dissection 97, symptomatic aortic aneurysm 26, pulmonary embolism 29, acute
coronary syndrome 528, and other diseases 207). The median (interquartile range) of d-dimer levels for each group were: 4.0 (1.7–7.0) for acute aortic dissection, 3.8 (2.0–6.6) for symptomatic aortic aneurysm, 8.0 (5.3–12.7) for pulmonary embolism, 0.5 (0.3–1.3) for acute coronary syndrome, and 0.7 (0.3–1.7) for other diseases. The distributions of d-dimer levels are shown in Figure.

When patients were divided into two groups according to the requirement of computed tomography for final diagnosis, the odds ratio of CT required group (acute aortic dissection, pulmonary embolism, symptomatic aortic aneurysm) according to the d-dimer levels were 5.2 (2.6–13.6) in d-dimer levels of 0.5–2.0 μg/mL, 21.4 (8.7–52.4) in 21.5–50.0 μg/mL, 92.4 (36.0–232.9) in 51.0–200.0 μg/mL, and 142.1 (50.7–378.0) in over 200 μg/mL for a control group of d-dimer level <0.5 μg/mL. In patients with acute chest pain, elevation of d-dimer levels was more pronounced in acute aortic and pulmonary artery disease. Measurement of d-dimer levels can help decision the requirement of further imaging for final diagnosis.

### P1516 | BEDSIDE

Use of antithrombotic therapy in patients with atrial fibrillation and prior stroke: insights from the global GLORIA-AF registry

G.Y.H. Lip1, J.L. Halperin2, H.C. Dienr3, S.J. Dubner4, C.S. Ma5, K.J. Rothman6, K. Zint7, A. Eliaesern8, M. Paquette9, M.V. Huism10

1University of Birmingham, Centre for Cardiovascular Sciences, Birmingham, United Kingdom; 2Mount Sinai School of Medicine, New York, United States of America; 3Departamento de Electrofisiología y Research Triangle Park, United States of America; 4Boehringer Ingelheim GmbH, Corporate Department Global Epidemiology, Ingelheim, Germany; 5Boehringer Ingelheim Corporation, Clinical Trial Portfolio, Burlington, Canada; 6Leiden University Medical Center, Department of General Internal Medicine, Endocrinology, Leiden, Netherlands

Background: Patients with atrial fibrillation (AF) and prior stroke present the highest risk category, given the substantial occurrence stroke if untreated. Such patients should therefore be prescribed oral anticoagulants (OAC) whether as a vitamin K antagonist (VKA) or non-VKA OAC (NOAC). Methods: We examined the use of antithrombotic therapy in AF patients included in the GLORIA-AF registry, in relation to their history of stroke. Results: From 10675 patients in the phase II of GLORIA-AF we identified 999 patients (median age 74 years, 55.3% male) with previous stroke, with a median CHA2DS2-VASc score of 5, compared with 3 in those with no previous stroke (n=8675). In those with previous stroke, VKA alone was prescribed in 26.5%, VKA plus antiplatelet therapy (AP) in 6.1%, NOAC alone in 44.8% and NOAC plus AP in 5.9%. In AF patients with previous stroke, AP alone was used in 10.8%; 5.8% received no antithrombotic therapy. Proportions were broadly between males and females, although VKA plus AP was more prevalent in males. In comparison, in patients with no prior stroke, proportions on AP and NOAC were higher (12.5% versus 7.8%). Amongst those with no previous stroke in these regions were 15.0%, 3.1%, 4.5% respectively, whilst proportions on no antithrombotic therapy in these regions were higher (12.5% versus 7.8%). Amongst those with prior stroke, proportions on VKA alone was prescribed in 26.5%, NOAC alone 44.8% and NOAC plus AP 5.9%. Conclusion: In AF patients with prior stroke with a mean CHA2DS2-VASc score of 5, approximately 16% were treated with AP or no antithrombotic therapy, with 15.0%, 3.1%, 4.5% respectively, whilst proportions on no antithrombotic therapy in these regions were higher (12.5% versus 7.8%). Amongst those with prior stroke, proportions on VKA alone was prescribed in 26.5%, NOAC alone 44.8% and NOAC plus AP 5.9%. We examined the use of antithrombotic therapy in AF patients included in the GLORIA-AF registry, in relation to their history of stroke.

### P1518 | BEDSIDE

Detection and dynamics of ventricular thrombus by CMR after reperfused ST-segment elevation myocardial infarction. Results of a large prospective registry

E. Cambroner Cortinas1, C. Bonanad1, J.V. Monmeneu1, M.P. Lopez-Lereu1, A. Paya1, D. Escribano1, J.T. Ortiz2, X. Bosch2, F.J. Chorro3, V. Bod1.

1Research Foundation Hospital of Valencia (INCLIVA), Cardiology, Valencia, Spain; 2Hospital Clinic de Barcelona, Cardiology, Barcelona, Spain; 3Boehringer Ingelheim Corporation, Clinical Trial Portfolio, Burlington, Canada

Purpose: In a large prospective registry, we aimed to predict the occurrence of non-extensive IS-MVO (IS <30% of LV mass and MVO <2.5% of LV mass) in patients without previous stroke treated with PCI and compared the ability of echocardiography to identify CMR-derived VTh. This study was funded by Boehringer Ingelheim.

Background: The ability of echocardiography to identify CMR-derived VTh was also addressed. The distributions of d-dimer levels are shown in Figure. When patients were divided into two groups according to the requirement of computed tomography for final diagnosis, the odds ratio of CT required group (acute aortic dissection, pulmonary embolism, symptomatic aortic aneurysm) according to the d-dimer levels were 5.2 (2.6–13.6) in d-dimer levels of 0.5–2.0 μg/mL, 21.4 (8.7–52.4) in 21.5–50.0 μg/mL, 92.4 (36.0–232.9) in 51.0–200.0 μg/mL, and 142.1 (50.7–378.0) in over 200 μg/mL for a control group of d-dimer level <0.5 μg/mL. In patients with acute chest pain, elevation of d-dimer levels was more pronounced in acute aortic and pulmonary artery disease. Measurement of d-dimer levels can help decision the requirement of further imaging for final diagnosis.

## Cardiovascular Magnetic Resonance in Clinical Practice

### P1516 | BEDSIDE

Detection and dynamics of ventricular thrombus by CMR after reperfused ST-segment elevation myocardial infarction

C. Bonanad Lozano1, J.V. Monmeneu2, M.P. Lopez-Lereu2, J. Gavara2, A. Paya1, D. Escribano1, P. Racugno1, A. Hervas1, F.J. Chorro2, V. Bod1.

1University Hospital Clinic, Department of Cardiology, Valencia, Spain; 2University Hospital Clinic, Imaging Unit-ERESA, Valencia, Spain

Abstract P1516 | Table 1

<table>
<thead>
<tr>
<th>N</th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>10675</td>
<td>999</td>
<td>552</td>
<td>447</td>
</tr>
<tr>
<td>Age (median, IQR, Q3)</td>
<td>71 (64.7, 78)</td>
<td>74 (67.1, 81)</td>
<td>69 (62.8, 79)</td>
</tr>
<tr>
<td>CHA2DS2-VASc (median, IQR, Q3)</td>
<td>3 (2.4)</td>
<td>5 (4.6)</td>
<td>4 (5.4)</td>
</tr>
<tr>
<td>VKA alone</td>
<td>2873 (26.9)</td>
<td>265 (26.5)</td>
<td>222 (27.4)</td>
</tr>
<tr>
<td>VKA plus AP</td>
<td>746 (7.0)</td>
<td>61 (6.1)</td>
<td>135 (16.3)</td>
</tr>
<tr>
<td>NOAC alone</td>
<td>4390 (41.1)</td>
<td>448 (44.8)</td>
<td>394 (46.4)</td>
</tr>
<tr>
<td>NOAC plus AP</td>
<td>700 (6.6)</td>
<td>59 (5.9)</td>
<td>641 (7.6)</td>
</tr>
<tr>
<td>AP alone</td>
<td>1315 (12.3)</td>
<td>108 (10.8)</td>
<td>1207 (15.0)</td>
</tr>
</tbody>
</table>

No antithrombotic therapy 814 (7.6) 58 (5.8) 31 (5.6) 27 (6.0) 756 (7.8) 407 (7.7) 349 (7.9) 9 patients had missing information on previous stroke.
P1510 | BEDSIDE
Natural history and clinical significance of infarct zone volume and remodelling in survivors of acute STEMI
J. Carberry1, D. Carrick1, C. Haig2, S.M. Rauhalmi2, N. Ahmed1, M. McIntegart2, A. Mahrous2, A. Radjenovic1, K.G. Oldroyd3, C. Berry1
1University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow; 2 University of Glasgow, Robertson Centre for Biostatistics, Glasgow; 3Golden Jubilee National Hospital, Glasgow, United Kingdom

Background: The natural history and clinical significance of extracellular volume (ECV) expansion in infarcted myocardium post-STEMI is unknown. Myocardial ECV can be estimated by cardiac magnetic resonance imaging (CMR) using T1 MOLLI before and after contrast. We aimed to measure infarct zone ECV post-reperfusion and evaluate follow-up in acute STEMI survivors and assess the relationships between ECV and other clinical findings.

Methods: Acute STEMI survivors were enrolled in a single centre cohort study (BHF MR-MI study - NCT02072850). Contrast-enhanced CMR was performed at 1.5 Tesla (Siemens MAGNETOM Avanto) 2 days and 6 months post-MI. T1 mapping with MOLLI was performed before and 15 minutes after contrast (0.15mmol/kg gadoterate meglumine). Analysis of ECV was performed by outlining regions of interest (ROIs) in infarcted myocardium and left ventricular (LV) blood pool. ROIs were representative of the infarct zone including microvascular obstruction (MVO) when present. ECV was calculated as the difference in relaxation rate (R1=1/T1) for myocardium and LV blood pool before vs. after contrast, corrected for haematocrit (HCT). Baseline and follow-up ECV were measured and compared. An increase in infarct zone ECV ≥1% was taken as a measure of infarct zone remodelling (interstitial expansion).

Results: 171 STEMI patients (mean age 59±11 years; 131 (77%) male) were enrolled. 117 (68%) had infarct zone ECV measured at baseline and follow-up. Mean infarct ECV at baseline and follow-up were similar (53.2±9.8% vs. 52.6±10.4% (p=0.117)). Mean infarct size reduced from baseline to follow-up (17.5±12.8% vs. 12.7±10.2% of LV (P<0.001)) (n=161). ECV was correlated with infarct size at baseline (r=0.6, P<0.001) (n=124) and follow-up (r=0.6, P<0.001) (n=160). 87 (51%) patients had MVO at baseline. Mean LV ejection fraction (LVEF) decreased from baseline to follow-up (55.1±8.8% vs. 62.2±9.6% (P=0.001)) (n=160). The within-subject change in ECV varied markedly. For an ECV deviation of ≥1% from baseline, 67 (57%) patients had no change or decrease and 50 (43%) had an increase. An increase in infarct zone ECV at follow-up was associated with higher peak troponin I, older age, presence of MVO at baseline, reduced LV ejection fraction (LVEF) and higher LV end systolic volume (LVESV) at follow-up (all P<0.05) (n=117).

Conclusion: Infarct zone ECV is increased in 6 months in approximately one half of STEMI patients. LVF, LVESV at 6 months, MVO at baseline and peak troponin were associated with infarct zone remodelling. Infarct ECV represents a biomarker for infarct characterisation in STEMI patients.

Acknowledgement/Funding: British Heart Foundation project grant, CB - Senior Fellowship, Scottish Funding Council

P1511 | BEDSIDE
Mitrail annular plane excursion measured during routine cine-cardiac magnetic resonance imaging is a predictor of adverse cardiac events in patients with known or suspected coronary artery disease
S.J. Chacko1, V. Rangarajan1, N. Jairwala1, S. Romano2, J. Chung1, S. McGraw1, A. Farzaneh-Far1,1 University of Illinois at Chicago, Section of Cardiology, Chicago, United States of America; 2University of Verona, Department of Medicine, Verona, Italy

Background: Longitudinal movement of the mitral annulus is a major component of normal left ventricular pump function, which involves the coordinated action of longitudinal, circumferential and radially oriented fibers. Longitudinal fiber dysfunction appears to be a very early marker of a number of pathological states, perhaps due to its subendocardial location. We therefore hypothesized that reduced mitral annular plane systolic excursion (MAPSE) measured during routine cine-Cardiac Magnetic Resonance (CMR) imaging reflects early changes in longitudinal fiber function and maybe associated with adverse cardiovascular outcomes.

Purpose: To assess the prognostic value of simple cine-CMR derived MAPSE for the prediction of adverse cardiac events.

Methods: 300 consecutive patients with known or suspected coronary artery disease undergoing CMR were prospectively enrolled. Lateral MAPSE was measured in the 4-chamber cine view by two independent observers. Patients were prospectively followed for major adverse cardiac events (MACE) - death, non-fatal myocardial infarction, hospitalization for heart failure or chest pain, and late revascularization.

Results: The mean age of the study population was 61 (±11) years, with a mean ejection fraction of 59 (±14%). 33% of the individuals had known coronary artery disease, and 35% were diabetic. 46 MACE occurred during a median follow-up of 15 months. By Kaplan-Meier analysis, patients with lateral MAPSE <11.3 (median) experienced higher incidence of MACE than patients with a MAPSE ≥11.3 (p=0.0399) (Figure).

Conclusions: Reduced longitudinal fiber function assessed with lateral MAPSE during routine cine-CMR is a predictor of MACE in patients with known or suspected coronary artery disease.

P1520 | BEDSIDE
The additive value of cardiovascular magnetic resonance first pass perfusion in diagnosis of microvascular disease in a population with chest pain and normal coronary arteries
C.E. Raphael1, L.Y. Hsu2, A. Greve2, P. Gatehouse3, C. Di Maro1, J. Collinson1, D.J. Pennell1, A.E. Ara1, S.K. Prasad1, 1Imperial College London, London, United Kingdom; 2National Institute of Health (Home), Washington, United States of America; 3Royal Brompton Hospital, London, United Kingdom

Introduction: Measurement of coronary flow velocity at rest and at peak hyperaemia allows calculation of coronary flow reserve (CFR). In patients with normal epicardial coronary arteries, a reduced CFR (typically <2) is considered diagnostic of microvascular dysfunction. Cardiovascular magnetic resonance (CMR) provides a non-invasive assessment of myocardial perfusion with high spatial resolution and no ionising radiation.

Purpose: We assessed the additive diagnostic value of CMR in the diagnosis of microcirculatory disease in a population of patients with suspected microvascular dysfunction.

Methods: Consecutive patients with a moderate-high pre-test probability of microvascular disease based on non-invasive testing, presenting with chest pain and angiographically normal epicardial coronary arteries were recruited. Patients underwent Doppler flow wire measurement of coronary flow and CFR in the proximal left anterior descending artery. They then underwent CMR assessment of first pass myocardial perfusion at rest and with adenosine stress perfusion on a 3.0T Skyra scanner (Siemens). Myocardial perfusion was assessed visually by two experienced observers blinded to the CFR result and quantified using a Fermi-constrained deconvolution algorithm.

Results: 37 patients (mean age 58±13, 70% male) were recruited. The mean CFR was 2.1±0.92. 22/37 (59%) patients had evidence of microvascular disease using the conventional criteria of a CFR<2. All of these patients had CMR evidence of microvascular dysfunction with a persistent circumferential subendocardial perfusion defect during adenosine stress. Four additional patients (11%) had CMR evidence of microvascular disease, despite a normal CFR (mean 2.42±0.16). There was no difference in age between these patients and the rest of the population (mean age 58±7, p=0.9).

Conclusions: CMR has additive diagnostic value in the assessment of coronary microvascular disease. A CFR greater than 2 does not rule out microvascular disease and further testing should be considered in patients with a history of chest pain suggestive of small vessel disease despite angiographically normal epicardial coronary arteries.

Acknowledgement/Funding: CER is supported by the BHF. This study is supported by the NIH.
by T2 mapping. T2 core was present in all patients with late MVO. 33 patients had T2 core in the absence of late MVO. The presence of T2 infarct core was more closely related to early MVO (186 patients (57%) vs late MVO. In multivariable regression, T2 in the infarct core was negatively associated with heart rate, Killip class, and peak neutrophil count at presentation (all p < 0.05). An increasing T2-core value (ms) was associated with a reduced risk of all-cause death or heart failure hospitalisation (HR 0.786, 95% CI 0.658, 0.939; p = 0.008) including after adjustment for baseline LVEF (p = 0.017) or LV end-diastolic volume (p = 0.009). In the serial imaging sub-set, the temporal evolution of T2 values within the infarct zone was analyzed in association with IMH. Patients with IMH a bimodal time-course in T2 values was observed within the infarct core, with a nadir at scan 2, corresponding with the greatest extent of IMH (p = 0.009). By contrast, this pattern differed in patients without IMH in whom T2 values increased progressively up to 10 days post-MI.

Conclusion: A hypointense infarct core revealed by T2-mapping was common and independently associated with all-cause death or heart failure hospitalisation post-discharge. T2 core reflects, not only IMH from microvascular destruction, but also functional MVO secondary to reduced tissue water as a result of reversibly obstructed capillary flow. T2 values are dynamic in the early reperfusion period and inversely associated with IMH. T2/IMH are biomarkers that may reflect the efficacy of therapeutic interventions in STEMI patients.

P1523 | BEDSIDE
Cardiac magnetic resonance findings in active rheumatoid arthritis
S. Kvistö1, R. Koivuniemi2, K. Korpi3, T. Kaasalainen1, M. Laine3, M. Kupari3, M. Leirisalo-Repo2, M. Holmström1,1. Helsinki University Central Hospital, Radiology, Helsinki, Finland;2. Helsinki University Central Hospital, Department of Rheumatology, Helsinki, Finland;3. Helsinki University Central Hospital, Heart and Lung Center, Helsinki, Finland

Background: In patients with rheumatoid arthritis (RA), cardiac involvement is common and congestive heart failure is an important contributor to the excess mortality. To our knowledge, only few studies of cardiac findings, mainly myocardial diffuse fibrosis and scarring have been reported.

Purpose: We aimed to assess diffuse myocardial fibrosis and local scarring in patients with active RA without cardiac symptoms using cardiac magnetic resonance (CMR) with native T1 mapping and late gadolinium enhancement (LGE) tests.

Methods: Fifty-eight consecutive patients (mean age of 50±12 years) with active RA underwent CMR. The study comprised with two female patient groups; patients with newly diagnosed RA starting treatment with conventional RA medication and patients with long-lasting active RA starting treatment with biological therapy. All patients with previously known cardiovascular disease or smoking were excluded.

CMR was performed to analyze native T1 mapping and LGE of the myocardium. Myocardial T1-mapping was performed in a mid-ventricular short-axis slice using a shortened Modified Look-Locker Inversion-recovery (shMOLLI) sequence. CMR imaging analysis was performed using tool developed for this purpose. LGE images were acquired after 15 min. after contrast agent. The location and pattern of LGE were visually estimated according to AHA 17-segment model.

Results: Mean native T1 relaxation times showed slightly elevated values compared to reference values: 1002±46 ms septum, 975±48 ms lateral wall in 1.5T. Out of 58 RA patients 38 (58%) exhibited myocardial fibrosis and scarring. LGE referring local scarring evaluated with CMR were visualized in 17-segment model. Out of 58 RA patients 1.5T and 3T). Out of 58 RA patients 38 (58%) exhibited myocardial fibrosis and scarring. LGE referring local scarring evaluated with CMR were visualized in 17-segment model. Out of 58 RA patients 38 (58%) exhibited myocardial fibrosis and scarring. LGE referring local scarring evaluated with CMR were visualized in 17-segment model.

Conclusion: In addition to commonly recognized risk criteria - particular caution is suggested in patients with classical CIEDs when: performing consecutive 1.5 T MRI and/or more than one region is scanned and in subjects with more-than-one or defibrillation lead.

P1524 | BEDSIDE
1.5 T MRI in patients with classical cardiac implantable electronic devices: previous uncomplicated MRI study does not guarantee safety but increases the risk of adverse events
L. Hawryluk. Institute of Cardiology, Second Department of Coronary Artery Disease, Warsaw, Poland

Magnetic resonance imaging (MRI) in subjects with cardiac devices (CIED), though approved in legitimate cases, is still the subject of awareness and investigations due to uncertain security profile.

Aim: To find the factors that contribute to the occurrence of serious (SAE) and minor (MAE) adverse events of 1.5 T MRI examination in patients with CIEDs not certified for MRI environment.

Results: Between September 2009 and December 2014 MRI examinations were performed in 24 patients with CIED, 33 studies were conducted and a total number of 43 different anatomical regions were scanned. No SAE were observed. As the result of 6 sessions (18.2%) in 6 different patients, a total number of 8 of MAE occurred: decrease of R wave on ventricular lead in DDD system; decrease of P wave/increase of pacing threshold on atrial lead in DDD system; increase of pacing threshold on atrial lead in DDD system; software reversible reset and decrease of impedance on atrial and ventricular electrodes in DDD system; increase of troponin level in 2pts with DDD and VVI systems. Statistical analysis showed that the highest relative risk was associated with: more-than one or ICD lead, with the next MRI examination performed in one patient or with the next examination or more than one region scanned during the same MRI examination. Statistical significance was achieved for the last two situations and – with lower relative risk – for the age of the patients and the number of regions scanned during one study.

Conclusions: In addition to commonly recognized risk criteria - particular caution is suggested in patients with classical CIEDs when: performing consecutive 1.5 T MRI and/or more than one region is scanned and in subjects with more-than-one or defibrillation lead.

Figure. The examples of distinctly different extent of left atrial delayed enhancement in low contrast fibrosis (AF): (A) 63-year-old female with paroxysmal AF. (B) 69-year-old male with persistent AF.

Acknowledgement/Funding: Nothing

P1525 | BEDSIDE
Relationship of left atrial delayed enhancement magnetic resonance imaging with clinical parameters and outcome after ablation in lone atrial fibrillation

Background: The extent of left atrial (LA) structural remodeling is expected to be minimal in lone atrial fibrillation (AF). This study was sought to determine whether the larger extent of delayed enhancement magnetic resonance imaging (DEMRI) was related to co-existence of multiple risk factors and then influenced the clinical outcome after catheter ablation (CA).

Methods: Between July 2013 and June 2014, a total of consecutive 65 patients with lone AF were divided based on the extent of LA DEMRI: the small group (Utah I-II; n=43, 66.2%) vs. the large group (Utah III-IV; n=22, 33.8%).

Results: The large group was older, had higher level of serum NT pro-BNP, LA volume index, and lower LA appendage emptying velocity. AF was more persistent in this group (63.6% vs. 37.2%, p<0.043). More extensive ablation was required to achieve endpoint in the large group (40.9% vs. 9.3%, p=0.006), but the acute success rate was significantly lower (71.4% vs. 95.3%, p=0.012). During mean 209.8 days of follow-up, the recurrence rate was significantly higher in the large group (45.5% vs. 20.9%, p=0.040). No factors were remained as independent predictors of large extent of LA DEMRI in multivariate logistic regression analysis. The largest extent of DEMRI was independently associated with early recurrence (EA) after CA (HR 3.909, 95% CI 1.177–12.982, p=0.026).

Conclusions: Large extent of LA DEMRI was shown in 33.8% of patients with lone AF. Patients belonged to this group required more extensive ablation, but achieved lower acute success rate. The large LA DEMRI was an independent predictor for EA after CA, but no conventional factors included in this study could predict its extent in the LA.

Acknowledgement/Funding: Nothing
P1526 | BEDSIDE
The left ventricular apical aneurysms in Chinese hypertrophic cardiomyopathy
C. Yan¹, H. Li², W. Fang¹, L. Li¹, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Department of Radiology, Beijing, China; People's Republic of; 2 Tong Ren Hospital, Capital Medical University, Beijing, China; People's Republic of

Background: The formation of left ventricular apical aneurysm (LVAA) is a distinctive subset in hypertrophic cardiomyopathy (HCM), however, it is still unknown about the prevalence and clinical characteristics of LVAA in Chinese HCM.

Purpose: The study was carried out to assess the prevalence and clinical characteristics of LVAA in Chinese HCM.

Methods: Of 1551 HCM patients, 30 (24 M/6 F) were identified as HCM with LVAA. Left cardiac catheterization was performed and coronary artery disease was ruled out. In addition, the LVAA was evaluated with late gadolinium enhancement magnetic resonance imaging (LGE-MRI). Pathological findings of LVAA were obtained in 5 patients.

Results: The prevalence of LVAA was 1.93% in Chinese HCM. In addition, LVAA occurred in 23 patients with mid-ventricular obstructive HCM and 7 patients with apical HCM. Two patterns of LVAA were identified with LGE-MRI: 21 LVAA with LGE and 9 LVAA with non-LGE. In particular, the transition from non-LGE to LGE was ruled out. In one patient, the LVAA was evaluated with late gadolinium enhancement magnetic resonance imaging (LGE-MRI). Pathological findings of LVAA were obtained in 5 patients.

Conclusions: The prevalence of LVAA in Chinese HCM approximates to that in Western world. Furthermore, LVAA with LGE tended to have worse prognosis in HCM, and non-LGE LVAA might develop into LGE-LVAA. Further research was required to reassess the mechanism, treatment considerations and prognosis of the disease.

P1529 | BEDSIDE
Significant improvement of survival by T2* CMR in thalassemia major
A. Pepe¹, E. Meloni¹, G.C. Del Vecchio², M.A. Romeo³, M.R. Gambirini⁴, F. Bonetti⁵, M.G. Nerli¹, G. Restaino¹, V. Postiáno¹, C. Bograna-Pignatti⁵, 1 Fondazione G. Monasterio CNR-Regione Toscana, CMR Unit, Pisa, Italy; 2 University of Pisa, Department of Medicine, Radiology, Padua, Italy; 3 University of Padova, Department of Medicine, Radiology, Padua, Italy; 4 Policlinico Vittorio Emanuele, University of Catania, Division of Hematology, Unit of Thalassemia, Catania, Italy; 5 Università Cattolica del Sacro Cuore, Dipartimento di Radiologia, Campobasso, Italy; 6 University of Ferrara, Dept of Pediatrics, Ferrara, Italy

Background: Thalassemia major (TM) is the most common form of thalassemia. Significant improvement of survival by T2* CMR in Thalassemia major (TM) was the most common cause of death (Borgna et al Haematologica 2004). In the same years the accurate and noninvasive assessment of cardiac siderosis was made possible in Italy by the introduction of the T2* cardiovascular magnetic resonance (CMR).

Purpose: To evaluate the potential of T2* CMR in the assessment of cardiac siderosis in patients with Thalassemia major.

Methods: We enrolled consecutive patients with suspected myocarditis, according to ESC position statement, in which the diagnosis was also confirmed by CMR fulfilling the Lake Louise criteria. Clinical presentation data, biochemical tests, electrocardiographic features and echocardiographic data were collected. CMR scan was performed on admission and the location and the amount of edema area and late enhancement (LE) were assessed in accordance with AHA-17 segments model. After 6 months, all patients underwent complete clinical follow up with cardiac function assessment.

Results: 83 patients were enrolled. All patients had troponin I releasing (meani peak 8 µg/L). Based on the presence of left ventricular dysfunction (LVEF <50%) population was divided in 2 groups: without (n=84) and with (n=19) ventricular dysfunction. Among all clinical parameters, only CMR parameters of extensive myocardial edema (more than 3 segments) and the presence of a LGE stria pattern in almost 3 segments were related to ventricular dysfunction in the acute phase. At follow up only the presence of a intra mural stria pattern and an extension of LGE in more than 3 segments were significantly associated with increased LVEF. At multivariable analysis the presence of edema was the only predictor of left ventricular dysfunction in the acute phase (p=0.03); while at follow up only the presence of LGE with stria pattern has been confirmed as a predictor of adverse cardiac event at 6 months with a p value close to statistical significance (p=0.07).

Conclusions: In the setting of acute myocarditis CMR is able both to identify the disease progression toward dilated cardiomyopathy at the follow up.
Cardiovascular magnetic resonance in clinical practice II

The study was restricted to the patients dead after 2004 (19/159=12%) or followed until August 2010 (N=357). In this subgroup of 376 patients, MRI was performed in the 52.4% of the survivors and in all dead patients (P<0.0001). The absence of a MRI exam was reconfirmed as a strong predictive factor for death (HR=3.47, 95% CI: 1.08–12.69, P=0.046). The Figure shows the Kaplan–Meier curve.

Conclusions: Our data suggests that the use of T2* CMR, that enables individually tailored chelation regimes reducing the likelihood of developing decompensated cardiac failure, allowed the reduction of cardiac mortality in chronically transfused TM patients.

P1530 | BEDSIDE

Combined high-resolution fibrosis and perfusion mapping by cardiac magnetic resonance in hypertrophic cardiomyopathy

A. Villa1, E. Sammut1, N. Zarinabad1, G. Carr-White2, N. Bettencourt3, A. Nagel1, R. Razavi1, A. Chiribiri1. 1King’s College London, Welcome Trust/ERSPC Medical Engineering Centre, Division of Imaging Science, London, United Kingdom; 2St Thomas’ Hospital, Cardiology Department, London, United Kingdom; 3Hospital Center Vila Nova Gaia, Porto, Portugal

Background: Microvascular ischaemia is one of the hallmarks of hypertrophic cardiomyopathy (HCM). Severe microvascular ischaemia is associated with poor outcomes. Myocardial fibrosis, seen on cardiac magnetic resonance (CMR) as late gadolinium enhancement (LGE), is a significant confounding factor in the assessment of microvascular ischaemia. LGE causes rest perfusion defects in 30% of patients with HCM, leading to overestimation of ischaemic burden. An association of microvascular ischaemia with outcomes has not yet been demonstrated independently from LGE. We investigated the interaction between LGE and perfusion abnormalities using novel high-resolution perfusion analysis techniques in conjunction with LGE quantification.

Purpose: To apply high-resolution quantitative perfusion analysis with and without pixel-wise correction for LGE maps and to compare high-resolution and standard segmental perfusion analysis.

Methods: 30 patients with HCM underwent CMR with Fermi constrained quantified perfusion analysis on segmental and high-resolution data. The latter were corrected for the presence of fibrosis on a pixel-by-pixel basis.

Results: High-resolution quantification proved more sensitive for the detection of microvascular ischaemia in comparison to segmental analysis (See table). Areas of LGE were associated with significant reduction of myocardial perfusion reserve (MPR) leading to an overestimation of the total ischaemic burden on non-corrected perfusion maps. Using a threshold MPR of 1.5, LGE caused an overestimation of the ischaemic burden of 28%. The ischaemic burden was more severe in patients with fibrosis, also after correction of the perfusion maps, in keeping with more severe disease in this subgroup of patients.

Average MPR according to patient groups using segmental and high-resolution quantification

<table>
<thead>
<tr>
<th>Group</th>
<th>PA-LGE (N=12)</th>
<th>PA-LGE (N=7)</th>
<th>PA-LGE (N=9)</th>
<th>PA-LGE (N=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segmental</td>
<td>2.2±0.5</td>
<td>2.1±0.5</td>
<td>2.1±0.5</td>
<td>2.0±0.5</td>
</tr>
<tr>
<td>High-resolution</td>
<td>1.8±0.7</td>
<td>2.1±1.1</td>
<td>2.0±0.8</td>
<td>2.5±0.9</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.0002</td>
<td>&lt;0.0004</td>
<td>&lt;0.001</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Conclusions: LGE is an important confounder in the assessment of the ischaemic burden in patients with HCM. High-resolution quantitative analysis with LGE correction enables the independent evaluation of microvascular ischaemia and fibrosis and should be used when evaluating patients with HCM.

Acknowledgement/Funding: Wellcome Trust/ERSPC WT 088441/Z/08/Z; BHF RE/08/003

P1531 | BEDSIDE

Prospective changes of left ventricular iron and function by MR in pediatric thalassemia major patients treated with different chelators or not chelated

A. Meloni1, L. Pitrolo2, M.G. Nerli1, C. Salvatori2, B. Pagano4, P. Preziosi5, M. Missere6, G. Valeri7, V. Positano1, A. Pepe1. 1Fondazione G. Monasterio CNR-Regione Toscana, CMR Unit, Pisa, Italy; 2Ospedale Cervello-Villa Sofia, Ematologia II con Talassemia, Palermo, Italy; 3Fondazione G. Monasterio CNR-Regione Toscana, Unità Operativa Sistemi Informatici, Pisa, Italy; 4PO Loci - A.S.L. n. 9, Centro Micrötomico, U.O. di Pediatria e Neonatologia, Loci (RC), Italy; 5Polichinico “Casilino”, U.O.C. Diagnostica per Immagini e Interventistica, Roma, Italy; 6Università Cattolica del Sacro Cuore, Dipartimento di Radiologia, Campobasso, Italy; 7Azienda Ospedaliero-Universitaria Ospedali Riuniti “Umberto I-Lancisi-Salesi”, Dipartimento di Radiologia, Ancona, Italy

Background: There are no prospective studies comparing the effectiveness of the three iron chelators commercially available in preventing or decreasing myocardial iron overload (MIO) in pediatric thalassemia major (TM) patients.

Purpose: Our aim was to evaluate the changes in cardiac iron and function by quantitative magnetic resonance imaging (MRI) over a follow-up (FU) of 18 months in pediatric TM patients treated with one of the 3 available iron chelators in monotherapy or non chelated.

Methods: Among the first 1611 TM patients enrolled in the MIOT (Myocardial Iron Overload in Thalassemia) network, we considered pediatric patients who had maintained the same chelation regimen between the two MRI scans. MIO was quantified by a multislice multiecho T2* sequence. Function parameters were evaluated by cine images.

Results: Four groups of patients were identified: 6 patients (3 F, 10±2.2 years) treated with desferioxamine (DFO—mean dosage 43.7±6.8 mg/kg/die), 7 patients (3 F, 15±1.7 years) treated with deferiprone (DFP—75.0±2.2 mg/kg/die), 39 patients (13 F, 13±3.4 years) treated with deferasirox (DFX—26.6±7.9 mg/kg/die), and 2 patients (2 F, 11±1.5 years) not chelated because they had performed a bone marrow transplantation. At baseline in DFO, DFP and no-chelated groups no patient showed a global heart T2* value <20 ms. In all 4 groups all patients who showed no MIO at baseline maintained the FU the same status. At baseline in DFX group 5 patients had heart T2* values <20 ms. The 4 patients with intermediate cardiac iron (T2* 20–40 ms) at the baseline showed no iron at the FU while the patient with severe MIO (T2* <10 ms) remained in the same status at the FU. No chelated patients had higher global heart T2* values at baseline (non-chelated 37.7±0.5 ms > DFP 35.3±4.9 ms > DFX 32.7±9.6 ms > DFO 31.9±10.5 ms) while DFP patients had higher global heart T2* values at the FU (DFP 39.5±6.1 ms > DFX 34.2±7.3 ms DFO 33.6±7.9 ms > on-chelated 28.9±4.0 ms).

In the DFO group at baseline patient showed pathological left ventricular ejection fraction (LVEF) and he recovered at the follow up. In the DFP group 2 baseline patients showed pathological LVEF. 2 recovered at the FU and 1 did not perform the evaluation of the cardiac function at FU due to technical reasons. Conversely 9 patients with normal LVEF at baseline showed pathological LVEF at the FU.

Conclusion: In this young population, DFP and DFO seem to be more effective versus the MIO with a concommitant positive effect on the global systolic function.

P1532 | BEDSIDE

Cardiac involvement in female Duchenne and Becker muscular dystrophy carriers in comparison to their first degree male relatives: A CMR study

A.R. Florian1, S. Roesch2, M. Bietenbeck1, U. Sechtem2, A. Yilmaz1. 1University of Munich, Cardiology, Munich, Germany; 2Robert Bosch Hospital, Department of Cardiology, Stuttgart, Germany

Background: Duchenne (DMD) and Becker (BMD) muscular dystrophies are X-linked recessive disorders associated with both skeletal myopathy and progressive cardiomyopathy in males. Female DMD/BMD carriers (DMDc/BMDc) are mostly free of skeletal muscle symptoms, but they are also prone to cardiomyopathy.

Purpose: The aim of the current study was to characterize the frequency, pattern and extent of cardiomyopathy in female DMD/BMD carriers (DMDc/BMDc) in comparison to their first degree male MD relatives.

Methods: Thirty-six (age 44±14 yrs) female MD carriers (20 DMDc and 16 BMDc) constituted the “MD carrier group” and were prospectively enrolled. All MD carriers underwent a complete CMR study comprising cine- and late gadolinium enhancement (LGE)-imaging. In 22 of these women (female MD carrier comparison group), 7 DMD and 15 BMD, at least one first degree male relative with a previously established diagnosis of MD underwent the same CMR protocol and was assigned to the “male MD comparison group” (N=24, 6 DMD and 18 BMD).

Results: In the total MD carrier group, 17 (47%) MD carriers had at least one pathological CMR finding (five (14%) with a reduced LV-EF and 16 (44%) with pathological LGE). All LGE-positive patients (N=16) showed non-ischemic LGE at the baseline. The presence of LGE was significantly lower in DMDc/BMDc compared to their first degree male MD counterparts (P<0.05). Combined high-resolution fibrosis and perfusion mapping by cardiac magnetic resonance in clinical practice II 247

In the DMDc/BMDc group at baseline 3 patients showed pathological LVEF: 2 recovered at the FU and 1 did not perform the evaluation of the cardiac function at FU due to technical reasons. Conversely 9 patients with normal LVEF at baseline showed pathological LVEF at the FU.

Conclusion: In this young population, DFP and DFO seem to be more effective versus the MIO with a concommitant positive effect on the global systolic function.
P1533 | BEDSIDE
A prospective CMR study of cardiac iron and function in non-trauma-dependent thalassemia intermedia patients treated with desferrioxamine
G. Restaino 1, V. Positano1, D. De Marchi 1, A. Pepe 1. Hospital, Centro T alassemici Adulti, Cagliari, Italy; 3 Ospedale S Maria alla Aim: In the setting of inflammatory cardiomyopathy this relationship remain to be origin. Electrocardiogram (ECG) is usually abnormal and up to 40% of patients with transmural edema (p = 0.001). Moreover both the number of segments with transmural edema and the myocardial edema volume are significantly higher in patients with TWI. Also the number of segments with LGE is higher in subjects with T-waves inversion. At multivariate analysis, the edema transmurality has been confirmed the only independent predictor of TWI on ECG. The 90% of patients were followed and all normalized the TWI during follow up.

Conclusions: In the setting of acute myocarditis, myocardial edema, especially in the form of a transmural pattern, relates to the presence of TWI. T-wave inversion might then be the electrical expression of the transmural dispersion of repolarization within edematous myocardial areas.

P1534 | BEDSIDE
Left ventricle myocardial edema as the substrate underlies transient T-wave inversion in acute myocarditis
M. De Lazzari1, A. Baritussio1, M. Siliotto1, A. Zorzi1, M.M. Marinato1, F. Marin1, B. Giorgi1, S. Illiceto1, M. Perazzolo Marra1, D. Corrado1. 1 University of Padua, Department of Cardiac, Thoracic and Vascular Sciences, Padua, Italy; 2 University of Padova, Department of Medicine, Radiology, Padua, Italy

Background: Myocarditis is defined as inflammation of the myocardium as histological evidence of myocardial edema associated with necrosis of non ischemic origin. Electrocardiogram (ECG) is usually abnormal and up to 40% of patients may present with T-waves inversion (TWI). Cardiac magnetic resonance (CMR) has emerged as a non-invasive modality for the diagnosis of acute myocarditis by identifying in vivo regions with myocardial edema and necrosis (late gadolinium enhancement, LGE). Previous studies demonstrate by CMR a cause-effects relationship between myocardial edema and TWI in Tako-Tsubo cardiomyopathy. In the setting of inflammatory cardiomyopathy this relationship remains to be established.

Aim: To disclose the relationship between myocardial edema and TWI in patients with acute myocarditis.

Methods: We enrolled consecutive patients with suspected myocarditis as suggested by ESC position statement in which the diagnosis was confirmed by CMR fulfilling Lake Louise criteria. The ECGs were recorded the same day of CMR as well as the presence of LGE and TWI. The presence of myocardial edema was quantified by both visual and semiquantitative analysis (using biventricular function parameters were quantified by cine SSFP sequences. Myocardial fibrosis was evaluated by late gadolinium enhancement (LGE) acquisition.

Results: Mean age was 39.69±8.12 years and 14 (48.3%) patients were females. Patients started regular chelation therapy at a mean age of 21.92±15.89 years. The mean administered dosage of DFO via subcutaneous route was 38.4±6.10.27 mg/kg body weight on 3.3±1.54 days/week. The percentage of patients with excellent/good levels of compliance to the chelation treatment was 82.1%. At baseline only one patient showed cardiac iron overload (global heart T2*<15.23 ms) but he recovered at the follow-up (FU) (global heart T2*=26.93 ms). All patients without cardiac iron maintained the same status at the FU. Due mainly to technical reasons, cardiac function was assessed at both baseline and FU MRIs in 24 patients. At baseline all patients had a normal LV ejection fraction (EF) and 4 of them showed a reduced LV ejection fraction (LVEF) at the FU. No patient had a pathological RV EF. No significant change between the two MRIs was detected in biventricular volume indexes, biventricular EFs and LV mass index.

For 21 patients the presence of myocardial fibrosis was investigated at both baseline and FU MRIs, and this subgroup was considered. Three (14.3%) patients had myocardial fibrosis at the baseline, all with a non ischemic pattern. At the FU two new instances of non-ischemic myocardial fibrosis were detected. Therefore, a sub-group of 24 patients were considered. During follow up.

Conclusions: In this small population of sporadically or non transfused T1 patients, the DFO therapy showed 100% efficacy in maintaining a normal global heart T2* value but it did not prevent the worsening of the LV function and the occurrence of new myocardial fibrosis.

P1535 | BEDSIDE
Pre-contrast T1-mapping and extracellular volume mapping for the assessment of myocardial fibrosis: A validation with histologic sample
M. Ota1, K. Dohi2, Y. Goto2, T. Omori2, N. Fujimoto2, T. Omori2, N. Fujimoto2, K. Kitagawa3, N. Yamada4, H. Sakuma3, M. Ito5,6. 1 Mie University Hospital, Tsu, Japan; 2 Mie University Graduate School of Medicine, Department of Cardiology, Tsu, Japan; 3 Mie University Graduate School of Medicine, Department of Radiology, Tsu, Japan

Introduction: Contrast enhanced T1 mapping allows for the detection of increased extracellular volume (ECV) in myocardial fibrosis. However, increased tissue collagen is also associated with prolonged pre-contrast T1. We investigated the value of pre-contrast T1 mapping for assessing increased collagen in dilated cardiomyopathy (DCM) by using histologic sample as a reference.

Methods: Twenty DCM subjects (18 men, 57±16 years old) underwent pre- and post-contrast T1 mapping as well as late gadolinium enhanced (LGE) MRI using a modified Look-Locker inversion recovery sequence at 3T. T1 values were quantified within the septal myocardium and LV blood pool with a heart rate correction. ECV was quantified from pre- and post-contrast T1 values of the blood and myocardial tissue. The tissue collagen volume fraction (CVF) was determined using picrosirius red staining.

Results: LGE was observed in 5 of the 20 patients on LGE MRI. While patients with non-ischemic LGE had significantly greater CVF than those without (27±15 vs. 13±8%, p<0.05), substantial overlap was found between patients with and without LGE. Both pre-contrast T1 and ECV were significantly associated with CVF (r=0.68, 0.71, p<0.05). Inter- and Intra- observer reproducibility for native T1 and ECV were 0.90, 0.98, 0.94 and 0.99, respectively.

Conclusion: The current results demonstrated that both native T1 and ECV have a good correlation with histological collagen fraction in DCM patients. Diffuse myocardial fibrosis in DCM may be reliably assessed by native T1 mapping without administration of gadolinium contrast agent contrast.

ECG, ARRHYTHMIA ANALYSIS, SIGNAL PROCESSING
P1536 | BENCH
Increased resting level of periodic repolarization dynamics predicts exercise-induced T-wave alternans
A. Bauer1, K.D. Rizas1, W. Hamm1, T. Nieminen2. 1 Ludwig-Maximilians University, Munich, Germany; 2 University of Helsinki, Helsinki, Finland

Background: T-Wave alternans (TWA) is linked to vulnerability to ventricular fibrillation but needs to be unmasked by cardiac stress. Periodic repolarization dynamics (PRD) is a novel electrocardiographic phenomenon that refers to low-frequency modulations of cardiac repolarization during rest (Rizas et al. JCI 2014). Increased PRD has been shown to be a strong and independent predictor of mortality after MI. Here, we postulated that increased resting PRD predicts exercise-induced TWA.

Methods: We tested the potential link between PRD and TWA in 3,223 patients of the Finnish Cardiovascular Study (FINCAVAS), who underwent a clinically indicated exercise test. We assessed TWA by the Modified Moving Average method. PRD was assessed as the low-frequency (≤0.1 Hz) spectral power of resting repolarization instability as previously described. Positive TWA was defined as a microvolt TWA>60 μV. Uni- and multivariable logistic regression analyses were used to test the association between resting PRD and exercise-induced TWA.

Results: 91 of 3,223 patients (2.9%) exhibited a TWA phenomenon during exercise. TWA-positive patients had significantly higher resting levels of PRD than TWA-negative patients (9.18 vs. 19.89, p<0.01). Increased resting PRD was the
strongest predictor of exercise-induced TWA and was independent from various covariates including age, sex, presence of diabetes, LVEF history of MI, treatment with b-blocker, as well as basal and maximum HR (Table). Univariate and multivariate regression analyses

<table>
<thead>
<tr>
<th>Risk Variable</th>
<th>Univariable logistic regression</th>
<th>Multivariable logistic regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.11 (0.04–0.18)</td>
<td>0.011</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.09 (0.02–0.15)</td>
<td>0.011</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.02 (−0.14–0.10)</td>
<td>0.932</td>
</tr>
<tr>
<td>Sex</td>
<td>−0.06 (−0.13–0.01)</td>
<td>0.112</td>
</tr>
<tr>
<td>Max HR</td>
<td>0.02 (−0.09–0.04)</td>
<td>0.339</td>
</tr>
<tr>
<td>Baseline HR</td>
<td>0.03 (−0.04–0.25)</td>
<td>0.252</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>0.11 (0.04–0.18)</td>
<td>0.003</td>
</tr>
<tr>
<td>History of MI</td>
<td>0.05 (−0.02–0.11)</td>
<td>0.183</td>
</tr>
<tr>
<td>PRD at rest</td>
<td>0.22 (0.16–0.29)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion: Increased resting levels of PRD predict development of exercise-induced TWA.

P1537 | BEDSIDE
Early repolarization pattern in patients with false tendons
A.M. Ragab, Y. Yazeed, W. El-Naggar, A.M. Abdelwahab. Cairo University Hospitals, Cardiovascular, Cairo, Egypt

Background: Although early repolarization pattern (ERP) has been considered for long to be a normal electrocardiographic finding, it has been recently linked to sudden cardiac death. Exact mechanism underlying this electrocardiographic phenomenon is not well established. False tendons are (FT) fibromuscular bands that traverse the left ventricular cavity and often contain conduction tissue which has been previously described in some case reports with ventricular tachycardias.

Objectives: To investigate the electrocardiographic characteristics of patients with FT and their association with ERP.

Methods: We studied 60 non-cardiac subjects with FTs and another 60 non-cardiac subjects with ERP. Patients were classified according to presence of ERP and FTs to: ERP+FT (Group 1, n=52), isolated ERP (Group 2, n=37 and isolated FT (Group 3, n=31). ERP was defined as J point elevation manifested either as QRS slurring (transition from the QRS segment to the ST segment) or notching (positive deflection on terminal S wave). Upper concavity ST segment elevation for more than 0.1mV and prominent T waves in at least 2 contiguous leads. False tendons were defined (by 2D TTE) as bands stretching across the left ventricle (LV) from the ventricular septum to the papillary muscle or LV free wall but not connecting, like the chordae tendineae, to the mitral leaflet. PRd, QRSd, QT, QTc, JT and JTC were calculated, site, morphology of ST elevation were identified and amplitude of ERP and number of leads with ST elevation were calculated. Site and number of FTs were identified and length, thickness and volume of FTs were measured.

Results: ERP was present in 48.3% of subjects with FTs and FTs were present in 38.3% of subjects with ERP. Horizontal ST segment elevation was found in 59.6% of subjects with ERP+FT which was more common than subjects with isolated ERP (27.8%, P=0.004). We found that 80% of subjects with ERP in the inferior leads had FTs (P=0.005) and 72% of subjects with ERP in the inferolateral leads had horizontal FTs (P=0.05).

Conclusion: Our results suggest that FTs may play a role in genesis and determination of site and morphology of ERP.

P1539 | BEDSIDE
Heart rate impact on heart rate variability prognostic value is different for different indices and outcomes
J. Sacha, S. Barabach, G. Statkiewicz-Barabach, K. Sacha, A. Muller, P. Barthei, G. Schmidt, T. Department of Cardiology, Regional Medical Center, Opole, Poland; 1 Wroclaw University of Technology, Institute of Physics, Wroclaw, Poland; 2 Jagiellonian University, Atom Optics Department, Institute of Physics, Krakow, Poland; 3 Medizinische Klinik und Deutsches Herzzentrum Munchen, Munchen, Germany

Background: Heart rate variability (HRV) indices are deemed to predict outcomes independently on heart rate (HR), however mostly of them correlate with HR, thus they may carry some prognostic information from HR. By normalization to HR one can explore how much the prognostic power of HRV depends on HR.

Methods: We calculated spectral HRV components (i.e. VLF, LF, HF, TP), and deceleration (DC) and acceleration capacities (AC) in two groups of post-infarction patients, i.e. 1455 in the exploratory (EXPL) group and 946 in the validation (VAL) one, followed up for 5 and 2.7 years (median). Normalization to HR was performed by division of the indices by the corresponding mean RR interval to the power 2.0 (spectral components) and 1.4 (DC and AC).

Results: Initially, all indices correlated with HR but after normalization no correlation was found. Areas under the curve (AUCs) of all indices decreased after normalization for each mode of death in both EXPL and VAL group (p<0.05 for all) – on average, AUCs decreased by 0.064 (VLF), 0.043 (LF), 0.101 (HF), 0.07 (TP), 0.039 (DC) and 0.085 (AC). The AUC decreased depended on AUC of HR for a given outcome, i.e. the higher prognostic power of HR for a given outcome the bigger decrease in the corresponding power of HRV after normalization (Figure) – for each index, the biggest AUC reduction was seen for cardiac death, but the smallest one for non-cardiac one. Of all indices, DC prognostic value revealed the weakest dependence on HR, in addition only DC presented significantly larger AUCs than HR before normalization (p<0.05).

Conclusions: HR participates in the HRV predictive value, however this impact depends on the prognostic power of HR and is different for different indices and outcomes. DC reveals the strongest predictive power with the least dependence on HR.

P1540 | BEDSIDE
Combination of ECG electrical myocardial instability markers in patients with idiopathic ventricular arrhythmia

Background: Ventricular arrhythmia (VA) is one of electrical myocardial instability (EMI) markers. It is important to study other markers, such as fragmentation of QRS (QQRS complex), microvolt T-wave alternans (mTWA), heart rate turbulence (HRT) and heart rate recovery (HRR).

Purpose: To study the markers of EMI (VA, QQRS complex, mTWA, HRT, HRR) during Holter ECG and exercise treadmill test (ETT) in patients with idiopathic VA.

Materials and methods: 49 patients (26 men, mean age 43±12 years) with idiopathic VA more than 300 VEC/hour without any therapy. Structural abnormality was excluded by an ECG, echoCG, stress ECG and cardiac MRI. EMI markers were analyzed using Holter ECG and ETT (protocol Bruse). ETT was performed up to submaximal heart rate 85% or more.

Results: During Holter ECG 59% of VA was monomorphic. Night type of arrhythmia was dominated by Holter ECG and exercise treadmill test (ETT) in patients with idiopathic VA. Materials and methods: 49 patients (26 men, mean age 43±12 years) with idiopathic VA more than 300 VEC/hour without any therapy. Structural abnormality was excluded by an ECG, echoCG, stress ECG and cardiac MRI. EMI markers were analyzed using Holter ECG and ETT (protocol Bruse). ETT was performed up to submaximal heart rate 85% or more.

Conclusions: HR participates in the HRV predictive value, however this impact depends on the prognostic power of HR and is different for different indices and outcomes. DC reveals the strongest predictive power with the least dependence on HR.
At the peak ETT VA was present in 44%, mean 3.4 SVEc/min. At the recovery period (RP) VA gradually returned to the pretest values. At the 1 min of RP VA was in 44% (3.5 SVEc/min), at the 3 min of RP – 48% (5.4 SVEc/min), at the 5 min of RP - 53% (7.9 SVEc/min).

Conclusion: We found no abnormal markers that could indicate structural changes of the myocardium. However, we observed the pathological changes due to autonomic nervous system modulation (the abnormal mTWA in VA and high detection of ventricular arrhythmias during ETT).

P1541 | BEDSIDE
Which QT correction formula should be implemented in a computer-based hospital-wide QT-monitoring system?

B. Vanderberk1, E. Vandaelf2, J. Spriet3, C. Garweg4, J. Vanderberge5, B. Van Den Bosch4, V. Foulot2, J. Ector1, R. Willems5, 1University of Leuven, Cardiovascular sciences, Leuven, Belgium; 2University of Leuven, Pharmacology, Leuven, Belgium; 3University of Leuven, Department of Neurosciences, Leuven, Belgium; 4University Hospitals (UZ) Leuven, Department IT, Leuven, Belgium

Background: QT prolongation carries risk for Torsades des Pointes and mortality. An algorithm monitoring QT in hospitalized patients might be useful to prevent arrhythmic death. It is unclear which correction formula should be implemented.

Methods: All ECGs in patients >18y in our University Hospitals during a 2 month period were included, one ECG per patient. Age, gender, heart rate (HR), QRS duration (QRSd), QT and 1 month survival were collected. QT correction was performed with Bazett (QTcB), Fridericia (QTcF) and Rautaharju’s (QTcR) correction formulas. QTc = 450ms for man and -470ms for women were considered normal, QTc < 500ms a high risk.

Results: In total 9648 ECGs were included: age 61.7±16.8y; 55.5% male, HR 74.5±17.3pm and QRSd 99.8±25.3ms. Sinus rhythm (SR) represents 87.9%, 7.5% AF-Aflutter, 4% ventricular pacing and 0.6% other. All patients were included in the analysis.

Overall, QTcB (435±38ms) was significantly longer than QTcF (421±35ms) and QTcR (422±26ms, p<0.001). Risk classification based on QTcF considered 41.5% less patients at risk vs QTcB (<0.001) and QTcR 60.4% less vs QTcB (<0.001). One month mortality was 1.8%. Sensitivity and specificity predicting 1 month mortality is shown in the table.

Conclusion: QTcF formulae have a major influence on the risk classification. The high sensitivity of QTcB for early mortality might reflect other parameters associated with mortality leading to a lower specificity, QTcF and QTcR have higher specificity and higher hazard ratios for early mortality in a multivariate analysis.

P1542 | BEDSIDE
ECG markers of electrical myocardial instability in patients with or without coronary artery disease

T.A. Kurilenko, E.V. Parmon, T.E. Tulintseva, T.V. Treshkur, E.V. Shlyakhto, T.A. Kurilenko, E.V. Parmon, T.E. Tulintseva, T.V. Treshkur, E.V. Shlyakhto, 1University Hospital of Fort de France, Department of Cardiology, Fort de France, Martinique; 2Hospital General, Department of Cardiology, Fort de France, Martinique; 3Federal North-West Medical Research Centre, Saint Petersburg, Russian Federation

Background: Electrical myocardial instability (EMI) markers in patients with coronary artery disease (CAD) are considered to be important in point of sudden cardiac death (SCD) risk stratification. A group of patients with ventricular arrhythmia (VA) without structural heart disease is still less studied. Appearance of VA is known to depend on autonomic nervous system modulation.

Purpose: To study the characteristics of VA: polymorphism of ventricular ectopic complexes (VEC), distribution during the day, presence of ventricular tachycardia (VT), markers of EMI: the fragmentation of QRS (QRSs complex, microtachyarrhythmias (mTWA) and heart rate turbulence (HRT) in patients without structural heart disease and patients with CAD.

Materials and methods: 52 patients with 500 VEC/day (28 males) were divided into 2 groups. Group I: 27 patients without structural heart disease, mean age 42±15y, 436±196VEC/hour, ejection fraction (EF) 65±6% by Simpson. Structural abnormality of the heart was excluded using an ECG, ecoCG, in some cases stress ECG and cardiac MRI.

Group II: 25 patients after myocardial infarction (mean age 59±11 years), VA (208±103 VEC/hour), EF 47±8% by Simpson. EMI markers were analyzed using holter ECG in both groups.

Results: In group I 59% VA was monomorphic, night type of arrhythmia was dominant (387±152 VEC/hour during the day, 495±203 VEC/hour at night, p<0.05), nonsustained VT was in 8% of patients. FQRS in sinus complex was not found in I group. FQRS in VEC was registered in 7% in the II, III, aVF leads. MTrWA was positive in 59%. Pathological turbulence onset (TO) was in 3.7%, while turbulence slope (TS) was in the normal range.

In II group polymorphism of VEC predominated (in 84% of patients), with a day type distribution of VA (247±125 VEC/hour during the day, 140±84 VEC/hour at night, p<0.05). Nonsustained VT was in 25%. FQRS in sinus complex was observed in 25%. FQRS in VEC was recorded in 92% in different leads, but more often in II, III, aVF and V1-M4. VT was positive in 50% of patients. 25% of patients had abnormalities in TO, 16% – in TS.

Conclusion: Abnormal mTWA and TO in patients without structural heart disease suggest that an imbalance of autonomic nervous system impacts on the maintenance of EMI in this group. While the daily type of arrhythmia, nonsustained VT, QRS fragmentation, pathological mTWA and HRT indicate the presence of EMI in patients with coronary artery disease, even when EF is preserved. ECG markers combination requires further studies.

P1543 | BEDSIDE
The electrocardiogram (ECG) is a poor diagnostic tool for the detection of left ventricular hypertrophy (LVH) in elderly patients with aortic stenosis

R. Kanyal, A. Constantine, P. Sawhney, A. Duncan, S.W. Davies, C. Di Mario, A.C. Lindsay, N.E. Moat, Royal Brompton Hospital, London, United Kingdom

Background and introduction: Several current scoring systems exist for assessing the presence of left ventricular hypertrophy (LVH) on the electrocardiogram (ECG). However, whether these scoring systems remain accurate in the setting of severe aortic stenosis has not previously been quantified.

Purpose: To determine the sensitivity and specificity of the electrocardiogram in determining the presence of left ventricular hypertrophy, as defined by CMR, in patients with severe aortic stenosis (AS).

Methods: 92 consecutive patients (Mean age 79±9.5 years, 49% Female) with severe aortic stenosis underwent CMR. The Romhilt-Estes LVH point score system was used to ascertain the presence of LVH on ECG. LVH on CMR was diagnosed using criteria of LV mass index >112 g/m² for men and >92 g/m² for females. The Marquette criteria were used to determine the presence of poor R wave progression.

Results: Overall 34/92 (36.9%) patients had confirmed left ventricular hypertrophy on CMR, 23/92 (67.6%) of these patients met ECG criteria for LVH. Of patients who did not have CMR evidence of LVH, 39/58 (67.2%) met ECG criteria for LVH. The overall sensitivity of the ECG for detecting LVH in patients with aortic stenosis was (67.6%) and specificity (32.7%). 17/92 patients (18.4%) showed poor R wave progression on the ECG. 7/17 (41%) had LVH on the ECG. The overall sensitivity of poor R wave progression for the detection of normal LV mass was 22.8% and specificity 88.5%.

Conclusions: The ECG is a poor diagnostic tool to determine LVH in patients with severe aortic stenosis. Current criteria have a poor sensitivity and specificity for diagnosing LVH, and poor R wave progression on the ECG does not exclude the presence of LVH if severe aortic stenosis is present.

P1544 | BEDSIDE
Clinical significance of ventricular arrhythmias in patients with sickle cell disease

J. Inamo1, G. Loko2, R. Itirm3, F. Demoniere1, S. Alexis-Fardini2, A. Inamo2, 1University Hospital of Fort de France, Department of Cardiology, Fort de France, Martinique; 2CHU Martinique, Centre Intégre de la Dresanocytose, Lamentin, Martinique; 3Clinical significance of ventricular arrhythmias in patients with sickle cell disease has been previously observed during acute crisis among patients with sickle cell disease (scd). No data is available for patients in stable conditions.

In the present study, we examined the frequency and clinical correlates of ventricular arrhythmias in 125 consecutive patients with homozygous sickle cell disease referred to our centre for routine cardiac evaluation, and compared them with 116 controls.

All participants completed a 24-hour Holter ECG monitoring, 6 min walking test distance (6MWT), echoCardiogram, and standard blood tests.

The incidence of ventricular ectopy was significantly higher in the scd patients than in controls (195±341 vs. 24±39, p<0.001). Also, non sustained ventricular
ECG, arrhythmia analysis, signal processing / e-Cardiology other 251
tachycardia occurred in 15% of the patients with SCD, but none of the controls (p=0.03). Ventricular arrhythmias were significantly associated with older age, creatinine levels, left atrial indexed volume, velocity of tricuspid regurgitation, and not with left ventricular size or ejection fraction. They were also associated with higher ProBNP levels, and reduced 6MW distance.

Arrhythmias in Sickle cell disease

Control (n=116) Sickle cell disease (n=125) p-value

Age, years med [min–max] 39.2 [20–65] 37.9 [19–65] 0.51
Hemoglobin, g/dl (mean ± SD) 13.4±1.4 8.2±1.5 <0.001
Creatinine level, µmol/l (mean ± SD) 75.3±13.9 56.2±26.3 <0.001
Heart rate, beats/min (mean ± SD) 71.8±9.7 79.5±8.8 <0.001
Total VPC, n (%) 5 1 0.001
NSVT, n (%) 0 14 (9.7) 0.03
Complex ventricular arrhythmies, n (%) 0 29 (20.0) <0.001

No life-threatening arrhythmias nor sudden death occurred in any participant during a mean three-year follow-up period. In conclusion, ventricular arrhythmias become common with aging in clinically stable patients with sickle disease, but do not demonstrate significant impact on the natural history of the disease

P1545 | BEDSIDE Evaluation of changes in T-wave alternans induced by 21-days of bedridden immobilization by head-down bed-rest A. Martin-Yebra1, J.P. Martinez2, V. Monasterio3, P. Laguna2, E.G. Caiani3, P1546 | BEDSIDE Cardiovascular deconditioning induced by microgravity exposure and reports on ventricular arrhythmias during space flight raise the question of whether reduced gravitational stimulus or immobilization could increase potential life-threatening arrhythmia susceptibility, and consequently, sudden cardiac death (SCD) risk. We hypothesized that T-wave alternans (TWA), a noninvasive marker for identifying patients at risk for SCD and ventricular vulnerability, and reflecting temporal and spatial repolarization heterogeneity, could be able to reflect these changes if present.

Introduction:
Cardiovascular deconditioning induced by microgravity exposure and reports on ventricular arrhythmias during space flight raise the question of whether reduced gravitational stimulus or immobilization could increase potential life-threatening arrhythmia susceptibility, and consequently, sudden cardiac death (SCD) risk. We hypothesized that T-wave alternans (TWA), a noninvasive marker for identifying patients at risk for SCD and ventricular vulnerability, and reflecting temporal and spatial repolarization heterogeneity, could be able to reflect these changes if present.

Purpose:
To assess changes in TWA induced by 21 days bedridden immobilization (~6 degrees head-down bed-rest, HDBR) by long-term average TWA activity. Methods: 22 healthy men (21–43 years old) were studied in two separate twin experiments conducted at MEDES, France and at DLR, Germany as part of the European Space Agency HDBR studies. High fidelity (1000 Hz) 24-h Holter ECG (12-leads,) was acquired before (PRE), the last day of HDBR (HTDT2), and the day after its conclusion (POST). To avoid potential confounding effects, the night period (23:00–06:00) was selected for analysis. Using a fully automated algorithm, TWA amplitude was measured in consecutive segments of 128 beats (50% overlap) using a multilead scheme, and was normalized by the corresponding T wave amplitude (expressed as %TWA). Then, the normalized TWA amplitude of all ECG segments was averaged, yielding the average night normalized alternating index (ANNAi). ANNAi was computed, together with the heart rate–restricted indices (ANNAAi), considering only those ECG segments with average HR ≤ X=(60,70,80,90), beats/min.

Results: Compared to PRE, at HTDT2 normalized ANNAi showed a trend to increase (median [25th,75th percentile]) from 0.29 (0.19,0.47) to 0.48 (0.31,0.52), p=0.084. Interestingly, when considering heart rate–restricted indices, ANNAAi showed a significant increase after 21 days of HDBR (p<0.05) for ANNAi60 (0.28 (0.19,0.43) vs 0.42 (0.31,0.52)) and with p=0.062 and p=0.055 for ANNAi70 and ANNAi90, respectively. At POST, all parameters returned to their control values.

Conclusions: In healthy subjects, normalized nocturnal TWA activity showed a reversible increase after 21 days of HDBR, which may be indicative of initial alterations in the myocardial substrate. These alterations likely suggest a potential increase in arrhythmia susceptibility induced by the sustained reduction of gravitational stimulus, which should also be taken into account in bedridden patients.

Acknowledgement/Funding: This study has been funded by the Italian Space Agency (contract 2013-033-R.O, recipient E.G. Caiani)

E-CARDIOLOGY OTHER

P1546 | BEDSIDE Non-invasive acoustic detection of coronary artery disease S.E. Schmidt1, S. Winther2, N.R. Holm3, H.E. Boetker4, E. Tøff5, P. Clemmensen6, J.J. Struik7, M. Boettcher8, Aalborg University, Department of Health Science and Technology, Aalborg, Denmark; 1Region Hospital Herning, Department of Cardiology, Herning, Denmark; 2Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark; 3Qatar University, College of Medicine, Doha, Qatar; 4Righospitalet - Copenhagen University Hospital, Heart Centre, Department of Cardiology, Copenhagen, Denmark

Recently, we have demonstrated that coronary artery disease (CAD) may be identified by diastolic heart sounds. The aim of this study was to optimize and validate the acoustic CAD-score algorithm in an independent study population.

Methods: Recordings of heart sounds were obtained from the 4th intercostal space at the left sternal border using a novel acoustic prototype sensor in subjects referred for coronary angiography (CAG) (n=179) or computerized tomography angiography (CTA) (n=119). The data were collected in three populations (see table). Population 1 and 3 were obtained at Aarhus University Hospital, Denmark and population 2 was collected at Copenhagen University Hospital, Denmark. The recordings were used for improvement, calibration and validation of the CAD-score algorithm. The algorithm automatically validates the suitability of the recordings and thus excluded 28.9% subjects (arrhythmias, excess noise or poor recording quality), providing a quantitative acoustic CAD-score in suitable subjects based on diastolic sound characteristics.

Quantitative coronary analysis (QCA) was performed after CAG. CAD was defined by at least one >50% diameter stenosis (DS). Non-CAD was defined as either: no coronary stenosis exceeding 30% DS in QCA or a negative CTA (no CAG performed). Subjects with a maximal CAG stenosis in the 30–50% DS interval and subjects with a stenosis identified by CTA, which was not confirmed by CAG, were defined as having insignificant-CAD.

Results: The CAD-score was higher in subjects with than subjects without CAD in all three populations (see table). Using CAD-score for classification of CAD and non-CAD cases gave areas under the receiver-operator curves (AUC) from 63.3% to 84.0%.

Conclusion: This study demonstrates the potential of a novel, non-invasive, non-radiation method for identification of CAD.

Acknowledgement/Funding: Acarix a/s
Heart failure telemonitoring in Japan and Sweden: the gap between research and practice
N. Kato\textsuperscript{1}, P. Johansson\textsuperscript{2}, I. Okada\textsuperscript{3}, A.E. De Vries\textsuperscript{4}, K. Kinugawa\textsuperscript{5}, A. Stromberg\textsuperscript{5}, T. Jaarsma\textsuperscript{3}, Linkoping University, Department of Social and Welfare Studies, Linkoping, Sweden; Linkoping University, Department of Cardiology, Division of Medicine and Health Sciences, Linkoping, Sweden; The University of Tokyo, Department of Therapeutic Strategy for Heart Failure, Tokyo, Japan; University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands; Linkoping University, Department of Nursing, Linkoping, Sweden

Background: Telemonitoring of heart failure (HF) patients is increasingly used in some countries in Europe and the US. Clinical impacts of reduced hospitalizations and mortality of some telemonitoring devices have been shown. However, little is known about the usage of non-invasive telemonitoring in daily clinical practice in Japan and Sweden. We therefore aimed at (1) describing the use of non-invasive telemonitoring, (2) exploring expectations of the telemonitoring among cardiologists and nurses and (3) assessing barriers to the implementation of telemonitoring in Japan and Sweden.

Methods: A total of 378 Japanese (120 cardiologists, 258 nurses) and 120 Swedish (39 cardiologists, 81 nurses) healthcare professionals from 165 Japanese and 61 Swedish hospitals/clinics nationwide (210 in Japan, 98 in Sweden) approached participated in the study. Data were collected between November 2013 and May 2014 with a questionnaire that was adapted from a previous Dutch study.

Results: In total, 7 Japanese (4.2\%) and none of the Swedish hospitals/clinics used telemonitoring for HF patients. One fourth (24\%) of the participants responded that they were familiar with the technology (22\% in Japan and 30\% in Sweden). The highest expectations of telemonitoring rated on a scale from 0–10 (low high expectations) were to reduce hospitalizations (8.3 in Japan and 7.5 in Sweden), increasing patients’ self-care (7.8 and 7.4), and offering high quality of care (7.8 and 7.0). The major reason for introducing telemonitoring would be to monitor effects of treatment and adjusting it remotely (87\%) and to remote diet titration (79\%). Three themes of the barriers were found by content analysis: organization (e.g., cannot envisage how it works, and lack of equipment), healthcare professionals (e.g., poor knowledge and lack of advice), and patients (e.g., physical dysfunction and lack of motivation).

Conclusions: In contrast to several European countries and the US telemonitoring has not been implemented for HF patients in Japan and Sweden. Only one fourth of healthcare professionals were familiar with HF telemonitoring, and several barriers for introducing telemonitoring were found. Further research is needed to intervene toward barriers of implementation of telemonitoring in the Japanese and Swedish healthcare context.

Acknowledgement/Funding: A Grant-in-Aid for Research Activity Start-up to the Japan Society for the Promotion Science

Body surface potential mapping in patients with arrhythmogenic rightventricular cardiomyopathy: spread of QRS notches and epsilon waves
D. Braja\textsuperscript{1}, A.Gapelyuk\textsuperscript{2}, U. Landmesser\textsuperscript{3}, O. Goeling\textsuperscript{1}, A. Schirdewan\textsuperscript{1}, Sana Klinikum Lichtenberg, Department Cardiology, Berlin, Germany;\textsuperscript{4} Institute for physics, Humboldt-University of Berlin, Berlin, Germany;\textsuperscript{5} Charite - Campus Benjamin Franklin, Berlin, Germany

Background: Most patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) show Q wave abnormalities, which play an important role in the diagnosis of the disease based on task force criteria as well as in the assessment of the disease progression. We investigated the surface distribution of QRS notching on top of the R-wave or in the nadir of the S-wave and of epsilon waves (EW) in patients with ARVC.

Methods: Twelve patients with task force criteria or genetically confirmed ARVC underwent 64 lead body surface potential mapping (BSPM). BSPM electrodes were applied to the chest in 8 vertical strips with each 8 electrodes, left and right anterior and posterior and 1 posterior strips. We were calculating the surface area corresponding to the electrodes detecting notchting and notching (Mean±standarddeviation). We create two subgroups: 1. Evidence of Piakophyllin mutation (PKP2), 2. Documentedventricular arrhythmia events (VTA). We compared the distribution of QRS notching and EW (magnitude, duration and the site of maximum) in these subgroups.

Results: Twelve patients with ARVC (mean age 57±20 years; 6 female) were included. 6 pts were PKP2 positive tested. Ventricular arrhythmias (VTA) were documented in 8 pts, 3 of them with PKP2. All pts showed a QRS notchting. The distribution of QRS notchting did not differ between PKP2 positive and negative and also VTA and non-VTA pts. EW were recorded in 8 pts, both-sided. Only the arrangement of the EW in the right anterior area for the VTA-subgroup differ significantly. The PKP2 mutation did not have any influence on the distribution area for the EW, on the duration or on the amplitude. In the VTA-group there was a trend for longer duration of the EW (p<0.07).

Conclusion: QRS Notching is common in our ARVC group but was not related to a PKP2 mutation or the history of VTA. Patients with VTA showed for the EW a focus on the distribution area for the right anterior side and on the duration of the amplitude. PKP-2 mutation seems to have no influence on it. BSPM can quantitatively characterize EW and should be applied for follow-up-investigation in order to document progressive changes.

Mechanisms Enabling Limited Ablation to Terminate Human AF: In silico and clinical studies
J.A.B. Zaman\textsuperscript{1}, G. Lalani\textsuperscript{2}, T. Baykaner\textsuperscript{3}, D.E. Krummen\textsuperscript{2}, P.J. Wang\textsuperscript{3}, S.M. Narayan\textsuperscript{4}, W.J. Rappel\textsuperscript{1}, 1 School of Medicine, Cardiovascular Medicine, Stanford, United States of America; 2 University of California San Diego, San Diego, United States of America; 3 Stanford University Medical Center, Stanford, United States of America

Background: Rotors are increasingly reported to maintain clinical AF; yet, it is unclear how localized ablation terminates an AF rotor. We hypothesized that variations in conduction velocity, e.g. from fibrosis, may anchor AF rotors and explain their termination by localized lesions. We tested this hypothesis by measuring atrial conduction in AF patients and translating this to physiologically relevant numerical models.

Methods: Clinical data: In 28 AF patients (left atria 43±5 mm; n=13 persistent), we measured atrial conduction at 64-pole catheters (Constellation, BSCI) while pacing into AF, using custom software to identify AF rotors as phase singularities. Computer models: Monodomain simulations used isotropic sheets and the Fenton-Karma (FK) model. Conduction slowing was coded by spatially varying FK parameters of excitability. AF was initiated and ablation lesions were modeled as 4 mm radius disks of inexctable tissue.

Results: In patients, conduction showed rate-dependent slowing at AF rotor sites (by 35\% p<0.001), that varied throughout atria (p<0.05). In computer models, several mechanisms enabled ablation to terminate AF. 1. For rotors anchored in low excitability (slowly conducting) regions (fig. 1A, circle), lesions enabled the wave front and back to meet, de-anchoing the rotor to terminate AF (fig 1B,C). Ablation can also 2. Create an excitable gap that can be invaded by fibrillary waves to terminate reentry (figure 2A-D); or 3. Anchor a rotor, converting AF to flutter.

Conclusions: Patients with AF exhibit marked spatial gradients in atrial conduc- tion velocity that provide several mechanisms by which localized ablation can terminate an AF rotor. Clinical studies should define if AF sources or regions of disorganization co-localize with sites of fiber anistropy.

Noninvasive measurement of stroke volume using impedance cardiography
I. Nederend\textsuperscript{1}, A.D.J. Ten Harkel\textsuperscript{2}, J.C.N. De Geus\textsuperscript{3}, N.A. Blom\textsuperscript{2}, 1 Sana Medical Center, Amsterdam, Amsterdam, Netherlands; 2 Leiden University Medical Center, Leiden, Netherlands

Introduction: Stroke volume is an important measure in the clinical evaluation of cardiac patients. Impedance cardiography can be used to noninvasively measure cardiac performance. Classically, three points are derived from the impedance cardiogram (ICG): 1. The “B point” represents the moment of opening of the aortic valves 2. The “C point” the moment of maximum flow velocity of blood through the thoracic aorta and 3. The “X point” depicts the moment of closing of the aortic valves. Stroke volume is computed using the product of the amplitude of the C point and ejection time, weighing for blood resistivity, baseline thorax impedance and the total volume enclosed by the measuring electrodes.

Objectives: This study aims to validate systolic time intervals and stroke volume measured by impedance cardiography.

Methods: 77 Healthy volunteers (41 girls, 36 boys) with an average age of 11.5 y (range 1–18) were recruited to undergo simultaneous recording of both impedance- and echocardiography. Impedance cardiography was measured using the SU Ambulatory Monitoring System (VU-AMS). In the echocardiogram, the 3 systolic time intervals of interest were mapped using a pulsed wave Doppler flow signal over the left ventricular outflow tract in a parasternal 5 chamber view. Stroke volume was assessed using velocity time integral. Bland-Altman plots and Intra Class Correlations were used for analysis of the agreement between TTE and ICG.
Results: Agreement between systolic time intervals measured by the two different modalities was moderate for opening of the aortic valves (B point) and maximal flow velocity (C point): ICC=0.47, (95% CI 0.26–0.63) and ICC=0.52. (95% CI 0.33–0.67) respectively. Agreement was high for the moment of closing of the aortic valves (X point): ICC=0.94 (95% CI 0.90–0.98). Agreement for stroke volume was ICC=0.58 (95% CI 0.40–0.72) correlation coefficient = 0.78 (p < 0.01).

Conclusions: Systolic time intervals derived from ICG show moderate to high agreement when compared to TTE. Agreement for stroke volume was moderate. The agreement between TTE and ICG is encouraging. A next step is to relate ambulatory recorded systolic time intervals and changes in stroke volume to clinical features in order to establish whether noninvasive (ambulatory) ICG might be of additional value in the clinical evaluation of (pediatric) cardiac patients.

P1554 | BEDSIDE
Interobserver and intraobserver validation of a novel echocardiographic 3D automated software for the assessment of mitral valve anatomy


Introduction: The increasing number of interventional procedures demands non-invasive techniques to be not only accurate but also reproducible for its use in clinical practice. In this regard, the future of 3D echocardiography requires not only superb image quality with high temporal and spatial resolution but also accurate and automatic quantification. For this reason new technological developments need to prove their accuracy with higher reproducibility before they can be used in clinical practice replacing the available conventional methods.

Purpose: Thus, the aim of our study was to evaluate the inter- and intra-observer reproducibility of a novel full-automated software in the evaluation of MV anatomy compared to routine clinical manual 3D assessment.

Methods: 36 out of 56 screened patients referred to our Cardiac Imaging Unit for TEE were included.3D TEE analysis was performed both manually and with the automated software. Same volume dataset and frame were used for both manual and software analysis, which included the following parameters: intercommissural distance, the area of mitral annulus and the leaflets length. 3D mitral valve images were imported for analysis into the software eSie Valves (Autovate prototype version 1.22).Manual measurements of the MV were performed using QLAB 11; Philips Medical System. To test interobserver variability between both methods, all images were analysed by 2 cardiologists that independently reviewed the 3D images. One observer repeated the measurements in 15 randomly selected cases where each observer noted down the time points to manual assessment, the inter- and intraobserver variability were analysed using the Bland-Altman method. Interobserver and intraobserver agreements for qualitative analysis score by 3D Echo manual and software assessments were calculated using intraclass correlation coefficient.

Results: Interobserver variability assessed by the intraclass correlation coefficient was superior for the automatic software: intercommissural distance 0.997 vs. 0.76; mitral annular area 0.957 vs. 0.858; anterior leaflet length 0.963 vs. 0.734 and posterior leaflet length 0.936 vs. 0.838. Intraobserver variability was good for both methods with a better level of agreement with the automatic software.

Conclusions: The novel 3D automated software is more reproducible in MV anatomy assessment compared to 3D manual evaluation. For this reason new technological developments with higher reproducibility can be used in clinical practice replacing the available conventional methods.

P1555 | SPOTLIGHT
Ritmo project (real time continuous web monitoring) a model of a multidisciplinary approach for safely managing of new therapies

S. Nodari1, M. Triggiani1, L. Lupi1, A. Manerba1, E. Rocco1, C. Villa1, N. Dasseni1, G. Milesi1, N. Berlinghieri1, F. Gilsanti1, 2University of Brescia, Department of Clinical and Surgical Specialties, Cardiology section, Brescia, Italy, 1Health Telematic Network srl, Brescia, Italy

Introduction: According to the decision of the Committee for Medicinal Products for Human use (CHMP), first dose administration of fingolimod must comply with the following conditions: 1) 12-lead electrocardiogram (ECC) and blood pressure (BP) measurement prior to administration of the first dose and thereafter 6 hours later; 2) Measurement of BP and heart rate every hour for 6 hours after first dose; 3) Field administration of the drug; 4) Continuous ECG monitoring (CEM) during the first 6 hours of treatment.

Aim of the study: To evaluate the effectiveness of our virtual intensive care unit connected with neurological departments for the continuous cardiology web monitoring.

Methods: A total of 50 frames with fibroatheromas were selected from the integration evaluation study of Intracoronary Stent from Porcine Characterised Experience (IBS). The fibroatheroma is relevant in research and clinical practice as previously shown by pathology studies. Traditional manual analysis of FC thickness of fibroatheroma by Weckesser ST area and thickness, however, is limited by intra- and inter-observer variability, thus limiting its reproducibility. This is of relevance for discrimination between thin and thick cap fibroatheroma and for longitudinal assessment of cap thickness changes, e.g. in response to medical interventions.

Aims: We aimed to assess the variability of the minimal cap thickness measurement and the reproducibility of fibroatheroma categorization based on a manual versus a novel software based semiquantitative assessment method.

Methods: A total of 50 frames with fibroatheromas were selected from the Interventional Study of Intracoronary Stent from Porcine Characterised Experience (IBS). The fibroatheroma is relevant in research and clinical practice as previously shown by pathology studies. Traditional manual analysis of FC thickness of fibroatheroma by Weckesser ST area and thickness, however, is limited by intra- and inter-observer variability, thus limiting its reproducibility. This is of relevance for discrimination between thin and thick cap fibroatheroma and for longitudinal assessment of cap thickness changes, e.g. in response to medical interventions.

Results: We aimed to assess the variability of the minimal cap thickness measurement and the reproducibility of fibroatheroma categorization based on a manual versus a novel software based semiquantitative assessment method.
monitoring during the first fingolimod dose administration in patients (pts) with multiple sclerosis (MS).

Materials and methods: Health Telematic Network (HTN), in cooperation with the Cardiology Department of the our University Hospital, has installed in a selected number of Neurology Departments, the web-connected information center IntelliVue Phillips M3150. Every of treated with fingolimod was remotely monitored during the first 6 hours thereafter the administration of the first dose. Reporting of ECG outcomes was carried out by HTN with 24 hour availability of a remote cardiology call-center, with either external reporting service (remote MS sites where the cardiologist was not available for consultation), or with the support of internal cardiology service where available (local MS sites).

Results: One hundred and eleven sites with active ECG and 61 sites with remote reading system have actively participated in the RITMO project and 845 pts were enrolled during 2014. CEM has recognized bradycardia in 619 pts, 1st degree atrio-ventricular block (AVB) in 30 pts, 2nd degree AVB Mobitz I 20 pts, 2nd degree AVB Mobitz II in 8 pts, prolongation of QTc interval in 55 pts, ventricular arrhythmias (singles or couples) in 75 pts and only 1 case of non-sustained ventricular tachycardia.

Conclusion: The RITMO project based on real-time web-based telemetry has represented an optimal solution for the first fingolimod dose administration, according to CHMP indications. RITMO project is the first example of telemonitoring in a network of neurology departments, and could pave the way for using a multidisciplinary approach in the management of new therapies.

REGULATORS OF VASCULAR GROWTH AND FUNCTION

P1556 | BENCH
The neuropeptide catestatin influences cardiac vascular cell function and inhibits cardiomyocyte apoptosis in vivo
M. Theuri, D. Lerner, U. Stanzl, A. Beer, W.-M. Franz, R. Kirchmair. Medical University of Innsbruck, University Hospital of Internal Medicine III, Department of Cardiology and Angiology, Innsbruck, Austria

Introduction: Myocardial infarction (MI) induces irreversible tissue damage, eventually leading to heart failure. The exogenous induction of angiogenesis is recognized to influence positively ventricular remodeling after a MI. Recently, we could show that therapeutic angiogenesis by the neuropeptide catestatin (CST) restores perfusion in the mouse hind limb ischaemia model by the induction of angiogenic, arterio- and vasculogenesis. Thus, we assumed that CST might exert beneficial effects in experimental MI.

Methods and results: To test the effect of CST on cardiac angiogenesis in vitro, matrigel assays with human coronary artery endothelial cells (HCAEC) were performed. CST significantly mediated capillary like tube formation comparable to basic fibroblast growth factor (bFGF), which was used as positive control (rel. tube formation vs. ctr.: CST 1 nM 2.6±0.3, n=3, P<0.001). Interestingly, blockade of bFGF either by a bFGF-antibody (Ab) or a specific receptor blocker (PD173074) (PD173074) resulted in abrogation of effects suggesting a bFGF-depending mechanism.

Moreover, CST induced proliferation of HCAEC and human coronary smooth muscle cells (HCASMC) as determined by BrdU-incorporation. Similar to the matrigel assay blockade of bFGF attenuated the effect (HCAEC: rel. proliferation vs. ctr.: CST 1 nM 1.5±0.1, P<0.001; CST-bFGF-Ab 1.1±0.1, P<0.001 vs. CST; PD173074 0.7±0.1, P<0.001 vs. CST; HCASMC: rel. proliferation vs. ctr.: CST 1 nM 1.8±0.3, P<0.001; CST-bFGF-Ab 1.2±0.1, P<0.001 vs. CST; PD173074 0.9±0.1, P<0.001 vs. CST; n=3). Consistent with these findings western blot analysis revealed a bFGF-dependent phosphorylation of extracellular signal regulated kinase 1/2 by CST in these cell lines.

To evaluate the effect of CST on cardiomyocyte apoptosis in vivo the mouse myocardial ischaemia/reperfusion model was performed. After reversible ligation of the left anterior descending artery an intra-myocardial injection of CST or saline 0.9% (control) was performed. In this animal model CST -treatment was associated with a significant reduction of cardiomyocyte apoptosis (apoptotic cardiomyocytes/HPF: CST 9.1±0.95 vs. ctr. 19.3±1.74, n=8,group, P<0.01).

Conclusion: Due to its favorable effects on cardiac vascular cells CST might qualify as potential candidate for therapeutic angiogenesis in MI.

P1557 | BENCH
Protein phosphatase 1 beta is modulated by chronic hypoxia and induces angiogenic events in vitro
D. Iacobazzi1, I. Garaeva1, A. Albertario1, M. Cherri1, G. Angelini1, M. Caputo2, M.T. Ghorbel1. 1University of Bristol, School of Clinical Sciences, Bristol, United Kingdom; 2Rush University Medical Center, Chicago, United States of America

Background and aim: Endothelial cell migration is required in the physiological angiogenic process, but also contributes to various pathological conditions, such as wound healing, tumor angiogenesis and arteriogenesis. The finding that PP1cβ is overexpressed in several cancers, and that angiogenesis is a hallmark of cancer development, with certain tumors developing a hypoxic microenvironment to further potentiate its vascularization and growth, suggest that PP1cβ might play an essential role in angiogenesis. Hence, the potential role of PP1cβ in angiogenesis is investigated in the present study.

Methods: We examined PP1cβ protein level in pediatric heart following chronic hypoxia and found PP1cβ upregulation in cyanotic compared with acyanotic myocardium. By treating HUVEC cells with hypoxia mimicking agent, PP1cβ protein level increased with maximum at 8 hours. The effect of PP1cβ pharmacological inhibition, in addition to knocking down and overexpressing PP1cβ, on endothelial cell migration and morphogenesis was examined in vitro using wound healing scratch assay and endothelial tube formation assay. The PP1cβ knockdown effect was mediated by a F-actin reorganization (vinculin staining) and local adhesion formation (vinculin) was evaluated by immunocytochemical staining with specific antibodies.

Results: PP1cβ knockdown significantly reduces endothelial cell migration, but does not have any effect on endothelial tube formation. Endothelial cell migration in the knockdown group is restored to the control level upon consequent transfection with PP1cβ CDNA. Furthermore, PP1cβ knockdown induces a profound cytotoxic skeletal reorganization, loss of focal adhesion sites and impairment of focal adhesion kinases (FAK) activation.

Conclusions: PP1cβ is regulator of endothelial cell migration, which is critical in the angiogenic process. PP1cβ inhibition reduces endothelial cell migration through focal adhesion turnover and actin polymerization pathways.

P1558 | BENCH
Glucagon-like peptide-1 (GLP-1) directly promotes angiogenesis via PKA/AMPK-dependent autophagy in endothelial cells
T.M. Mitsui, Y. Kureishi Bando, A.H. Monji, M. Aoyama, H.K. Kawase, H.K. Nakamura, T.M. Murakawa. National University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan

Background: We recently reported the impact of glucagon-like peptide-1 (GLP-1) on myocardial remodeling observed in type 2 diabetic mice (T2DM) via cyclic AMP-dependent activation of autophagy in myocardium; however, it remains unclear whether GLP-1 may modulate angiogenesis in heart.

Purpose: To evaluate the impact of GLP-1 in angiogenesis and its link to endothelial autophagy.

Methods: T2DM was treated with Ex4 (24 nmole/kg/day for 4 weeks). Cardiac capiary density was measured by CD31 immunohistochemical staining Cultured human umbilical venous endothelial cells (HUVECs) were used for in vitro experiments. Analyses for the changes in activities of autophagy (LC3-turnover assay and protein levels of p62 and Beclin1), and angiogenesis (tube formation assay and Akt/AMPK/eNOS activity), were evaluated. Role of PKA was assessed by CREB phosphorylation and RNA interference (siRNA). Effect of autophagy was assessed by use of pharmacological inhibitor 3MA and siRNA of autophagy-related gene (ATG) 5, ATG7, and p62.

Results: Immunohistochemical analyses revealed that T2DM exhibited reduced cardiac capillary density, which was reversed by Ex-4 treatment with concomitant amelioration of systemic diabetic condition. The Ex-4 treated heart exhibited increase in myocardial cyclic AMP concentration. We thus observed direct impact of Ex-4 and cyclic AMP elevation on ECs, in which GLP-1 receptor expression was confirmed by immunoblot and QPCR. In vitro angiogenesis assay revealed increased tube formation and phosphorylation of PKA in T2DM. Ex-4 and PKA activation enhanced GLP-1 facilitated angiogenesis and autophagy in HUVECs and the PKA/AMPK/eNOS phosphorylation levels of Ex-4 treated HUVECs were enhanced. Of note, each Akt activity remained unchanged. PKA inhibitors (H89, RP-AMP; and siRNA for caspase-6) abolished the Ex-4- and PKA-induced autophagy as well as GLP-1-mediated angiogenesis in ECs.

Conclusion: GLP-1 directly promotes angiogenesis via the PKA/AMPK-dependent autophagic activation.
murine endothelial cells. Hindlimb ischemia (HLI) was induced in a murine model of DM in wildtype (WT) and PPARα knockout (KO) mice with/without fenofibrate. Ischaemic recovery was assessed by laser Doppler (LDI) and capillary density analysis. Results: Fenofibrate (FA), the active component of fenofibrate, reduced high glucose-induced impairment in EC migration (82.5±0.1% vs. 52.8±0.4% of control, p<0.05) tubulogenesis (89.5±0.2% vs. 56.5±0.3% of control, P<0.05) and apoptosis (12.5±0.2% vs. 28.6±0.8%, P<0.001) in a PPARα-independent manner. FA action was associated with PPARα-independent reversal of high glucose-induced upregulation of thioredoxin-interacting protein (TXNIP) (P<0.05), an exquisitely glucose-sensitive regulator of angiogenesis. Interestingly, overexpression of TXNIP abrogated the protective effects of FA on tubulogenesis under high glucose (p<0.05). In vivo, fenofibrate rescued diabetes-related impairment in ischaemic recovery and angiogenesis in both WT (LDI: P<0.05, Capillary density: p<0.001) and PPARα KO mice (LDI: P<0.01; Capillary density: p<0.01), consistent with a PPARα-independent effect. Fenofibrate also reversed diabetes-related overexpression of TXNIP in WT (P<0.05) and KO mice (P<0.01). In normal brain, we have found that the expression level of the HH inhibitory protein (HIP) was significantly and constantly downregulated in all ten human brain AVM specimens, compared to control tissue. We also show that when pellets containing Sonic hedgehog (SHH) - a prototypical member of the HH family proteins - were implanted into the cornea of mice to induce angiogenesis, they stimulate the growth of both arterial and venous vessels, which are interconnected by a complex set of arteriovenous shunts that lack an interposed capillary bed, as seen in AVMs in humans. We have further detailed the unique characteristics of the arteriovenous angiogenesis induced by SHH by using ephrinB2-lacZ mice, which carry the lacZ reporter gene under the control of the promoter of the ephrinB2 gene, which is specifically expressed in arteries and not in veins. SHH is known to be an indirect angiogenic agent, which is able to induce the expression of various families of angiogenic growth factors in interstitial cells. Based on this notion, we have analyzed the expression of a large set of angiogenic genes in the corneas of mice implanted with pellets containing SHH. We have found a significant upregulation of crucial angiogenic genes, including VEGF, Angiogenin, PDGF, PIGF, and HGF. Interestingly, we have found that the same genes are significantly upregulated in human brain AVMs, compared to normal human brain. Our findings show that both HH inhibitory protein HIP is consistently and significantly downregulated in brain AVM tissues. They also demonstrate that the activation of the HH signaling pathway results in a robust angiogenic process which is characterized by the growth of both arterial and venous vessels, with several arteriovenous shunts which mimic the tangle of abnormal vessels that directly shunt blood from the arterial to the venous circulation in human AVMs. Finally, HH-induced angiogenesis is characterized by the upregulation of various families of growth factors, similar to what occurs in brain AVMs. Taken together, these data strengthen the hypothesis that the HH pathway plays a role in the pathogenesis of brain AVMs, with potentially important fundamental and clinical implications.

P1561 | BENCH
Colchicine reduces plaque inflammation and fibrosis and potentiates vascular remodelling in atherosclerotic rabbits
N. Merlet1, F. Rouble1, E. Rheaume2, Y. Shi1, T. Mihalache-Avram1, D. Rivais1, M. Mecteau1, G. Brand1, D. Busseuil2, J.C. Tardif1.

Background: The anti-inflammatoty agent colchicine is gaining interest as a potential treatment for coronary artery disease given the recent results of the LoDoCo study. The effects of colchicine in atherosclerotic animal models are mostly unknown.

Methods: Twenty-two male New-Zealand White rabbits were fed a 0.5% cholesterol-enriched diet for 10 weeks. Animals were then randomized to oral saline (placebo group, n=11) or colchicine (350 µg/kg/day; colchicine group, n=11) for 6 weeks, with 0.2% cholesterol diet during the treatment period. We performed echocardiograms, intravascular ultrasound (IVUS) imaging of the descending thoracic aorta (at start and end of treatment) and histology. Results: Colchicine prevented vascular remodeling of the descending thoracic aorta, as revealed by the increase over time in total vessel volume on IVUS in the placebo group (−29%, p<0.001) and the non-significant change with active treatment (p=0.299). This was confirmed by serial echocardiograms of the ascending aorta, which diastolic diameter increased in the placebo group (+12%, p=0.005) but remained stable with colchicine (p=0.206). There was a significant interaction between colchicine on atherosclerotic plaques evaluated by histomorphological analyses, with significant decreases in atherosclerotic plaque and media areas in rabbits presenting higher cholesterol levels (−57%, p=0.031 and −17%, p=0.039, respectively). Recent findings in the progression of thoracic aneurysms in mice showed −35%, (p=0.038) and macrophage area (RAM11: −49%, p=0.037) in plaques compared to placebo, and these effects were again greater for rabbits with higher plasma cholesterol levels (fibrosis: −41%, p=0.027; macrophages: −76%, p=0.005). Treatment with colchicine also decreased type I collagen in the media by 16% compared to placebo (p=0.026), with a more marked effects in animals with high plasma cholesterol levels at start of treatment (−33%, p<0.002).

Conclusion: Long-term oral colchicine treatment favourably affects plaque inflammation and fibrosis, reduces media fibrosis and prevents positive vascular remodelling (enlargement). Interestingly, colchicine effects were greater in rabbits with high plasma cholesterol levels.

Acknowledgement/Funding: NH/MRC

P1562 | BENCH
WARS2 regulates cardiac angiogenesis
M. Wang1, P. Sips2, E. Khin1, M. Rovtali2, X. Sun3, N. Hubner4, M. Pravenev3, E. Petretto1, C. Macrae2, S.A. Cook1.

Background: In the absence of epicardial coronary arterial disease (CAD), coronary flow (CF) is largely determined by small capillary resistance vessels. While the genetic architecture of CAD has been characterized extensively, the genetic regulation of inheritable CF remain unknown.

Purpose: To identify genes underlying CF variation and to explore mechanisms regulating CF.

Methods: We combined genetic mapping in the rat with loss- and gain-of-function approaches in vitro and in vivo in both the zebrafish and the rat. Molecular studies were performed using unbiased and genome wide genomics and proteomics approaches.

Results: We mapped and replicated a CF locus on rat chromosome 2, which was associated with capillary vessel density. Mitochondrial triphosphat (IFNA) synonyms of WARS2, encoding an L53F protein variant within the "HGXH motif" that defines class I aminoacyl IFNA synthetases (AARSs), was identified as the candidate locus. WARS2 L53F had low canonical enzymatic activity and inhibition of WARS2 in endothelial cells (ECs) caused cell cycle arrest and impaired angiogenesis in vivo. Knockdown of WARS2 resulted in dysfunction of the endocardium from myocardium and marked cardiac dysfunction, as observed following inhibition of critical angiogenesis factors. In the rat WARS2 loss-of-function caused cardiac vein abnormalities, reduced cardiac capillary vessel density and diminished CF.

Conclusions: Our data in the heart demonstrate a novel EC-specific, pro-angiogenic function for WARS2, which is a candidate gene for human cardiovascular traits and breast cancer. These studies highlight important non-canonical functions of AARS2 genes, which are known attributes of their cytosolic counterparts, while identifying new biology underlying CF.

Acknowledgement/Funding: MRC UK, NMRC Singapore, British heart foundation and NIH

P1563 | BEDSIDE
Circulating annexin A5 levels are related to carotid intima-media thickness but not coronary plaque composition
M. Burgmaier1, S. Reith1, L. Schurges2, N. Marx1, C. Reutelingsperger1.

Background: Several effects of annexin A5 (anxA5) on vascular cells and atherosclerosis have been described. However, the relationship between circulating anxA5 levels and atherosclerotic lesion extension as well as plaque composition in high risk patients is currently unclear.

Objective: To characterize the relationship between circulating anxA5 levels with atherosclerosis burden and plaque composition in patients with type 2 diabetes.

Methods: Intima-media thickness (IMT) has been determined in 96 patients with
type 2 diabetes and stable coronary artery disease. Furthermore, intracoronary optical coherence tomography (OCT) has been performed in 106 lesions to determine coronary plaque composition.

**Results:** AxAnxA plasma levels of patients with increased IMT were significantly higher (3.49±2.19ng/ml) compared to patients with normal IMT (2.24±1.67ng/ml, p<0.002). Furthermore, axAnxA predicted thickened IMT in univariate (OR 1.445 (1.106–1.889), p<0.007) and multivariable (OR 1.643 (1.166–2.314), p<0.005) binary logistic regression analysis when adjusted for multiple cardiovascular risk factors and biomarkers. Receiver-operating-characteristic analysis demonstrated that axAnxA predicted thickened IMT with low-moderate diagnostic efficiency (AUC 0.700 (0.592–0.808), optimal cut-off value 1.907ng/ml, sensitivity 74.2%, specificity 65.8%, positive predictive value 76.4%, negative predictive value 61.0% at the optimal cut-off). However, no association was found between circulating axAnxA levels and coronary plaque composition as assessed by OCT including the presence of lipid, calcified, fibrous plaque or the minimal thickness of the fibrous cap overlying the necrotic lipid core (p>ns).

**Conclusion:** Circulating axAnxA plasma levels are related to carotid IMT but not coronary plaque composition in high-risk patients with type 2 diabetes.

**P1564 | BEDSIDE**

The comparison of flow-mediated dilation and EndoPAT-reactive hyperemia index in patients with impaired glucose metabolism

H. Tsutsui, T. Sawada, Y. Yasaka, H. Kawai, M. Yokoyama. Himeji Cardiovascular Center, Himeji, Japan

**Background:** Patients with impaired glucose metabolism (IGM) tend to create endothelial dysfunction and are highly associated with cardiovascular disease (CVD). Therefore, assessment of endothelial function in such patients is important to mark of endothelial function, flow-mediated dilatation (FMD) and EndoPAT-reactive hyperemia index (RHI) were widely used in clinical setting. However, there were no studies that evaluate characteristics of FMD and EndoPAT-RHI simultaneously in patients with IGM.

**Methods and results:** In 439 IGM patients (age 66.2±11.2 y.o, male n=322, 73%), which included the patients who had diabetes mellitus (DM; OGTT > 200 and HbA1c > 6.5%), who had a fasting plasma glucose of 110mg/dL or higher, or who took oral diabetic agents, we measured FMD and EndoPAT-RHI at the same time. The scatter diagram showed no significant correlation between FMD value and EndoPAT-RHI. While FMD value was significantly associated with the number of conventional risks of CVD, such as age (over 75 years old), DM, hypertension [systolic blood pressure (SBP)] > 135mmHg], dyslipidemia (High LDL cholesterol, triglycerides, and HDL cholesterol), current smoking, obesity (Body Mass Index>25kg/m²), uric protein (albuminuria > 30mmol/d) (P<0.01). EndoPAT-RHI was not significantly associated with the number of CVD risk. Then, we analyzed correlation between each measurements and several biomarkers. While FMD value was negatively associated with SBP and albuminuria (SBP: P=0.002, r=−0.24, albuminuria; P=0.005, r=−0.10). On the other hands, although there was no correlation between FMD and HOMA-R, insulin resistance index which calculated fasting plasma glucose×fasting insulin (405), EndoPAT-RHI was negatively correlated with HOMA-R (P<0.002, r=−0.17).

**Conclusions:** Although both FMD and EndoPAT-RHI is same kind of examination which evaluates endothelial function, they each may evaluate different state of endothelial function. In patients with IGM, FMD may be useful to stratify CVD risk classification compared with EndoPAT-RHI, because FMD and EndoPAT-RHI may indicate opposite reaction in patients with high SBP and albuminuria. Meanwhile, EndoPAT-RHI may be able to show endothelial dysfunction in IGM patient with insulin resistance which FMD could not catch in the early stages.

**P1565 | BEDSIDE**

Usefulness of brachial flow-mediated dilation and platelet function to predict long-term adverse clinical events in subjects without heart disease

M. Shechter1, *, A. Shechter1, *, H. Hod1, R. Beigel1, N. Koren-Morag2, S. Matekzy1, M. Sheba Medical Center, Tel Hashomer, Israel; 2 Tel Aviv University, Sackler Faculty of Medicine, Tel Aviv, Israel

**Background:** Platelet activation occurs in an endothelium-dependent flow-mediated dilation (FMD) impairment environment.

**Methods and results:** An association between FMD, platelet function, cardiovascular (CV) events and non-CV events in healthy subjects, we prospectively assessed brachial FMD in 89 consecutive healthy subjects 64 (72%) men, mean age 51±11 years. Following overnight fasting for 12 hours FMD and EndoPAT-reactive vasodilatation (NTG) were assessed. Platelet aggregation was assessed by conventional aggregometry, and platelet adhesion and aggregation under flow conditions by cone-and-plate(let) technology (Impact-R).

**Results:** After a mean follow-up of 7±2 years there were 29 total adverse clinical events, of which 11 were CV event points. Subjects with CV events had significantly lower FMD compared to those without CV events (10.4±8.0% vs 17.5±9.7%, p=0.02), while NTG was similar in both groups. Furthermore, 73% with and 37% without CV events had FMD < the median (p=0.02). Additionally, subjects with the highest (FMD>16.8%) compared to the lowest baseline FMD tertile (FMD<9.6%) had significantly the less CV events compared to the associated with low CV events (p=0.01) (Figure). ADP- and arachidonic acid-induced platelet aggregation were significantly higher in subjects with compared to those without CV events (p=0.01). In addition, platelet adhesion which reflects platelet reactivity, as seen by surface coverage (SC) under flow conditions, was greater in those with than without CV events (142±8% vs 9±6%, p=0.05). Furthermore, more subjects without compared with CV events had SC < the median (62% vs 27%, p=0.02).

**Conclusion:** Tissue accumulation of AGEs is increased in patients with an Abdominal Aortic Anomaly but does not predict all-cause mortality during 7 year follow-up

J. Boersemb1, *, L.C. De Vos1, D.J. Mulder1, R.P.F. Dullart2, A.J. Smit1, C.J. Zeebregts1, *, J. D. Leeflang1, *, 1 University Medical Center Groningen, Vascular Medicine, Groningen, Netherlands; 2 University Medical Center Groningen, Endocrinology, Groningen, Netherlands; 3 University Medical Center Groningen, Vascular Surgery, Groningen, Netherlands

**Background:** Accelerated accumulation of tissue advanced glycation endproducts (AGEs) in patients with peripheral arterial occlusive disease (PAD) is associated with increased mortality. Aneurysmatic disease is characterized by tunica media weakening rather than by intima thickening. Whether AGEs are increased in patients with an abdominal aortic aneurysm (AAA) is not known.

**Purpose:** To study whether tissue accumulation of AGEs is increased and predictive of mortality in AAA.

**Methods:** 142 consecutive patients with AAA (131 men, 11 women, mean age 69±10 y) and 113 with PAD (positive controls) were included between 2007 and 2015. In 82 patients with AAA and PAD, AGEs were measured with the AGE-reader, using Skin Autofluorescence (SAF). Follow-up was 7 years. Optimal cut-of values for SAF were sought with ROC-analysis.

**Results:** SAF differed among the groups: mean 2.82±0.58 in AAA, 2.71±0.70 in PAD and 2.53±0.61 in controls. ANOVA p=0.001, 43 AAA patients (30%) and 27 (24%) PAD patients died during a median follow-up of 4.3 (IQR 2.7–6.2) years. SAF>2.88 was associated with increased mortality in PAD, HR 2.48 (95% CI: 1.19–5.18) p=0.02, but not in AAA, HR 1.08 (0.60–1.94) p=0.80, see figure. In PAD, HR 1.93 (1.00–3.73) p=0.05, but not in AAA, HR 1.26 (0.76–2.11) p=0.38, SAF was predictive after adjustment for age, gender, diabetes, smoking and history of coronary or cerebrovascular disease.

**Conclusion:** Tissue accumulation of AGEs is increased in both AAA and PAD patients compared to controls. However, AGEs accumulation is not predictive of mortality in AAA patients, in contrast to PAD patients. This conceivably suggests that AGEs may play a role in the pathogenesis of dilating disease but does not to an important extent contributes to metabolic pathways that result in death.
P1567 | BENCH
Lower level of serum asymmetric dimethylarginine contributes to improving vascular endothelial function after short-term resistance training in healthy elderly people
R. Shimizu, M. Kato, Y. Kamada, S. Tanaka, N. Hamazaki, D. Kamekawa, A. Akiyama, T. Nakamura, K. Yabu, T. Masuda. Kitasato University, Graduate School of Medical Sciences, Sagamihara, Japan

Background: Moderate- or high-intensity exercise training is well known to activate endothelial nitric oxide synthase (eNOS), resulting in the improvement of vascular endothelial function. Although asymmetric dimethylarginine (ADMA), endogenous NOS inhibitor, is reported to decrease NO production, it is still unknown whether ADMA affects the improvement of vascular endothelial function in exercise training. This study aimed to investigate the effect of serum ADMA on vascular endothelial function after short-term resistance training in healthy elderly people.

Methods: We recruited 20 healthy elderly people (71±4 years, 17 males and 3 females) who had no habit of regular exercise. We measured serum ADMA and divided subjects into two groups based on the median of ADMA level: high ADMA and low ADMA groups. All subjects performed resistance training 20 minutes a day for 4 weeks. We measured serum thrombomodulin (TM), plasma tissue plasminogen activator-plasminogen activator inhibitor-1 complex (tPAIC) and reactive hyperaemic index (RHI) using finger plethysmograph (Endo-PAT2000) before and after the 4-week training period as parameters of vascular endothelial function.

Results: Serum ADMA ranged from 0.24 to 0.35 µM/m, and the median was 0.42 µM/m. The TM and tPAIC decreased significantly after the training period in the low ADMA group (-12.8% and -25.4%, respectively). There were no significant changes in TM and tPAIC before and after the training period in the high ADMA group. The RHI measured after the training period was significantly higher in the low ADMA group than in the high ADMA group (P=0.01).

Conclusion: Lower level of serum ADMA contributed to improving vascular endothelial function after short-term resistance training in healthy elderly people.

P1568 | BENCH
Angiotensin II downregulates microRNA-145 to regulate kruppel-like factor 4 and myocardin expression in human coronary arterial smooth muscle cells under high glucose conditions
K.G. Shyu, W.P. Cheng, B.W. Wang. Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan, ROC

Aims: MicroRNA (miR)-145 is the most abundant miR in vascular smooth muscle cells (VSMCs). However, the effect of hyperglycemia on the regulation of miR-145 is unknown. We hypothesized that hyperglycemic condition activates a pro-inflammatory response which mediates the expression of miR-145 in VSMCs. We investigated whether miR-145 serves as a critical regulator to regulate the downstream proliferation factor (such as Kruppel-like factor 4 (KLF4) and myocardin) in VSMCs under hyperglycemic conditions.

Methods and results: Human coronary artery smooth muscle cells (HCASMCs) were cultured under high glucose conditions. Sustained high glucose at 25 mM significantly decreased the expression of miR-145 in HCASMCs. High glucose significantly increased angiotensin II (Ang II) secretion from HCASMCs and Ang II suppressed miR-145 expression in HCASMCs. Exogenous addition of valsartan, enalaprilat dehydrate, and anti-agamir-145 before high glucose stimulation reversed KLF4 and myocardin expression induced by high glucose stimulation, indicating the involvement of autocrine Ang II and miR-145 in the regulation of KLF4 and myocardin expression in HCASMCs. Ang II mediated the KLF4 and myocardin expression in high glucose state. MiR-145 significantly decreased KLF4 and increased myocardin expression in high glucose state. High glucose stimulation for 1 h and Ang II alone for 4 h without high glucose stimulation significantly increased KLF4 promoter activity as compared to control cells. Overexpression of miR-145, addition of valsartan and enalaprilat significantly attenuated the promoter activity induced by high glucose. When the conserved site of miR-145 in the promoter area of KLF4 was mutated, the increased promoter activity induced by high glucose and Ang II was abolished.

MiR-145 significantly inhibited HCASMCs proliferation and migration induced by high glucose. Balloon injury of carotid artery in diabetic rats was performed to investigate the miR-145 and KLF4 and myocardin expression. The expression of miR-145 was maximally increased at 7 days after carotid injury and gradually declined thereafter. Overexpression of miR-145 and treatment with valsartan reversed KLF4 and myocardin protein expression induced by balloon injury and improved vascular injury.

Conclusions: Our study reveals that Ang II downregulates miR-145 to regulate KLF4 and myocardin expression in HCASMCs under high glucose conditions. Ang II plays a critical role in the regulation of miR-145 under hyperglycemia conditions.

P1569 | BENCH
Acute administration of dietary nitrate improves endothelial function and vascular stiffness in hypercholesterolemia
S. Velmurugan, S.M. Ghosh, R.S. Kambatta, S. Van Eijl, A. Robertson, T.A. Chowdhury, A. Ahluwalia. William Harvey Research Institute, Barts and The London School of Medicine, London, United Kingdom

Background: Orally ingested inorganic nitrate undergoes sequential chemical conversion in vivo first to nitrite and then to nitrous oxide. We recently demonstrated that daily dietary nitrate for six weeks improves flow-mediated dilatation (FMD) and vascular stiffness in hypercholesterolemics (ESC 2014. Abstract 86922). In half of this cohort we also sought to examine whether the first dose of dietary nitrate might alter vascular function acutely. (NCT01493752)

Methods: 34 of 67 otherwise healthy non-diabetic untreated hypercholesterolemic patients completed this assessment of the acute effects of a once daily dietary nitrate dose (n=17, nitrate-rich beetroot juice, 250 ml of 24.1±7.7 mM) vs placebo (n=17, nitrate-depleted juice, 250 ml of 0.05±0.1 mM) in this randomised double-blind placebo-controlled parallel study. The primary end point was change in ultrasound FMD at baseline and after 3 hours. Pulse wave analysis (PWA) and pulse wave velocity (PWV) were also measured (values shown as mean±SD). Plasma nitrate and nitrite measurements were conducted using ozone chemiluminescence. All averaged values shown as mean±SD.

Results: In the Nitrate-limb plasma levels of nitrate increased –8-fold (p<0.0001) and nitrite –2.0-fold (p=0.0005) and was associated with a ~29% increase in FMD (5.3±2.3% to 6.8±2.3%, p=0.01) vs no change in all parameters in the Placebo: (4.8±2.0% vs 4.8±1.9%, p=0.86). A small improvement in PWV (8.1±4.4 to 7.9±1.2 m/s, p=0.02) and PWA augmentation index (30.1±8.0 to 27.6±7.5 m/s, p=0.02) was also noted with worsening values in the Placebo: 8.4±1.0 to 8.8±1.5 m/s, p=0.73, PWV and 25.4±9.1 to 28.4±9.4 m/s, p=0.01, PWA).

Conclusions: Acute dietary nitrate ingestion improves endothelial function and vascular stiffness in hypercholesterolemics: an effect that is sustained with long-term ingestion. These findings indicate that dietary nitrate may be an effective strategy in preventing cardiovascular disease in hypercholesterolemics ordinarily at risk.

Acknowledgement/Funding: British Heart Foundation Clinical Research Fellowship

P1570 | BENCH
Pharmacological effects of K-877, a potent and selective PPAR alpha modulator (SPPARM alpha) - Controlling the plasma HDL-C and triglycerides, and prevention of atherosclerosis in experimental animals

Background: K-877 is a new highly potent and selective PPAR alpha modulator (SPPARMA). Clinical trials are in Phase II in EU and Phase III in Japan; increases in HDL-C and reduction in Triglycerides (TG) have been observed. MOKA-2 and MOKA-3 are mouse model of macrophages in atherosclerotic tissues.

Purpose: The purpose of this study was to confirm the effects of K-877 on plasma HDL-C and TG, and the prevention of atherosclerosis in experimental animals.

Methods: (1) Human apoA-I transgenic mice, normolipemic rats, dogs and fructose-fed hypertriglyceridemic rats were administered K-877 once a day for 2 weeks. Plasma cholesterol and/or TG were measured. (2) LDL receptor deficient mice were loaded with a high-fat high-cholesterol diet (WD) and were administrated K-877 or fenofibrate for 12 weeks. The heart and aortas were immersed in neutral buffered paraformaldehyde fixative for a night. MOKA-2 positive area in aortic sinus was measured by immunohistochemical methods. Total RNA in the remaining aorta was extracted using the RecoverAll™ Total Nucleic Acid Isolation Kit (Agilent Technologies) with some adaptation of its protocol. Messenger RNA level of Cd11c (C-C chemokine receptor type 7) was evaluated by quantitative (qPCR).

Results: (1) Plasma HDL-C and apoA-I was increased in K-877 (0.1, 0.3, 1mg/kg)-treated apoA-I transgenic mice up to 243% and 250% respectively, comparing with vehicle-treated mice. Plasma triglycerides, and prevention of atherosclerosis in experimental animals. (2) Administration of K-877 (0.03mg/kg) or fenofibrate (100mg/kg) to WD-fed LDL receptor deficient mice resulted in decrease of MOKA-2 positive area by 33% and 22%, respectively, comparing with vehicle-treated mice. Relative gene expressions of Cd11c in MOKA-2 were evaluated by quantitative (qPCR).

Conclusions: K-877 increased plasma HDL-C and decreased TG in experimental animals. K-877 also prevented infiltration of macrophages into the aortic sinus and reduced gene expression of Cd11c. These results support the results.
in clinical studies and suggest there is an anti-atherogenic effect in patients with dyslipidemia.

P1571 | BEDSIDE

Vascular ageing is apparent during an oral glucose challenge in healthy persons

H. Dominguez¹, O. Bin Abdullah², J. Raunso³, T.S. Hermann², T.J. Guterbaum¹, A.T. Major-Pedersen¹, N. Ihlнем³, G.T. Torp-Pedersen⁴, ¹Bispebjerg Hospital of the Copenhagen University Hospital, Copenhagen, Denmark; ²Herlev Hospital - Copenhagen University Hospital, Department of Cardiology, Herlev, Denmark; ³Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark; ⁴Aalborg University Hospital, Aalborg, Denmark

Hyperglycaemia is associated with a poor outcome after coronary revascularization. Furthermore, per-conditioning may prevent the repercussion injury that follows prolonged myocardial ischemia, a mechanism that may be impaired during hyperglycaemia. We therefore hypothesized that endothelial dysfunction during prolonged ischaemia followed by repercussion can be reversed in persons without diabetes but not in persons with diabetes during postprandial hyperglycaemia. In our preliminary studies, post-prandial endothelial dysfunction was not apparent in younger control persons. Therefore, we investigated the effect of an OGTT on vascular function in younger and older healthy individuals.

Methods and results: Seven younger (median 25, range 23–28) and seven older (median 65, range 54–70) healthy persons underwent forearm blood flow (FBF) measurements by venous occlusion plethysmography, stimulated by the repercussion that follows 10 minutes forearm ischemia, and by increasing doses of intra-arterial infusion of serotonin (5HT) (7, 21 and 70 ng/min). One hour after glucose intake, glycemias did not differ in younger and older persons while of intra-arterial infusion of serotonin (SHT) (7, 21 and 70 ng/min). One hour after glucose intake, glycemias did not differ in younger and older persons while FBF increased in young persons both at repercussion and during SHT infusion, while it tended to decrease in older persons. Results were reproducible in short ischemia/reperfusion alone (n=8 young and n=7 older).

Conclusion: Postprandial endothelial dysfunction is apparent in older but not younger healthy persons without diabetes.

P1572 | BEDSIDE

Metabolic syndrome accelerates endothelial aging in younger subjects

D. Terentes-Printzios, C. Vlachopoulos, P. Xaplanteris, N. Ioakeimidis, P. Pietri, K. Aznaouridis, M. Abdelrasouli, I. Gourgouli, E. Paschalidis, D. Tousoulis. Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Purpose: Vascular aging, as assessed by structural and functional properties of the arteries, is an independent indicator of cardiovascular risk. We sought to investigate whether the presence of metabolic syndrome accelerates the progression of vascular aging.

Methods: One hundred and forty-two subjects (mean age 51.9±10.8 years, 94 men) attending the Peripheral Vessels Unit with no established cardiovascular disease were investigated in two examinations over a 2-year period (mean follow-up visit 1.84 years). Metabolic syndrome was defined by the ATP III criteria. Subjects had at the beginning and end of the study determinations of carotid-femoral pulse wave velocity (PWV), aortic augmentation index corrected for heart rate (AIx75), brachial flow-mediated dilatation (FMD) and carotid intima-media thickness (cIMT). Based on these measurements the annual absolute changes were calculated.

Results: At baseline patients with metabolic syndrome compared with patients without metabolic syndromes had lower values of FMD (6.0% vs. 7.0%, P=0.025), but there were no statistically significant differences for PWV (7.04±1.67 vs. 7.26±1.67, P=0.424), AIx75 (19.9% vs. 20.3%, P=0.846) and cIMT (0.68 mm vs. 0.68 mm, P=0.957). For the overall population, there were no statistically significant differences in the annual absolute changes of PWV, FMD, AIx75 and cIMT. However, when a subgroup of patients <60 years with more rapid progression of endothelial aging was investigated, metabolic syndrome was associated with almost 7 times higher annual change of FMD (p=0.001) in patients with metabolic syndrome vs. −0.13% (95% CI: −0.15 to −0.23) vs. −0.36% (95% CI: −0.15 to −0.23) in patients without metabolic syndrome, P=0.003.

Conclusions: The presence of metabolic syndrome is associated with both worse endothelial function as well as accelerated progression of endothelial aging and dysfunction, especially in the younger subjects.

P1573 | BEDSIDE

Role of metabolomics in interpreting the origin of pulmonary arterial hypertension in patients with systemic sclerosis

A. Fassouli1, F. Ascedu1, M. Deidda1, C. Cadeddu1, S. Orofino1, S. Palmisano1, G. Giau1, M. Mura2, P.E. Manconi1, G. Finco2, G. Mercuro1, 1University of Cagliari, Department of Internal Medicine “M. Aresu”, Monseanno, Italy; 2University of Cagliari, Department of Public Health, Clinical and Molecular Medicine, Monserrato, Italy

Introduction: The presence of arterial pulmonary hypertension (PH) in systemic sclerosis (SSc) identifies a subset of patients with poor prognosis. Recent studies suggested a “metabolic theory” for the development of PH. Metabolomics (MBS) is an “omics” science, which allows the identification and evaluation of a wide range of metabolites that provide a picture of the metabolic changes that underlie a disease.

Methods: To assess whether, in SSc patients with increased pulmonary vascular resistance (PVR), differences in pulmonary arterial blood metabolomics could be identified.

Methods: We enrolled 18 SSc patients (age 58.7±15.6 years) who underwent a control evaluation with standard, Tissue Doppler and Speckle tracking echocardiography, and a right heart catheterization (RHC). A blood sample was collected during the RHC in the distal peripheral circulation of the pulmonary arteries to perform the metabolic analysis. Samples were analysed with a 1H-NMR 500MHz spectrometer. An Orthogonal Signal Correlation (OSC) and a Projection on Latent Structures Discriminant Analysis (PLS-DA) were applied.

Results: Based on PVR we divided the population in Group A (N=8; PVR ≤1.6 uW/mm²) and Group B (N=10; PVR > 1.6 uW/mm²). A clear clustering was observed with the PLS-DA, achieving good values of R2 (R2X=0.364, R2Y=0.889) and Q2 (0.721), with significant ANOVA cross-validation (p=0.003). The discrimination were related to a metabolic fingerprint depending on a limited set of metabolites: Group B was characterized by higher values of Lactate, Glycerol, fatty acids, Acetobacetate, Valine, Leucine, Isoleucine and VLDL/LDL, whereas Group A showed higher values of Choline, Betaine, Alanine, Glycine, Taurine, Arginine and 3-OH-butyrate; worthy of note is that all the compounds higher in Group A were related to the NO metabolism and endothelial function.

Conclusions: Increased PVR appear to be related to the presence of specific metabolites, in turn closely connected with endothelial dysfunction. Additionally, MBS was able to accurately identify the metabolic imbalance of vasoactive factors, able to determine and maintain the increased PVR. This approach could be useful for a better understanding of the pathophysiology of this severe complication of SSc.
nificantly more pronounced increase in VO2peak compared to patients with low L-arginine/ADMA-ratio (p=0.004) and high ICAM-1 (p=0.007), respectively. The odds ratio for no improvement of VO2peak during the intervention was 4.6 (95% CI 1.2 to 17.2) (p=0.024) for patients with low compared to high L-arginine/ADMA-ratio, and 6.3 (95% CI 1.4 to 27.0) (p=0.015) for patients with high compared to low ICAM-1.

Conclusion: In our population of patients with type 2 diabetes and CAD, patients with impaired endothelial activation, indicated by low L-arginine/ADMA-ratio or high ICAM-1, experienced significantly poorer improvement of exercise capacity after exercise training compared with patients with less endothelial activation.

P1575 | BENCH

JNK inhibition mimics the beneficial effect of Roux-en-Y gastric bypass surgery on obesity-induced endothelial dysfunction

D. Tousoulis1. G. Siasou1, G. Siasos 1, M. Moschos 2, N. Gouliopoulos 1, E. Oikonomou 1, T. Paraskevopoulos1, M. Zaromytidou2, K. Mourouzis1, S. Tsalamandris1, D. Tousoulis1. 1 University of Athens Medical School, Dept. of Cardiology, Hippokration Hospital, Athens, Greece; 2 University of Athens Medical School, Division of Ophthalmology, Athens, Greece

Background: Preeclampsia (PE) occurs in 3% of pregnancies. Women who develop PE are at increased risk of developing sPE to those observed in healthy pregnant controls (n=20) are recruited to undergo baseline assessment at 22–26 weeks of pregnancy.

Aim: To evaluate whether in vivo inhibition of JNK activity with two different JNK inhibitors in sham-operated ad libitum-fed rats mimics the beneficial endothelial effects of RYGB.

Methods: DIO rats underwent RYGB or sham surgery, and sham-operated ad libitum-fed rats received either vehicle (sham AL) or the specific JNK inhibitor SP600125 20mg/kg/day s.c. (sham SP) for 8 days post-surgery. In a separate experiment, sham-operated ad libitum-fed rats received either control peptide TAT (sham TAT) or the highly specific JNK peptide inhibitor D-JNKi-1 20mg/kg/day s.c. (sham DJNK) for 8 days post-surgery. Thereafter, thoracic aortic rings were isolated and subjected to ex vivo isometric tension recordings. After submaximal contraction with norepinephrine (10–6mol/L), cumulative relaxation responses were performed to GLP-1 (7–36) amide (10–12 to 10–6mol/L) or insulin (10–11 to 10–5mol/L). Western blot analysis of JNK and eNOS was performed on aortic tissue lysates.

Results: Body weight did not differ between sham SP and sham AL rats, while the weight loss of RYGB rats was significant 8 days after surgery. GLP-1- and insulin-induced vasorelaxation responses improved in RYGB and showed a tendency for improvement in sham SP compared to sham AL rats. Interestingly, treatment of sham-operated rats with the more specific JNK inhibitor D-JNKi-1 completely mimicked the effects of RYGB surgery on both body weight loss and improvements in endothelial function 8 days after surgery or start of treatment, respectively. JNK protein phosphorylation was decreased and eNOS activation was increased in aortic lysates of RYGB, sham SP and sham DJNK rats in comparison with sham AL rats, respectively.

Conclusion: Our study underlines a crucial role of JNK activation in obesity-induced endothelial dysfunction. Chronic in vivo JNK inhibition mimics the rapid endothelial protection of RYGB, suggesting a novel JNK-dependent mechanism for the cardiovascular beneficial effects of RYGB.

P1576 | BEDSIDE

Maternal cardiovascular effects of preeclampsia in the 2nd trimester

K. McLaughlin1, R. D’Souvza1, M. Hladunewich2, J. Parker1, J. Kingdom1, 1Mount Sinai Hospital of the University Health Network, Toronto, Canada; 2Sunnybrook Health Sciences Centre, Toronto, Canada

Background: Preeclampsia (PE) occurs in 3% of pregnancies. Women who develop severe/early-onset PE (sPE) demonstrate extensive cardiovascular abnormalities. Low-molecular weight heparin (LMWH) significantly reduces the incidence of sPE in women at high risk of developing sPE, although the mechanism is unknown.

Purpose: I) Compare baseline measures of cardiovascular function in pregnant women at high-risk of developing sPE to those observed in healthy pregnant controls in the 2nd trimester and ii) determine if LMWH modifies cardiovascular function in high-risk pregnant women.

Methods: Pregnant women at high-risk of sPE (n=20) and healthy pregnant controls (n=20) are recruited to undergo baseline assessment at 22–26 weeks of gestation. Cardiovascular function is assessed by heart rate (HR), blood pressure (BP), non-invasive cardiac output (OC) measurement (INCON), flow-mediated dilation (FMD), and uterine artery Doppler. High-risk women are then randomized to LMWH or saline placebo (30mg IV bolus and 1mg/kg subcutaneous dose). Cardiovascular function is assessed 1.5 and 3 hours post-randomization.

Results: 20 high-risk women and 10 controls have participated in the study. Gestational delivery was significantly earlier in the high-risk group when compared to controls (34±0.6 vs 39±0.6 weeks; p<0.003), with 58% of the high-risk women developing PE vs 0% of the healthy controls. At baseline, HR was higher in the high-risk group as compared to controls (84±3 vs 73±2 bpm; p<0.01). Systolic and diastolic BP were higher in the high-risk group, although the difference was not significant (117±3 vs 109±3 mmHg; p=0.107, 68±3 vs 62±1 mmHg; p<0.09). Despite their higher HR, CO was significantly lower in the high-risk group as compared to controls (5.9±2 vs 7.5±3 L/min; p<0.0001). Systemic vascular resistance was also higher in the high-risk group (917±51 vs 900±45 dyn/cm²; p=0.003), consistent with the phenotype of established PE. There was no significant difference in FMD between high-risk and control groups (6.4±1% vs 9.8±2%; p=0.07). Uterine artery Doppler-based pulsatility index was significantly higher in the high-risk group compared to controls (1.5±0.1 vs 1.0±0.01; p<0.0001). LMWH significantly increased FMD in high-risk women 3 hours following administration (7.6% to 10.8%; p<0.005), while no differences were observed in placebo subjects (5.3% to 6.1%; p=0.92).

Conclusions: Women at high-risk of developing sPE exhibit abnormalities in baseline cardiovascular function. Acute improvements in endothelial function in response to LMWH suggest that this drug may prevent sPE via direct cardiovascular actions.

P1577 | BEDSIDE

Impaired endothelial function and arterial stiffness in patients with pseudoexfoliative glaucoma

G. Siasou1, G. Siasos 1, M. Moschos 2, N. Gouliopoulos 1, E. Oikonomou 1, T. Paraskevopoulos1, M. Zaromytidou2, K. Mourouzis1, S. Tsalamandris1, D. Tousoulis1. 1 University of Athens Medical School, Dept. of Cardiology, Hippokration Hospital, Athens, Greece; 2 University of Athens Medical School, Division of Ophthalmology, Athens, Greece

Background: Primary open-angle glaucoma (POAG) is one of the most prevalent causes of irreversible blindness and is associated with endothelial dysfunction and arterial stiffness. Pseudoexfoliative glaucoma (PEG) is another type of glaucoma observed in pseudoexfoliation syndrome. It is characterized by the deposition of pseudoexfoliative material not only to the anterior part of the eye, but also to the vessels, heart and other organs.

Purpose: We evaluated the association of endothelial function and arterial stiffness with POAG and PEG.

Methods: Forty four POAG patients, 22 PEG and 38 healthy subjects (Cl) were included in this study. All subjects were free of cardiovascular or inflammatory diseases. Endothelial function was evaluated by flow-mediated dilation (FMD). Cardiol-femoral pulse wave velocity (PWV) was measured as an index of aortic stiffness and augmentation index (AIx) as a measure of arterial wave reflections.

Results: Between the three study groups Cl, POAG, PEG there was no difference in age (67±10 years vs. 70±9 years vs. 66±12 years; p=0.12) or prevalence of male sex (70% vs. 57% vs. 50%; p=0.21). Importantly, there was a linear impairment of FMD (7.3±2.7% vs. 6.5±1.9% vs. 4.8±1.2%; p=0.006) and PWV (7.9±0.8/6.5/sec vs. 9.2±1.5/6.4/sec vs. 11.8±1.3/6.6/sec; p=0.004) and AIx (21.9±9.7% vs. 25.1±5.7% vs. 28.5±7.5%; p=0.002) from Cl to POAG and PEG. Interestingly post hoc test after Scheffe correction revealed that only POAG subjects had not only significantly impaired FMD, compared to controls, but also to compared to POAG subjects (4.8±3.2% vs. 6.5±3.8%; p=0.02).

Conclusion: Endothelial function and arterial stiffness is significantly impaired in POAG and PEG in comparison with pseudoexfoliative glaucoma. These alterations in the pathophysiology of pseudoexfoliative glaucoma and support the theory that pseudoexfoliative fibrils may also accumulate and damage the arterial wall.

LIPIDS IN ATHEROSCLEROSIS

P1578 | BENCH

Modulation of cardiac structure by epicardial adipokines


Introduction: Heart failure is a condition with increasing prevalence in developed countries and is associated with obesity. Adipose tissue is now considered an ‘endocrine organ’ that secretes numerous bioactive peptides, termed adipokines. In obesity, due to adipocyte hypertrophy and dysfunction, there is an increased secretion of pro-inflammatory adipokines. These adipokines secreted by adipose tissue can act in a paracrine manner directly on the myocardium and influence their structure and function. In this work we aim to evaluate the changes in cardiac structure caused by adipokines secreted by the epicardial adipose tissue of obese rats.

Methods: Epicardial adipose tissue of 20-weeks-old lean and obese ZSF1 rats was collected for adipokines’ expression and adipocytes cross-sectional area assessment as well as for a 24h DMEM incubation to acquire conditioned medium. Thereafter, epicardial adipocytes were prepared by enzymatic digestion, washed, and labeled with propidium iodide and incubated for 24h with the conditioned media previously obtained from both groups. After incubation, cross-section area of cardiomyocytes and fibrosis were evaluated.
P1579 | BEDSIDE
Differentially expressed microRNAs in human peripheral blood mononuclear cells are potential markers for statin response
L. Salazar1, T. Zambrano1, M. Hirata2, A. Cerda1, R.D.C. Hirata2. 1 University of La Frontera, Center of Molecular Biology & Pharmacogenetics – BIOREN, Temuco, Chile; 2University of Sao Paulo, Sao Paulo, Brazil

Background: During years, statins have been the lipid-lowering drug of choice to attain lower LDL-C levels and reduce cardiovascular risk. In spite of being a safe agent, a recent study of statin use 260 Lipids in atherosclerosis

Methods and results: Methods: A total of 120 statin-naïve patients were randomly assigned to atorvastatin 10 mg/day for 12 weeks. Results from both treatments were analyzed using a PCR array platform, including 84 microRNAs previously selected and linked to cholesterol homeostasis.

Results: From the 84 microRNAs selected, six (miR-29a-3p, miR-29b-3p, miR-30e-5p, miR-454-3p and miR-590-3p) were downregulated after atorvastatin treatment (P < 0.05). Regulatory pathway examination showed that deregulated microRNAs interact with key genes of lipid metabolism (HMGCGR, LDLR, ABCA1, SCAP, INSIG1, LPL and SREBP1). Moreover, after sub grouping LDL-C reduction into quartiles of response according to specific lipid-lowering therapy, quartile 1 - poor response to atorvastatin - showed reduced expression of miR-106b-5p, miR-17-3p and miR-590-5p, whereas in the quartile 4 - enhanced response to simvastatin- miR-106b-5p, miR-17-3p and miR-183-5p were overexpressed.

Conclusions: Our results show, for the very first time worldwide, that statins modulate the microRNA expression pattern in vivo. Also, miRNAs miR-106b-5p and miR-17-3p, together with miR-590-5p and miR-183-5p, can be markers of decreased response to atorvastatin and high response to simvastatin therapy, respectively.

Acknowledgement/Funding: CONICYT (No. 21090417); FAPESP (No. 2011/21967-1) & FONDECYT (No. 11030675).

P1580 | BENCH
Local production of fatty acid-binding protein 4 in the extracellular perivascular fat and macrophage leads to coronary atherosclerosis
M. Fujihashi, T. Fuseya, S. Ishimura, T. Mita, K. Hoshina, Y. Watanabe, A. Omori, M. Tanaka, H. Yoshida, T. Mura. Sapporo Medical University, Department of Cardiovascular, Renal and Metabolic Medicine, Sapporo, Japan

Purpose: Fatty acid-binding protein 4 (FABP4) is mainly expressed in adipocytes, and elevated circulating FABP4 level is associated with obesity-mediated metabolic phenotype. We have systemically searched for roles of FABP4 in the development of coronary artery atherosclerosis.

Methods: Coronary atherosclerotic plaques and epicardial/perivascular fats in autopsy cases and coronary thrombi obtained by thrombectomy in patients with acute coronary infarction were immunohistochemically stained with FABP4 antibody. Release of FABP4 from adipocytes and macrophages into the conditioned medium and effects of exogenous FABP4 on inflammatory responses in several vascular cells were examined in vitro. Severity of angiographic coronary stenosis assessed by the modified Gensini score and serum FABP4 level in the coronary sinus (CS-FABP4) and aortic root (Ao-FABP4) bloods were determined in 34 male patients with suspected or known coronary artery disease.

Results: FABP4 was expressed in adipocytes and macrophages within coronary atherosclerotic plaques, epicardial/perivascular fats and coronary thrombi. FABP4 was secreted from both adipocytes and macrophages into the vitro. Treatment with recombiant FABP4 significantly increased expression of inflammatory markers in macrophages and human coronary artery-derived smooth muscle cells and endothelial cells. Coronary stenosis score was weakly correlated with CS-FABP4, but not with Ao-FABP4. Stronger correlation (r=0.59, p<0.01) was observed for the relationship between the coronary stenosis score and coronary veno-arterial difference in FABP4 level (CS-Ao-FABP4), indicating local production of FABP4 in the heart. Multivariate analysis adjusted by conventional coronary risk factors.
indicated that CS—Ao-FABP4 was an independent predictor of severity of coro-
nary stenosis.

Conclusions: FABP4 locally produced by epicardial/perivascular fats and/or macrophages in vascular plaques contributes to the development of coronary atherosclerosis.

P1583 | BENCH
Expression level of fatty acid-binding protein 5 increased in pro-inflammatory macrophage with atherosclerotic lesion formation; evaluation as a potential biomarker for atherosclerosis imaging
Y. Shimizu1, H. Hanzawa2, Y. Zhao3, S. Zhao3, T. Sakamoto2, N. Tamaki2, Y. Kuge1, 1Hokkaido University, Central Institute of Isotope Science, Sapporo, Japan; 2Hitachi, Ltd. Central Research Laboratory, Kokubunji, Japan; 3Hokkaido University, Graduate School of Medicine, Sapporo, Japan

Background: In diagnosing atherosclerosis, detailed evaluation of biomarkers relating to lesion formation is desired for estimation of its progression rate. In our previous proteomic studies of atherosclerotic model mice, the protein level of fatty acid-binding protein 5 (FABP5) in aorta but not in plasma elevated relatively with the atherosclerotic plaque formation; therefore, we supposed that FABP5 would be a potential biomarker for diagnostic imaging of atherosclerosis progression.

Purpose: To confirm our hypothesis, we performed pathological analysis of FABP5 expression in atherosclerotic lesions and compared the results against FABP4, a conventional biomarker of atherosclerosis. Furthermore, we evaluated their expression levels in macrophage cells under polarized states.

Methods: B6C3F1 mice were obtained from male B6C3F1 mice (n=12). Lesions were classified by their phenotypes according to AHA classification with Movat's pentachrome staining. FABP4, FABP5, Mac-2 (a macrophage marker) and -SMA (a smooth muscle marker) staining were examined using specific antibodies. RAW264.7 mouse macrophage cells were polarized into M1 (pro-inflammatory) or M2 (anti-inflammatory) cells by incubation with lipopolysaccharide (LPS) and interferon gamma or IL-4 for 48 h. The mRNAs were isolated, and then analyzed their expression levels of FABP4, FABP5, and -actin by quantitative PCR method (n=5/group).

Results: The expression level of FABP5 reached the highest in the Type IV lesion possessing the vulnerable-like characteristics, and preferentially localized in macrophage infiltration areas (the correlation rate: r=0.75, P<0.05), but not in the smooth muscle cells and other connective tissues. The similar result was also seen in the FABP4 study. As for the outside tissues of aorta such as connective tissues, FABP4 but not FABP5 highly expressed. Furthermore, M1-polarized RAW264.7 cells showed significant higher expression levels of FABP5 and FABP4 compared to M2-polarized or non-polarized (MC) cells (FABP5/ -actin: 1.29±0.47 (M1) vs. 0.50±0.17 (M2), 0.42±0.17 (M0) (P<0.05), FABP4/ -actin: 0.56±0.20 (M1) vs. 0.19±0.10 (M2), 0.15±0.09 (M0) (P<0.05)).

Conclusion: FABP5 preferentially expressed in unstable atherosclerotic plaques as well as FABP4, and the expression level strongly correlated with macrophage, especially pro-inflammatory, M1 macrophage. Furthermore, FABP5 showed less expression in non-lesion related areas compared to FABP4. Our results suggest that FABP5 has an advantage as a biomarker for diagnostic imaging of atherosclerotic plaque formation.

P1584 | BEDSIDE
Impact of statin therapy on coronary plaque composition: a systematic review and meta-analysis of virtual histology-intravascular ultrasound studies
1Resverlogix Corporation, Calgary, Canada; 2Resverlogix Corporation, San Francisco, United States of America

Introduction: Foam cells derived from human vascular smooth muscle cell

and necrotic core (SM3: +0.011 mm3, 95% CI: −0.144, +0.165; p=0.882) tissue volumes were not statistically significant.

Conclusions: This meta-analysis indicates a significant effect of statin therapy on plaque and external elastic membrane volumes and fibrous and dense calcium volumes. There was no effect on lumen volume, fibro-fatty and necrotic tissue volumes.

P1585 | BENCH
RXV-208, an orally active BET inhibitor, lowers CVD risk by activities beyond raising ApoA-1/HDL
E. Kulkowsk1, L. Tsujikawa2, D. Gilham3, S. Wasiak1, C. Halliday1, K. Lebioda1, J. Johansson2, M. Sweeney3, N. Wong1 on behalf of None. 1Resverlogix Corporation, Calgary, Canada; 2Resverlogix Corporation, San Francisco, United States of America

Background: RXV-208, an orally active small molecule, selectively inhibits bromodomain extra-terminal (BET) proteins by competing with acetylated histones for binding to acetylated lysines. RXV-208 binds to the second domain of the ligand domains. Post-hoc analysis of SUSTAIN and ASSURE trials showed patients given RXV-208 had a 55% relative risk reduction of major adverse cardiac events (MACE). This marked reduction is explained, only in part, by the RXV-208 induced rise of ApoA-1 and HDL to 10.3% and 7.7%, respectively suggesting RXV-208 has added biological properties that could benefit CVD risks.

Methods: Primary human hepatocytes and whole blood from healthy donors were exposed to RXV-208 and surveyed using microarray panels. Dominant effects on biological pathways arising from these studies were confirmed by measuring plasma protein levels.

Results: In primary hepatocytes, RXV-208 decreased the expression of many genes within pathways for; cholesterol synthesis, fatty acid synthesis, innate immunity and glucose processing. Most profound were the marked effects on the complement and coagulation pathways. There was wide spread downregulation of most (19 of 26) components in the complement pathway and a similar suppression (20 of 33) of the components within the coagulation cascade. Findings from the microarray data were confirmed by measuring hepcytotic mRNA of key genes. Function of the pathways or individual components, mRNA data, levels of specific proteins were measured in plasma from SUSTAIN and ASSURE trials. Results showed significant decreases ranging from 7–12% vs. baseline in complement (i.e. complement factor 3 and H) and coagulation components. Next, donor whole blood was exposed ex-vivo to RXV-208 followed by microarray analysis leading to the identification of several pathways with known roles in atherosclerosis including; pro-inflammatory signaling, cell-cell interactions and extracellular matrix organization. The actions of RXV-208 significantly downregulated several (8 of 11) pro-atherogenic genes but in contrast, upregulated (5 of 7) anti-atherogenic genes, that control monocyte recruitment, migration and activation, macrophage function, inflammatory signaling and plaque stability. Together, these findings suggest an overall anti-atherosclerotic benefit of RXV-208 that extends beyond its effects on ApoA-1/HDL.

Conclusion: RXV-208 affects multiple pathways that play important roles in CVD risk. RXV-208 induces ApoA-1/HDL and shown here are its potential; anti-thrombotic, anti-atherosclerotic and anti-inflammatory effects in hepatocytes and whole blood that may all act in concert to reduce MAE in patients with CVD risks.

Acknowledgement/Funding: None

P1586 | BENCH
Circulating soluble low density lipoprotein receptor-related protein 1 (sLRP1) is related to vascular lipid burden
D. De Gonzalez Calvo1, A. Cenarro2, M. Martinez-Bujod2, L. Badimon1, A. Bayes-Genis1, J. Ordovanes-Llano2, F. Civeira2, V. Llorente-Cortes1
1Cardiovascular Research Center (CSIC-CCCC), Barcelona, Spain; 2University Hospital Miguel Servet, Lipid Unit and Molecular Research Laboratory, IIS Aragon, Zaragoza, Spain; 3Hospital de la Santa Creu i Sant Pau, 3 Biochemistry Department, IIB-Sant Pau, Barcelona, Spain; 4Germanias Trias i Pujol University Hospital, Cardiology Service, Badalona, Spain

Background: Foam cells derived from human vascular smooth muscle cell
Gold nanoparticles, conjugated to HDL Reduces Lp-PLA2 level in human macrophages

E. Harari1, D. Leshem-Lev1, R. Ankri2, D. Fixler2, R. Kornowski2, E.I. Lev2, 1Rabin Medical Center, Cardiac Research Laboratories - The Felsenstein Medical Research Center and The Cardiology Department, Petah Tikva, Israel; 2Bar Ilan University, Faculty of Engineering and Institute of Nanotechnology and Advanced Materials, Ramat Gan, Israel

Background: Inflammation leads to macrophage accumulation in unstable atherosclerotic plaques, which eventually weakens the extracellular matrix and calcifies plaques.

Methods: Lipoprotein-associated phospholipase A2 (Lp-PLA2) is an enzyme produced by inflammatory cells, co-travels with circulating low-density lipoprotein (LDL), and hydrolyzes oxidized phospholipids in LDL. The product of Lp-PLA2 bioactive lipids, oxidative phospholipids, are generated in lesion-prone vasculature, and are known to elicit inflammatory responses. HDL is known for its anti-atherosclerotic properties, and it may protect against inflammatory cell infiltration by binding to scavenger receptors. We hypothesized that gold nano-particles which are scavenged by macrophages, can be used to deliver HDL to inflammatory plaques and thereby reduce inflammatory responses. We tested the hypothesis in an in-vivo model of injured carotid artery that was treated with gold nano-particles conjugated to HDL. To test the hypothesis that Lp-PLA2 activity is reduced by conjugating gold nanoparticles to HDL, we incubated Lp-PLA2 positive macrophages (monitored by confounding factors in human macrophages. Principal Component Analysis included Lp-PLA2 in a pro-atherogenic-related component together with LDL-C, ApoB and non-HDL-C. Lp-PLA2 concentrations decrease after statin treatment and increase after atherogenic lipid feeding. A logistic regression model showed that the presence of plaque in carotid artery was associated with Lp-PLA2 (p=0.014), even after adjusting for traditional atherosclerosis risk factors. This association was higher than for traditional lipid parameters. Lp-PLA2 slightly improves the discrimination and calibration of a model of carotid atherosclerosis based on classical atherosclerosis risk factors.

Conclusions: Our combined in vitro and patient-based approach point to circulating Lp-PLA2 as a new lipid-related parameter highly related to vascular lipid burden that may be considered as a potential biomarker of atherosclerosis.


P1587 | BENCH

Release of interferon-gamma by activated CD8-positive T cells in human calcified aortic valves fosters formation of osteoclasts with advanced calcium resorption

E. Nagy1, Y. Lei1, E. Martinez Martinez1, S.C. Body1, A. Assmann1, P. Libby1, G.K. Hansson2, E. Aikaara2, B. Brigham and Women’s Hospital, Division of Cardiovascular Medicine, Harvard Medical School, Boston, United States of America; 2Brigham and Women’s Hospital, Center for Perioperative Genomics; Department of Anesthesiology, Boston, United States of America; 3Karolinska Institute, Department of Medicine, Stockholm, Sweden

Background: The valve calcium content in human calcific aortic valve disease (CAVD) correlates with clinical stenosis severity and independently predicts outcomes. Histologically, large numbers of activated T-lymphocytes, predominantly memory-effector CD8+ cells localize in close proximity to calcified regions. The role of CD8+ cells and their association with osteoclasts, the cells with specialized calcium resorptive potential, remains unknown in CAVD.

Purpose: To test the hypothesis that CD8+ T cells promote calcification in CAVD.

Methods: CAVD valves (n=46) from valve replacement surgeries were dissected into non-calcified and calcified parts followed by mRNA extraction and quantitative PCR. Gene expression patterns were confirmed by immunohistochemistry and ELISA. To recapitulate a CAVD environment with high interferon (IFN) expression, calcified parts were stimulated with phorbol 12-myristate 13-acetate and ionomycin, qPCR detected signatures molecules of CD8+ cells activation and differentiation. Valve calcium content was detected using ex vivo fluorescence reflectance molecular imaging with near-infrared calcium tracer. In addition, CD14+ cells isolated from healthy donors were treated with either recombinant human IFNg or IFNg from conditioned medium (CM) derived from stimulated organ cultures with or without neutralizing anti-IFNg antibody.

Results: CAVD valves exhibited significantly elevated transcript levels for CAVD valves treated with IFNg or IFNg from conditioned medium (CM) derived from stimulated organ cultures with or without neutralizing anti-IFNg antibody. Results: CAVD valves exhibited significantly elevated transcript levels for CD8: 2.8±0.6-fold, p<0.03; IFNg: 2.2±0.5-fold, p<0.01; CXCCL9: 3.9±0.9-fold, p=0.01; Perforin1: 4.3±0.8-fold, p<0.003; Granzyme B: 6.1±1.8-fold, p<0.003; fold, p=0.01; CD14: 1.2±fold, p=0.01; and mRNAs, including CD14, $sLRP1$: 6.4±1.9-fold, p<0.01, and TRAP: 8.3±2.9-fold, p=0.01 increased significantly, whereas Cathepsin K: 1.6-fold, p=0.8 did not change. In stimulated organ cultures, elevated levels of IFNg, confirmed by ELISA in CM (13.6±3.5-
fold, p<0.01) and qPCR (44.3±24.8-fold, p<0.001) reduced mRNA levels of RANKL (0.03±0.01, p<0.01) and Cathepsin K (0.013±0.01, p<0.001), whereas TRAP did not change (0.4±0.2, p=0.6) compared to unstimulated regions. In addition, calcium signal intensity was increased in stimulated vs. unstimulated calcified (p<0.001). Moreover, IFNγ reduced transcripts for Cathepsin K, TRAP, RANK, and TRAF6, which were decreased in parallel with reduced osteoclast resorptive function, which was restored by neutralizing anti-IFNγ antibody.

Conclusion: Our results indicate that CD8+ cells highly expressing IFNγ in CAVal disease, which do not promote valvular calcification.

Acknowledgement/Funding: Dr E Nagy: Swedish Research Council (grant no: 537-2013-484), Swedish Heart and Lung Foundation; Dr E. Akawa: NIH R01 HL 114805, NIH R01 HL 109506.

P1590 | BEDSIDE
Clinical use of the cardiovascular medicine heart failure (CVM-HF) index in mitral clip population
V. Cammalleri, S. Muscoli, M. Macrini, A. Aroschitz, G. Piascuzzo, E. Maior, F. De Persis, M. Marrochi, G.P. Ussia, F. Romeo. Tor Vergata Polyclinic, Rome, Italy

Background: The CardioVascular Medicine Heart Failure (CVM-HF) index is a prognostic model to predict outcomes in stable heart failure patients. Aim of our study is to validate the feasibility of the score in HF patients undergoing MitraClip procedure.

Methods: We performed a prospective study in patients with left ventricle dysfunction and functional mitral regurgitation, who underwent Mitrclip procedure in our institute from January 2012 to December 2013. The CVM-HF index is the sum of the scores assigned by 13 parameters, 7 not cardiac (age, anaemia, hypertension, chronic obstructive pulmonary disease, diabetes mellitus, moderate to severe kidney dysfunction, cancer and metastatic cancer) and 6 cardiac (no blockers, no ACE-I, NYHA III or IV, lef ventricular ejection fraction 20%, severe valvar heart disease, atrial fibrillation). According with the index patients were divided into 4 categories: low risk if the score was <6 (group A), medium risk if the score was from 6 to 11 (group B), high risk if the score was from 12 to 16 (group C) and very high risk 17 (group D). Adverse events were registered during in-hospital stay and 6 months of follow-up.

Results: 47 patients (mean age 73±9 y.o., males 76%) were included in the study population. The evaluation of CVM-HF showed that 3 patients (6%) were included in low risk category; 30 patients (64%) were included in medium risk category and 14 patients (30%) in high-risk category. At 6-months all patients in group A were in NYHA functional class I-III (100%) and no adverse events were observed; in group B one patient died for HF (3%) and one patient was admitted in hospital (3%) for percutaneous closure of the residual interatrial communication after Mitrclip intervention; in group C two patients were in NYHA III (14%) and two rehospitalizations valve-related were observed (14%); 2 no-cardiac (14%) and 2 cardiac-deaths were observed. Although the incidence of adverse event was not statistically significantly different between the groups, the Logistic EuroSCORE was significantly higher in group C, when compared to group A (37.7±25.1 vs. 5.1±2.9, p<0.044) and group B (37.7±25.1 vs. 17.1±14.8, p<0.001).

Conclusion: CVM-HF index is a not invasive and practical tool, which can be easily used to assess the clinical risk of HF patients undergoing Mitrclip procedure. Poor 6-months outcomes have been observed in patients belonging to the high-risk Group.

P1591 | BEDSIDE
Differential effects of percutaneous edge-to-edge mitral valve repair on endothelial function based on left ventricle function
D. Duesing1, E. Lubos1, U. Schaefer1, S. Blankenberg1, S. Baldus2, V. Rudolph2.
1 University Heart Center Hamburg, Hamburg, Germany; 2 Cologne University Hospital - Heart Center, Cologne, Germany

Background: Endothelial dysfunction is thought to aggravate heart failure by increasing systemic vascular resistance and decreasing coronary flow. Whether the acute hemodynamic changes of percutaneous edge-to-edge mitral valve repair (PMVR) have an impact on endothelial function has so far not been reported.

Methods and results: 25 patients (74.5±8.3 years and 36% female) underwent PMVR. Using ANOVA for repeated measurements FMD improved significantly from baseline to first follow-up and second follow-up (3.6±0.5 vs. 9.0±0.1 vs. 8.2±5.9, F=6.75, p<0.003), which was accompanied by a significant increase of endothelial forward stroke volume (41±14 vs. 49±13 vs. 48±13 ml, F=3.49, p<0.044). These changes were more pronounced in patients with an left-ventricular ejection fraction (LVEF) <35% with significant improvements in FMD (2.5±5.6 vs. 11.5±6.7 vs. 11.7±6.6, F=1.79, p=0.089), a significant increase of FSV (32±11ml vs. 45±11 ml vs. 38±10ml; F=4.04; p=0.048), whereas no significant changes were observed in patients with a LVEF>35%.

Conclusions: Our data suggest an improvement of endothelial function and FSV following reduction of mitral regurgitation with PMVR. Interestingly, these changes were more prominent in patients with reduced LVEF, which likely is a reflection of the overreaching compensatory mechanisms in these patients translating to more direct effects of MR reduction on systemic vascular function.

P1592 | BEDSIDE
Morphometric differences between primary and secondary mitral regurgitation evaluated by 3D transoesophageal echocardiography
E. Bourni, R. Rajani, V. Bapat, A. Krommydas, S. Kapetanakis. St Thomas’ Hospital, London, United Kingdom

Real-time 3D imaging of the mitral valve offers the possibility of advanced quantification of the mitral valve complex, however the clinical significance of the derived parameters is unknown. We investigated the value of these in patients with mitral regurgitation.

Methods: 26 unselected patients with mitral regurgitation were assessed with 3D Transoesophageal Echocardiography (3DTEE). The 3D data set was analysed with TomTec MV Analysis 2.3 for both static and dynamic analyses. Static analyses were performed for annular geometry, coaptation and leaflet geometry, while dynamic analyses were performed for annular displacement, tenting volume and annulus area fraction.

Results: 9 patients had secondary regurgitation (SMR), 17 had primary valve disease (PMR). There were no significant differences between groups in annular geometry, including linear diameters, 3D area, circumference, non-planar angle or aorto-mitral angle. Leaflet geometry assessment on the other hand showed significant differences in tenting volume (1.14 [0.5–2.35] vs 3.12 [1.77–5.55], p=0.0161 for PMR vs SMR respectively, figure - left column) and tenting area (0.93 [0.55–1.38] vs 1.79 [1.78–5.89], p=0.0191, figure - middle column, for PMR vs SMR respectively). Interestingly there was no significant difference in tenting height between these 2 groups (5.65 [3.4–7.6] vs 5.93 [5.0–11.1], p=0.266, figure - right column).

Conclusions: 3D quantification of mitral geometry offers many tantalising parameters but these in their majority do not offer incremental diagnostic benefit. The novel 3D PISA method has important technical limitations for mitral valve orifice area (MVA) assessment in mitral stenosis (MS), mainly the geometric assumptions of PISA shape and the requirement of an angle correction factor. Recently developed single-beat real-time three-dimensional (3D) color Doppler imaging allows direct measurement of PISA without geometric assumptions nor the requirement of an angle correction factor. (see Figure 1). Our aim is to assess the correlation be-

P1593 | BEDSIDE
Mitral valve area obtained by the novel 3D PISA method has a statistically significant correlation with pulmonary artery systolic pressure in mitral stenosis
H. Meija, J.A. De Agustin Loeches, D. Villani, J.J. Gomez De Diego, C. Almería, J.L. Rodrigo, P. Mahia, M.A. García-Fernandez, C. Macaya, L. Perez De Isla. Hospital Clinico San Carlos, Madrid, Spain

Introduction: Two-dimensional (2D) proximal isovelocity surface area (PISA) method has important technical limitations for mitral valve orifice area (MVA) assessment in mitral stenosis (MS), mainly the geometric assumptions of PISA shape and the requirement of an angle correction factor. Recently developed single-beat real-time three-dimensional (3D) color Doppler imaging allows direct measurement of PISA without geometric assumptions nor the requirement of an angle correction factor (see Figure 1). Our aim is to assess the correlation be-

Figure 1
between MVA obtained by both 2D and 3D PISA methods with pulmonary artery Doppler echocardiography is feasible in the clinical setting and has a statistically significant PISA in patients with mitral stenosis.

### Methods

**Background:** Ischemic mitral regurgitation (MR) carries adverse prognosis after myocardial infarction (MI). Functional ischemic MR in acute phase of MI remains unstable and deteriorates due to its often transient nature.

**Purpose:** To assess left ventricular (LV) mechanics by two-dimensional (2D) speckle-tracking echocardiography (STE) in acute inferior MI and ischemic MR.

**Methods:** 69 patients with first acute inferior MI treated with percutaneous coronary intervention, and no structural cardiac valve abnormalities and 45 healthy individuals (age 49.3±10.9 years, 48.9% males) were enrolled. Study patients were divided into NMR gr. (no or mild MR, N=34, age 60.38±11.36 years, 79.4% males) and IMR gr. (grade ≥ 2 MR, N=35, age 61.86±12.02 years, 54.3% males).

2D STE was performed within 48 h of presentation and reperfusion therapy. 2D STE analysis was performed offline (GE EchoPAC software). Statistical analysis was carried out with SPSS 21.0.

**Results:** LV ejection fraction (EF) and longitudinal deformation parameters were significantly better in healthy subjects, but did not differ between the study groups. All circumferential deformation parameters were significantly worse in IMR group compared to control and NMR groups. Radial strains did not differ between control and NMR groups neither globally nor regionally. Global, basal and mid-ventricular strain was significantly lower in IMR group compared to both – healthy subjects and NMR group.

**Conclusion:** Ischemic MR in acute inferior MI is associated with worse radial and circumferential LV deformation parameters assessed by 2D STE.
of the Kaplan-Meier curves and the log-rank test revealed that the all-cause mortality was significantly different between the four groups (p < 0.001). Furthermore, Cox regression analysis revealed that NYHA class IV (HR 1.89, 95% CI 1.086–3.286, p = 0.024) and NT-pro BNP > 5000 pg/mL (HR 2.638, 95% CI 1.503–4.630, p = 0.001) independently associated with the mortality after mitraclip.

Conclusion: NYHA class and NT-pro BNP levels are not always correlated and independently have a predictive value in mitraclip patients. Since the baseline HF status is strongly associated with the survival after mitraclip, we may need to evaluate the HF status of mitraclip patients carefully by using both objective and subjective parameters.

Acknowledgement/Funding: Japan Society for the Promotion of Science

P1599 | BEDSIDE
Survival and clinical outcome in functional mitral regurgitation: percutaneous mitral valve repair or conservative treatment
F. M. Aggioni, F. Fiorelli, C. Gianmini, M. De Carlo, A. S. Petronio, F. Guaracino. Azienda Ospedaliero-Universitaria Pisana, Dipartimento Cardio-Toracico e Vascolare, Pisa, Italy

Background: Percutaneous mitral valve repair (PMVR) using the MitraClip System is feasible and entails clinical improvement in high-surgical risk patients with asymptomatic severe mitral valve regurgitation (MVR), rejected by the surgical option. The lack of randomized clinical trials weighs on the clinical decision between conservative and interventional treatment.

Purpose: The aim of the present study was to assess survival rates and clinical outcome of patients with severe functional MVR treated conservatively compared with those who received PMVR with MitraClip.

Methods: Between December 2009 and February 2015, 237 consecutive patients were referred to our center for assessment. 83 underwent PMVR and 154 were treated with conservative medical therapy (OMT), according to the current guidelines. To the purpose of our retrospective study, we analyzed data of patients in both groups with optimal medical therapy (OMT) who reached 1-year follow-up (OMT n=39; PMVR n=50).

Results: There was no significant differences between the two selected groups (OMT vs PMVR). Mean age was 76±9 vs 73±9 years, p=0.12; 69.2 vs 78% were male, p=0.35. The surgical risk was comparable as assessed by Logistic EuroSCORE and EuroSCORE II (24.3±12.8 vs 27.5±20.2, p=0.10; 8.1±6.5 vs 10.8±8.5, p=0.09). Mean creatinine and hemoglobin values were 1.43±0.5 vs 1.63±1.2 mg/dl, p=0.31, and 12.9±1.9 vs 12.0±1.8 g/dl, p=0.10, respectively, and glomerular filtration rate was 49.5±21.1 vs 50.1±17.8 ml/min/1.73 m², p=0.89. The echocardiographic assessment showed comparable volumes and biventricular function between the two groups in terms of left ventricle end-diastolic and end-systolic volumes (185.1±58.4 vs 202.1±70.8 ml, p=0.23; 119.1±55.9 vs 132.2±59 ml, p=0.37). Respectively, left ventricular ejection fraction (35.1±12.7 vs 34.6±11.4%, p=0.89), left atrium area (30.5±7.1 vs 31.9±8.7 cm², p=0.43), systolic pulmonary artery pressure (48.9±14 vs 49.9±7.9, p=0.69) and tricuspid annular plane systolic excursion (19.6±6 vs 16.8±4, p=0.24). Procedural success rate of PMVR was 99% and 1 month mortality rate was 2%. We observed a significant clinical improvement in the PMVR group, assessed as NYHA functional class: at 1-year follow-up, 85% vs 17% were in NYHA class III, respectively (p < 0.0001). The one-year survival rate in the PMVR was higher (69.2 vs 84%, p=0.05), with higher overall survival (46.2% vs 70%, p=0.02).

Conclusion: PMVR in high-risk surgical patients with severe functional mitral regurgitation entails clinical benefit and displays higher survival rates compared to optimal medical therapy.

AORTIC VALVE DISEASE

P1599 | BEDSIDE
Gender-related comparison in early and late outcomes after transcatheter aortic valve replacement

Background: An independent effect of gender on late mortality after transcatheter aortic valve replacement (TAVR) remains controversial. This controversy can be partially explained by a balance between a higher risk of complications in women, and a higher late risk attributable to a higher prevalence of comorbidities in men.

Purpose: From a single center cohort we sought to determine the independent effect of gender on one-year mortality after TAVR using Cox regression analysis.

Methods: We identified the correlates of one-year mortality by univariable analysis. Subsequently, variables with p < 0.10 were selected to enter into the multivariable Cox regression analysis. The sex-independent effect was assessed in the overall cohort and after excluding life-threatening bleeding and transfusion.

Results: From 2007 to 2014, 682 patients underwent TAVR at our Institution of whom 348 (51%) were women. Women were less likely to have baseline comorbidities as compared to men such as atrial fibrillation (37% vs. 47%; p=0.01), chronic renal failure (41% vs. 53%; p=0.01), resulting in a higher average STS score (9.9±4.6 vs. 8.2±2.4, p=0.01). Conversely, women had a higher rate of VARC-vascular complications (9% vs. 5%), life-threatening bleeding (10% vs. 5.5%) and in-hospital cardiac death (8% vs. 4%) (p=0.05 for all). After adjusting for confounders no gender-independent effect was shown considering the entire cohort and after excluding vascular complications and transfusion (Table).

Conclusion: A gender-independent effect on late mortality after TAVR does not seem to exist, even after accounting for the higher rate of vascular complications in women.

P1600 | BEDSIDE
Concomitant mitral regurgitation increases mortality in high-risk patients with severe aortic stenosis treated with transcatheter aortic valve replacement
S. Haussi1, M. Mangner1, F. Woitek1, J. Wilde1, G. Stachel1, S. Leontyev2, D. Holzhey2, F. W. Mohr2, G. Schuler1, A. Linke1. 1University of Leipzig - Heart Center, Department of Internal Medicine / Cardiology, Leipzig; 2University of Leipzig - Heart Center, Department of Cardiac Surgery, Leipzig, Germany

Background: The impact of concomitant mitral regurgitation (MR) on outcome in high-risk patients with severe aortic stenosis undergoing transcatheter aortic valve replacement (TAVR) appears to be unclear. Therefore, it was aim of this study to evaluate the impact of MR on outcome after TAVR.

Methods and results: Patients with severe aortic stenosis in which TAVR was performed between 2006 and 2013 were included into the analysis. MR was measured by echocardiography at baseline, 30 days and at one year, 30-day, 1-year and 2-year mortality was calculated. Between January 2006 and February 2013 a total of 1196 consecutive patients (Age 80±7.6 years, Logistic EuroScore 21.2±13.2%, STS PROM 9.3±6.4%) with severe aortic stenosis were treated with TAVR at our institution. At baseline 11.9% of these patients presented with no MR, 75.5% with mild MR (grade 1), 12.0% with moderate MR (grade 2) and 0.5% with severe MR (grade 3).

Compared to baseline MR at 30 days and 1 year after TAVR remained unchanged (p=0.10 were selected to enter into the multivariable Cox regression analysis. The sex-independent effect was assessed in the overall cohort and after excluding life-threatening bleeding and transfusion.

Conclusion: A gender-independent effect on late mortality after TAVR does not seem to exist, even after accounting for the higher rate of vascular complications in women.
Conclusion: Pre-existing moderate or severe mitral regurgitation is associated with an 64% higher mortality at 30 days, a 35% higher mortality at one year and a 38% higher mortality at two years as compared to patients with no or mild MR. Further studies are necessary to investigate whether additional treatment of MR in patients with concomitant moderate to severe MR will improve the prognosis in a TAVR population.

P1601 | BEDSIDE
Peak aortic velocity correlates with serum leukotriene B4, metalloproteinase-2 and IFN gamma in calcified aortic valve disease
M. Springall, R. Bojallj, J. Cossio-Andrada, N. Espinola, J. Verdejo-Paris, S. Trevethan, National Institute of Cardiology Ignacio Chavez, Immunology and Outpatient Care, Mexico City, Mexico

Background: An increment of the peak aortic valve jet flow velocity (PAJV) is associated with a progression of aortic valve sclerosis (AVS) to stenosis (AS). Increased serum concentrations of leukotriene (LT) B4 have been associated with fibrosis of connective tissue through regulating the synthesis, secretion and activation of matrix metalloproteinases (MMPs). IFN-γ is a marker of inflammation. We assessed the association of these surrogate markers of inflammation and fibrosis with PAJV in patients with AVS and AS.

Methods: The data of 150 consecutive patients from 59 patients (AVS= 31 and AS=28) and 28 healthy donors. Serum concentrations of LT4, MMP-1, 2 and 9 and IFN-γ were determined by a quantitative immunoassay technique with commercial kits. PAJV was evaluated with coronary computed tomography angiography in all patients. A one-way ANOVA nonparametric test (Kruskall-Wallis) and a Spearman test for correlation were performed. Both Research and Ethics Committees of our Institution approved the present study.

Results: Both patient groups had higher concentrations of all three markers than controls. AS patients had higher concentrations of LTB4 and lower concentrations of IFN-γ than AVS patients. We found a direct significant correlation of LT4 (r=0.349, p=0.007) and MMP-2 (r=0.318, p=0.014), and an inverse correlation of IFN-γ (r=-0.247, p=0.060) with PAJV.

Conclusion: Our results suggest that as PAJV increases, fibrosis as a resolutive phase of inflammation, gradually takes place over the overt inflammation associated with AVS.

P1602 | BEDSIDE
When does the bicuspid aortic valve begin?
E.G. Milano, M.A. Prioli, L. Zanolla, M. Rebonato, C. Sandrini, G. Dolci, L. Rossetti, C. Vassanelli, University of Verona, Department of Medicine, Section of Cardiology, Verona, Italy

Background: Bicuspid aortic valve (BAV) has a population prevalence of 0.5–2%. It is well accepted that the disease involves not only the valve function but also the entire aorta, with the development of the so-called BAV aortopathy. However, few studies have addressed to the onset of aortic dilation and the determinants of aortic growth. We postulate that the aortopathy in a subset of BAV pts is caused by a defect in the early development of the aorta and thus is detectable in early stages of life.

Purpose: To identify the onset of the aortic dilation and which part of the aortic arch is primarily involved in BAV pts.

Methods: Serial retrospective echocardiographical data on 191 consecutive pts with isolated BAV (150 males, mean age 21y) were analyzed. Aortic diameters at different levels were recorded. Aortic diameters at different levels were compared with normal subjects (162 males, mean age 18y) with a tricuspid aortic valve morphology was defined according to cusp fusion pattern in right-left coronary arteries. Asc. aorta/BSA BAV 33.61±9.3* 23.23±4.1 18.83±2.9 20.17±4.1
STJ/BSA BAV 29.43±8 21.32±4 16.85±2.8 17.98±3.2
Sinus/BSA BAV 36.29±8.7** 24.61±4 19.27±3 19.86±2.7
Anulus/BSA BAV 26.41±7.1 18.48±3 15.61±2.3 13.4±1.8

Table 1

Anulus/BSA BAV 26.41±7.1 18.48±3 15.61±2.3 13.4±1.8
N 24.05±6.2 17.83±2.8 13.99±1.7 12.54±1.2
Sinus/BSA BAV 36.29±8.7** 24.61±4 19.27±3 19.86±2.7
N 29.73±6.5 22.57±3.7 17.99±1.9 16.39±2.1
STJ/BSA BAV 29.43±8 21.32±4 16.85±2.8 17.98±3.2
N 26.69±6.3 19.55±3.1 15.32±1.8 14.75±2.2
Asc. aorta/BSA BAV 33.61±9.3* 22.33±4.1 18.83±2.9 20.17±4.1
N 28.35±6.7 20.55±3.2 16.99±1.7 15.5±2.1

*p value <0.05; **p value<0.01; ***p value<0.001.

Conclusion: BAV is a complex condition and BAV aortopathy begins early in childhood and progresses during adolescence till adult age. According to this data, it is necessary to start medical therapy with betablocker or sartan still in pediatric age?

P1603 | BEDSIDE
The influence of endothelin-1, hs-CRP, coronary artery plaque burden and plaque morphology on calcific aortic valve disease
V. Appadurai, 1, K. Nei, 2, C.M. Anterley, 3, R. Senior, 4, C.D. Byrnes, 5, J.C. Kaski, 1, R. Bull, 1, C.J. Boos, 1, E. Carlton, 1, G. Kereves, 1, S. Sunshine Coast Hospital and Health Service, Department of Cardiology, Nambour, Australia; 3 Bournemouth University, Centre for Postgraduate Medical Education and Research, Dorset, United Kingdom; 2 Sunshine Coast Hospital and Health Service, Department of Intensive Care Medicine, Nambour, Australia; 4 Royal Brompton Hospital, Biomedical Research Unit, National Heart and Lung Institute, Imperial College, London, United Kingdom; 3 University Hospital Southampton NHS Foundation Trust, National Institute for Health Research Biomedical Research Centre, Southampton, United Kingdom; 5 St George's Healthcare NHS Trust, Cardiovascular Science Research Centre, London, United Kingdom; 1 Royal Bournemouth Hospital, Department of Radiology, Dorset, United Kingdom; 4 Poole Hospital NHS Foundation Trust, Department of Cardiology, Dorset, United Kingdom; 6 Sunshine Coast Hospital and Health Service, The University of Sunshine Coast, Department of Cardiology, Nambour, Australia

Background: Calcific aortic valve disease (CAVD) affects 1 in 4 of the population >65 years. Subsequent progression to severe aortic valve stenosis has a high morbidity and mortality. The pathophysiology of CAVD is poorly understood. Understanding the processes involved is important if successful non-surgical treatments are to be developed. Both systemic levels of inflammation and coronary atherosclerotic artery disease (CAD) – itself an inflammatory process - are predictors of CAVD. However, whether their effects are independent of each other is not clearly shown. Further studies are necessary to investigate the influences of plaque burden, differing coronary plaque morphology and systemic levels of the inflammatory mediator endothelin-1 (ET-1), on CAVD are unknown.

Purpose: To investigate the inter-relationships between coronary artery plaque burden and markers of inflammation (hs-CRP and ET-1), with aortic valve calcification (AVC).

Methods: Patients undergoing CT coronary angiography (CTCA) for investigation of chest pain were recruited. Those with significant CAD (≥50% luminal stenosis) and significant valvular dysfunction were excluded (aortic valve velocity >2.0m/s). Coronary artery plaque burden, plaque morphology, and AVC were assessed with CTCA. Inflammatory markers were obtained from venous sampling.

Results: 183 patients, 53% male, mean age 59.8 (±9.6) years were recruited. Understanding the processes involved are important if successful non-surgical treatments are to be developed. Both systemic levels of inflammation and coronary atherosclerotic artery disease (CAD) – itself an inflammatory process - are predictors of CAVD. However, whether their effects are independent of each other is not clearly shown. Further studies are necessary to investigate the influences of plaque burden, differing coronary plaque morphology and systemic levels of the inflammatory mediator endothelin-1 (ET-1), on CAVD are unknown.

Conclusion: To identify the onset of the aortic dilation and which part of the aortic arch is primarily involved in BAV pts.

P1604 | BEDSIDE
Transcatheter aortic valve replacement improves functional mitral regurgitation
E. Ouzan, 1 B. Kinya, 2 Y. Ko, 3 P. Block, 4 C. Deviredy, 5 B. Leshnower, 4 V. Babalaros, 4 V. Thourain, 5 S. Lerakis, 5 K. Movromatis, 5 Hadassah University Medical Center, Jerusalem, Israel; 2 Emory University School of Medicine, Atlanta, United States of America; 3 Emory University, Atlanta, United States of America; 4 Emory University Hospital, Atlanta, United States of America

Background: Severe aortic stenosis (AS) is commonly associated with mitral regurgitation (MR) in patients undergoing transcatheter aortic valve replacement (TAVR). The progression of such MR after TAVR has not been well defined.

Purpose: To examine the effects of TAVR on functional MR.

Methods: Echocardiograms (at baseline and 1 year) were evaluated in consecutively selected patients undergoing TAVR for AS between 2007 and 2011. MR was classified as functional or organic and was graded as minimal (none-nil) or moderate-severe. Pulmonary artery systolic pressure (PASP) as well as other parameters were estimated as well.

Results: 164 patients underwent TAVR with mean aortic valve gradients diminishing from 47 to ≤10 mmHg. 87 (53%) of the patients had functional MR at baseline, 32 of which had significant MR. Of those with significant functional MR, 53% improved at least one MR class, and 85% of those had only minimal MR 1 year after TAVR. PASP was reduced from 55±20 mmHg (p<0.001) at baseline to 56±17 mmHg in the entire MR group as well (see Table 1). Multivariable analysis showed baseline functional MR to be an independent predictor of improved LVEF and PASP.

Conclusion: Patients undergoing TAVR for severe AS who have concomitant...
functional MR show important reductions in grade of MR and pulmonary artery pressures.

P1605 | BEDSIDE
Prognostic Implications of fibrosis in low risk aortic stenosis patients
C. Gavina1, I. Falcao-Pires2, B. Marinho1, J. Rodrigues1, J. Almeida1, P. Pinho1, F. Rocha-Goncalves2, A. Leite-Moreira1, 1Hospital São João, Porto, Portugal; 2Faculdade de Medicina do Porto, Porto, Portugal

Introduction: In aortic stenosis (AS), fibrosis is associated with progression to heart failure and worse prognosis.

Objectives: We aimed to evaluate the impact of myocardial fibrosis on clinical events after aortic valve replacement (AVR) in low risk severe AS.

Methods: Prospective cohort of 56 severe AS patients with ejection fraction (EF) > 40%, who underwent AVR with myocardial biopsies and collagen volume fraction (CVF) determination. Mean follow-up was 5 ± 2 years. Outcomes were all-cause death and the combined endpoint of all-cause death or non-fatal cardiovascular hospitalization after 8 years of follow-up.

Results: Patients’ mean age was 66 ± 12 years, 67.9% women, mostly mildly symptomatic (NYHA class I/II, 76.8%), with low risk of operative mortality (Euroscore I 1.5 ± 1.0%), and mean EF was 63 ± 7 ± 6%. Mean value of CVF was 16.9 ± 13.5%. There were 7 deaths (12.5%) and 48 non-fatal cardiovascular hospitalizations (7.1%). Baseline clinical and echocardiographic characteristics were similar between patients with or without an event. Patients who suffered a fatal event or the combined endpoint had higher degree of fibrosis (27.1 ± 20.7% vs 15.4 ± 11.8%, p = 0.035, 24.0 ± 18.2% vs 15.3 ± 12.0%, p = 0.038, respectively). Patients with CVF > 15.4% had lower survival (37.5% vs 97.0%, p < 0.001) and survival free of the combined endpoint (0 vs 91.2%, p < 0.001). On Cox regression analysis, CVF was the only independent predictor of all-cause death (HR 1.88, 95% CI: 1.06–3.29 for 10% increase; p = 0.026) and the combined endpoint (HR 1.73, 95% CI: 1.03–2.911 for 10% increase; p = 0.038).

Conclusions: In low risk AS, higher levels of fibrosis are independent predictors of all-cause death and of all-cause death and non-fatal cardiovascular hospitalization. Further advances on anti-fibrotic therapies in the setting of AS are needed.

P1606 | BEDSIDE
Transfemoral Implantation of the Edwards SAPIEN 3 Aortic Valve without Predilation is Safe and Feasible in the Majority of Patients
K. Bijukcic1, J. Witt2, K. Krause2, L. Hansen2, J. Schofer1, 1Medical Care Center Prof. Mathey, Prof. Schofer, University Cardiovascular Center, Hamburg, Germany; 2Albertinen Hospital, Hamburg, Germany

Objectives: To evaluate the feasibility and safety of transfemoral implantation of the Edwards SAPIEN 3 aortic valve without balloon predilation.

Background: Aortic valve implantation without balloon predilation may facilitate the procedure, reduce rapid pacing duration and may impact the stroke rate. For the self-expandable CoreValve in small studies this strategy has been shown to be feasible and safe. Whether direct aortic valve implantation is applicable to the Edwards SAPIEN 3 valve is unknown.

Methods: Ninety six consecutive patients with severe symptomatic aortic stenosis and high surgical risk were prospectively enrolled to receive the Edwards SAPIEN 3 aortic valve. 84 patients were treated with direct Edwards SAPIEN 3 aortic valve implantation without predilation.

Results: Mean age of the patients was 83 ± 5.7 years, 55.8% were male. Mean aortic pressure gradient was 42 ± 16 mmHg, aortic valve area 0.8 ± 0.3 cm². In the first 40 patients (Group A) direct implantation was attempted in all, in two the prosthesis could not cross the native aortic valve. Both patients had severe asymmetrical calcification and an AWA < 1.5 cm². 10 patients (25%) experienced an intraprocedural cardiogenic shock due to difficult prolonged valve crossing and died at day 2. Post-dilation was performed in one patient due to moderate aortic regurgitation.

Conclusions: Transfemoral implantation of the Edwards SAPIEN 3 aortic valve without balloon predilation is feasible and safe in the majority of patients, limitations are severe asymmetrical valve calcification in combination with AWA of 0.5 cm² or less.

P1607 | BEDSIDE
Incidence and predictors of late recurrence of left ventricular dysfunction after aortic valve replacement for chronic aortic regurgitation: long-term follow-up data
M. Amano, C. Iizumi, M. Miyake, Y. Tamaki, S. Enomoto, T. Tamura, H. Kondo, K. Kaitani, Y. Nakagawa, Tenri Hospital, Nara, Japan

Background: Left ventricular (LV) dysfunction is sometimes seen at aortic valve replacement (AVR) in patients with severe chronic aortic regurgitation (AR). We have experienced late recurrent LV dysfunction despite ejection fraction (EF) was once normalized early after AVR, but there are few reports about chronological changes of LV function during long-term follow-up.

Purpose: The purpose of this study is to clarify chronological changes of LV function and predictors of recurrent LV dysfunction late after AVR.

Methods: Among 80 consecutive patients with AR for severe chronic AR between 1995 and 2010, we retrospectively investigated 55 patients who were followed-up with echocardiography more than 5 years after AVR. LV function before, early (1 year) and late (5–10 years) after AVR were evaluated. Late recurrent LV dysfunction was defined as EF < 50% late after AVR and 10% reduction in the EF compared with that seen 1 year after AVR. In order to determine the predictors of late recurrent LV dysfunction, laboratory data, medications, clinical background, and echocardiographic data were evaluated.

Results: The mean follow-up period was 10.7 ± 4.4 years. LVDD, LVDVs, and EF before, early and late after AVR were as follows; LVDD: 69 ± 7, 50 ± 6, and 52 ± 6 mm, LVDVs: 47 ± 9, 32 ± 6, and 33 ± 7 mm, EF: 54 ± 15, 65 ± 9, and 62 ± 11%. EF was < 50% in 19 (35%) patients before AVR, 1 (2%) early and 7 (13%) late after AVR. Late recurrent LV dysfunction developed in 7 (13%) of the 55 patients. Compared with the 48 patients without late recurrent LV dysfunction, the seven patients displayed significantly larger LVDD before (77 ± 5 vs 67 ± 7 mm, p < 0.01) and early after AVR (54 ± 13 vs 49 ± 6 mm, p = 0.03), larger LVDVs before (62 ± 7 vs 45 ± 8 mm, p = 0.01) and early after AVR (37 ± 5 vs 31 ± 6 mm, p = 0.01), lower EF before (36 ± 7% vs 57 ± 13%, p < 0.01) and early after AVR (59 ± 9 vs 66 ± 10%, p = 0.04), greater LVMI early after AVR (134.7 ± 22.7 vs 110.2 ± 28.5 gm/m², p = 0.02), and a higher incidence of postoperative AF (71% vs 17%, p < 0.01). There were no significant differences in the ages at the AVR (p = 0.24), laboratory data, medications, or underlying diseases between the two groups. In multivariate analysis, the preoperative LVDD and the incidence of postoperative AF were found to be independent predictors of late recurrent LV dysfunction.

Conclusions: Late recurrent LV dysfunction developed in 13% of the patients after AVR for chronic severe AR, thus long-term follow-up is important even if EF was once normalized. Early operation preceding remarkable LV enlargement and the maintenance of sinus rhythm are important for maintaining LV function late after AVR.
transfemoral implantation of the DFM aortic valve is feasible. Significant valve and mild paravalvular in 1 pt. In 1 pt., 3 days post procedure, the valve embolized there were 2 pull-throughs in 1 pt and 3 in another pt with the valve successfully tion. The annulus diameter was measured by MSCT and the size of the prosthesis in 3 centers in Germany and Italy. All patients were in NYHA III, ejection fraction ranged from 20% to 70%. The mean logistic EuroScore/STS score were 20.7 and 15.5. The intervention in the 46-year-old patient was a bridge to heart transplant. The annulus diameter was measured by MSCT and the size of the prosthesis (i.e., to ensure proper positioning) was measured by 3D CT. In 1 pt, 3 days post procedure, the valve embolized into the left ventricular outflow tract. This finding was confirmed by an echocardiogram performed 3 days post procedure, and the valve was successfully retrieved using a rededicated catheterization laboratory.

Aim of the study: To evaluate the safety and feasibility of the DFMs in patients with severe AR.

Methods and results: Five high surgical risk patients (77.2 years, range 67 to 87, 1 male) with severe AR and no or trivial valvular calcification were enrolled in 3 centers in Germany and Italy. All patients were in NYHA III, ejection fraction ranging from 20% to 70%. The mean logistic EuroScore/STS score were 20.7 and 15.5. The intervention in the 46-year-old patient was a bridge to heart transplant. The annulus diameter was measured by MSCT and the size of the prosthesis (i.e., to ensure proper positioning) was measured by 3D CT. In 1 pt, 3 days post procedure, the valve embolized into the left ventricular outflow tract. This finding was confirmed by an echocardiogram performed 3 days post procedure, and the valve was successfully retrieved using a rededicated catheterization laboratory.

Background: Pure aortic regurgitation (AR) without leaflet calcification is considered a contraindication for most percutaneous aortic valve prostheses because calcification is required for a stable valve position. The DFM aortic valve may be suitable for pure AR, because it is fixed by 2 expandable rings placed below and above the native valve which may not need calcification for stable positioning.

Aim of the study: To evaluate the safety and feasibility of the DFMs in patients with severe AR.

Methods and results: Five high surgical risk patients (77.2 years, range 67 to 87, 1 male) with severe AR and no or trivial valvular calcification were enrolled in 3 centers in Germany and Italy. All patients were in NYHA III, ejection fraction ranging from 20% to 70%. The mean logistic EuroScore/STS score were 20.7 and 15.5. The intervention in the 46-year-old patient was a bridge to heart transplant. The annulus diameter was measured by MSCT and the size of the prosthesis (i.e., to ensure proper positioning) was measured by 3D CT. In 1 pt, 3 days post procedure, the valve embolized into the left ventricular outflow tract. This finding was confirmed by an echocardiogram performed 3 days post procedure, and the valve was successfully retrieved using a rededicated catheterization laboratory.

Conclusion: In high-risk pts with severe non-calcified pure aortic regurgitation, transfemoral implantation of the DFM aortic valve is feasible. Significant valve embolization, however, is critical to achieve a stable position of the prosthesis. Further studies are needed to learn more about appropriate patient selection.

AORTIC VALVE INTERVENTIONS

P1600 | BEDSIDE

Transformal implantation of the direct flow medical (DFM) aortic valve for pure noncalcified aortic regurgitation

L. Hansen1, K. Bijkic2, A. Laib3, A. Colombo4, F. Gatto4, C. Oezbek5, J. Schofer5
1 Abertinen Hospital, Hamburg, Germany; 2 Medical Care Center Prof. Mathey, Prof. Schofer, University Cardiovascular Center, Hamburg, Germany; 3 San Raffaele Hospital of Milan (IRCCS), Milan, Italy; 4 SHG Kliniken Völklingen, Völklingen, Germany

Background: Pure aortic regurgitation (AR) without leaflet calcification is considered a contraindication for most percutaneous aortic valve prostheses because calcification is required for a stable valve position. The DFM aortic valve may be suitable for pure AR, because it is fixed by 2 expandable rings placed below and above the native valve which may not need calcification for stable positioning.

Aim of the study: To evaluate the safety and feasibility of the DFMs in patients with severe AR.

Methods and results: Five high surgical risk patients (77.2 years, range 67 to 87, 1 male) with severe AR and no or trivial valvular calcification were enrolled in 3 centers in Germany and Italy. All patients were in NYHA III, ejection fraction ranging from 20% to 70%. The mean logistic EuroScore/STS score were 20.7 and 15.5. The intervention in the 46-year-old patient was a bridge to heart transplant. The annulus diameter was measured by MSCT and the size of the prosthesis (i.e., to ensure proper positioning) was measured by 3D CT. In 1 pt, 3 days post procedure, the valve embolized into the left ventricular outflow tract. This finding was confirmed by an echocardiogram performed 3 days post procedure, and the valve was successfully retrieved using a rededicated catheterization laboratory.

Conclusion: In high-risk pts with severe non-calcified pure aortic regurgitation, transfemoral implantation of the DFM aortic valve is feasible. Significant valve embolization, however, is critical to achieve a stable position of the prosthesis. Further studies are needed to learn more about appropriate patient selection.

P1610 | BEDSIDE

Assessment of operative mortality risk in patients with active infective endocarditis undergoing cardiac surgery: performance of the EuroScore I and II logistic models


Background and aims: The European System for Cardiac Operation Risk Evaluation (EuroSCORE) has been established as a tool for assisting decision-making in surgical patients and as a benchmark for quality assessment. Infective endocarditis (IE) often requires surgical treatment and is associated with high mortality. This study was undertaken to 1) validate both versions of the EuroSCORE, the older logistic EuroSCORE (ES-I) and the recently developed EuroSCORE II (ES-II); 2) to compare their performances and 3) to identify new variables that could further improve the performance of previous models.

Methods: Data from all (n=128) patients undergoing surgery for active IE between January 2007 and November 2014 was retrieved from a single center prospective registry and accordingly, the ES-I and ES-II were calculated for each individual case. The discriminative power of each score was assessed by determining the area under the Receiver Operating Characteristic (ROC) curve. Relative performances of the scores were compared using the DeLong method and calibration was assessed by the Hosmer-Lemeshow goodness-of-fit method and calibration curves.

Results: One hundred and twenty-eight patients were analyzed. The observed perioperative mortality was 16.4%. The median ES-I and ES-II were 13.8% IQ [0.05-31.7] and 6.6% IQ [3.5–18.2]). Discriminative power was higher for ES-II (AUC of 0.82, 95% CI, 0.74–0.88) than for ES-I (AUC of 0.73, 95% CI, 0.65–0.81), although the difference was not statistically significant (p<0.1). The Hosmer-Lemeshow test showed good calibration, however ES-I tended to over predict and ES II to under predict. Among variables known to be associated with greater IE severity, only prosthetic valve IE and elevated white blood cell count were independent mortality predictors (OR 8.0; 95% CI: 2.6-20.0; p<0.0001 and an OR 3.5; 95% CI: 1.2–10.0; p=0.02, respectively). The new model including the ES-II variables and the independent predictors of mortality showed an AUC of 0.85, 97.7-0.93, and did not differ significantly from ES-II (p=0.65).

Conclusion: Both ES-I and ES-II adequately stratify risk in active IE, however ES II in the overall comparison performed slightly better. ES I tends to over predict and ES II to under predict mortality. Specific endocarditis features will increase model complexity without an unequivocal improvement in predictive accuracy.

P1611 | BEDSIDE

Evolution of 18F-FDG PET/CT findings under therapy in patients with infective endocarditis: first description

E. Ravis, L. Tessonnier, L. Saby, S. Hubert, C. Lavoute, E. Salaun, M. Suniam, J.P. Casalta, S. Camilleri, G. Habib. la Timone Hospital, Marseille, France

Introduction: Infective endocarditis (IE) is associated with difficult and delayed diagnosis, high mortality, and risk of recurrence during the first year following diagnosis.

Methods: Among 186 patients that underwent 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET/CT) has recently proved useful for the diagnosis of IE and has been proposed as a new major diagnostic criterion for prosthetic valve IE. However, repeat 18F-FDG PET/CT has never been performed in IE, and the significance of a positive uptake has remained unclear.

Purpose: First description of the evolution of a positive 18F-FDG PET/CT after treatment of IE and its correlation with patient outcome.

Methods: During the first week of their admission, 235 patients with definite IE (177 men, aged 24 to 91) underwent 18F-FDG PET/CT. Among them, 98 (42%) presented with a positive 18F-FDG PET/CT and were scheduled for 1 month follow-up PET/CT after the end of the antibiotic therapy. Patients treated by early surgery were excluded, to avoid false positive uptake related to the postoperative inflammatory process. After exclusion of operated patients, 1-month repeat 18F-FDG PET CT was obtained in 33 patients. These 33 patients underwent repeat clinical, biological and echocardiographic follow-up at 1, 3, 6 months and 1 year. Primary end point was mortality and/or recurrence of IE at 1 year.

Results: The 33 patients in which repeat 18F-FDG PET/CT was obtained included 22 (66%) men, 22 (66%) prosthetic valves, and 15 (45%) aortic IE. Repeat 18F-FDG PET/CT remained positive in 26 (78%) patients and became negative in 7 (22%) patients.

Conclusion: A persistent positive 18F-FDG PET/CT is frequently observed despite an apparently healed IE, when performed 1 month after the end of antibiotic therapy, irrespective of the clinical evolution. Negative follow-up 18F-FDG PET/CT after antibiotic therapy predicts the absence of recurrence of IE or death. Repeat 18F-FDG PET/CT under therapy is potentially useful for the follow-up of patients with IE under antibiotic therapy and may help optimizing patient management.
Factors associated with progression or regression of non-specific valvular changes detected during echocardiographic screening for rheumatic heart disease

M.G.W. Remond1, D. Atkins1, A. White2, A.D. Brown3, J.R. Carapetis5, E. Marijon1, X. Jouven1.

Background: The significance of Borderline rheumatic heart disease (RHD) or other non-specific valvular abnormalities (NSVAs) detected during echocardiographic screening for RHD is unclear.

Purpose: To determine which valve abnormalities are associated with future progressive damage or regression.

Methods: A prospective cohort study of high-risk Indigenous Australian children. Cases had Borderline RHD or NSVAs on prior echocardiography. Controls had a previous normal echocardiogram. Follow-up echocardiography was performed 2.5–5 years later to assess for deterioration or improvement. Logistic regression models were developed to identify factors associated with progression or regression of valvular changes.

Results: Of 442 individuals enrolled, 42 (9.5%) exhibited deterioration and 27 (6.1%) improvements in valvular lesions.

Changes in valvular lesions

<table>
<thead>
<tr>
<th>Category – number (%)</th>
<th>Deterioration</th>
<th>Improvement</th>
<th>No change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Borderline A (MV)</td>
<td>4 (31)</td>
<td>2 (15)</td>
<td>7 (54)</td>
</tr>
<tr>
<td>Borderline B (MV)</td>
<td>6 (29)</td>
<td>6 (29)</td>
<td>9 (42)</td>
</tr>
<tr>
<td>Borderline C (AV)</td>
<td>3 (14)</td>
<td>7 (33)</td>
<td>11 (53)</td>
</tr>
<tr>
<td>NSVA (MV)</td>
<td>8 (19)</td>
<td>3 (7)</td>
<td>31 (73)</td>
</tr>
<tr>
<td>NSVA (AV)</td>
<td>2 (13)</td>
<td>4 (25)</td>
<td>10 (62)</td>
</tr>
<tr>
<td>NSVA (MV + AV)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>4 (100)</td>
</tr>
<tr>
<td>Normal</td>
<td>19 (6)</td>
<td>5 (2)</td>
<td>301 (93)</td>
</tr>
</tbody>
</table>

Conclusions: Some children with Borderline RHD or NSVAs progressed but this was not invariable and a proportion improved. AV changes were not independently associated with progression, and were more likely to improve, suggesting more intensive follow-up should focus on MV changes. The counter-intuitive effect of secondary prophylaxis on the odds of progression and regression is likely to reflect the selective use of this in those deemed by clinicians to be at highest risk of RHD.

Acknowledgement/Funding: Supported by the National Health and Medical Research Council (Australian Government)

P1614 | BEDSIDE

Adverse effect of aortic insufficiency after TAVI on short term outcome in patients with renal impairment

M. Posser1, J. Vontobel2, C. Zindel1, E.W. Hohy3, S.F. Staempfli1, M. Zuber1, F. Niedipspach1, P.A. Kaufmann1, N. Niemann1, F.C. Tanner1, 1University Heart Center, Zurich, Switzerland; 2University Hospital Zurich, Nuclear Medicine, Zurich, Switzerland

Purpose: To assess the effect of aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI) on short term outcome in patients with impaired kidney function.

Methods: Short term outcome was assessed in 546 patients (mean age 81.9±7.7 years) who underwent TAVI for severe native aortic valve stenosis. The main endpoint was defined as a combined early safety endpoint at 30 days according to the valve academic research consortium-2 (VARC-2) criteria. Post-procedural transhoracic echocardiography was performed in each patient and AR was classified as none/mild versus moderate/severe. Univariate and multivariate logistic regression analyses to evaluate predictors of the early safety endpoint were then performed in groups with none/mild (estimated glomerular filtration rate [eGFR] >30ml/min/1.73m²) and patients with eGFR <30ml/min/1.73m² (95 patients [11%]) reduction in kidney function.

Results: The early safety endpoint occurred in 88 patients [16%]. Moderate/severe AR after TAVI was present in 66 patients (12%), with 60 patients (12%) having an eGFR >30ml/min/1.73m² versus 6 patients (10%) exhibiting an eGFR <30ml/min/1.73m². In patients with eGFR >30ml/min/1.73m², hemoglobin [per 1 g/L increase: OR (odds ratio) 0.993, 95% CI (confidence interval) 0.988–0.999; p=0.016] and NT-proBNP (per 1000 ng/L increase: OR 1.000, 95% CI 1.000–1.000; p=0.016) before intervention were the only independent predictors of the early safety endpoint at multivariate analysis. In contrast, in patients with eGFR <30ml/min/1.73m², moderate/severe AR was the only independent predictor of the early safety endpoint (OR 7.591, 95% CI 1.144–43.962), independently of hemoglobin and NT-proBNP.

Conclusion: The development of moderate/severe AR after TAVI independently predicts the early safety endpoint in patients with moderate/severe reduction in kidney function, but not in patients with normal or mildly reduced kidney function.

P1615 | BEDSIDE

Analysis of the learning curve for transcatheter aortic valve implantation via the transfemoral approach

T. Arai, T. Lefevre, T. Hovasse, H. Benamer, B. Cormier, E. Bouvier, M.C. Morice, B. Chevalier. ICPS - Générale de Santé - Hôpital Privé Jacques Cartier, Massy, France

Purpose: To assess the effect of aortic regurgitation (AR) after transcatheter aortic valve implantation (TAVI) on short term outcome in patients with impaired kidney function.

Methods: Short term outcome was assessed in 546 patients (mean age 81.9±7.7 years) who underwent TAVI for severe native aortic valve stenosis. The main endpoint was defined as a combined early safety endpoint at 30 days according to the valve academic research consortium-2 (VARC-2) criteria. Post-procedural transhoracic echocardiography was performed in each patient and AR was classified as none/mild versus moderate/severe. Univariate and multivariate logistic regression analyses to evaluate predictors of the early safety endpoint were then performed in groups with none/mild (estimated glomerular filtration rate [eGFR] >30ml/min/1.73m²) and patients with eGFR <30ml/min/1.73m² (95 patients [11%]) reduction in kidney function.

Results: The early safety endpoint occurred in 88 patients [16%]. Moderate/severe AR after TAVI was present in 66 patients (12%), with 60 patients (12%) having an eGFR >30ml/min/1.73m² versus 6 patients (10%) exhibiting an eGFR <30ml/min/1.73m². In patients with eGFR >30ml/min/1.73m², hemoglobin [per 1 g/L increase: OR (odds ratio) 0.993, 95% CI (confidence interval) 0.988–0.999; p=0.016] and NT-proBNP (per 1000 ng/L increase: OR 1.000, 95% CI 1.000–1.000; p=0.016) before intervention were the only independent predictors of the early safety endpoint at multivariate analysis. In contrast, in patients with eGFR <30ml/min/1.73m², moderate/severe AR was the only independent predictor of the early safety endpoint (OR 7.591, 95% CI 1.144–43.962), independently of hemoglobin and NT-proBNP.

Conclusion: The development of moderate/severe AR after TAVI independently predicts the early safety endpoint in patients with moderate/severe reduction in kidney function, but not in patients with normal or mildly reduced kidney function.
of 30-day mortality and 1-year mortality significantly decreased in the late experience group (20% to 6%, p=0.033; 38% to 15%, p=0.040, respectively). The groups including both valves were also analyzed after propensity-matching (early [n=52] vs late [n=52]). This model showed also that 30-day and 1-year mortality was significantly lower in the late experience group (13% to 1%, p=0.028; 34% to 20%, p=0.042, respectively).

Conclusions: Appropriate level of experience is needed to reduce the complication rate and mortality in TF-TAVI.

P1616 | BEDSIDE
Platelet size and bleeding following transcatheater aortic valve implantation
1 Independent Public Central Clinical Hospital, 1st Department of Cardiology, Medical University of Warsaw, Warsaw, Poland; 2 Independent Public Central Clinical Hospital, Department of Cardiosurgery, Medical University of Warsaw, Warsaw, Poland; 3 Independent Public Central Clinical Hospital, 2nd Department of Anesthesiology and Intensive Therapy, Medical University of Warsaw, Warsaw, Poland

Background: Bleeding complications are frequent and independently predict mortality after transcatheater aortic valve implantation (TAVI).

Purpose: To determine the correlation between baseline platelet indices and bleeding complications in patients undergoing TAVI.

Methods: Platelet indices: platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT) were measured in 110 consecutive patients on the day preceding TAVI. Any bleeding, major/life-threatening bleeding and need for transfusion were assessed according to VARC-2 criteria. In-hospital follow-up was performed.

Results: ROC analysis revealed only MPV distinguished patients with and without any bleeding (area under the curve [AUC] 0.629, 95% confidence intervals [CI] 0.531–0.719, p=0.0342), major/life-threatening bleeding and need for transfusion were assessed according to VARC-2 criteria. In-hospital follow-up was performed. ROC analysis revealed only MPV distinguished patients with and without any bleeding (area under the curve [AUC] 0.629, 95% confidence intervals [CI] 0.531–0.719, p=0.0342), major/life-threatening bleeding and need for transfusion were assessed according to VARC-2 criteria.

Discussion: (1) Do the data acquired from randomized studies and registers justify expansion of the procedure to include younger and healthier patients? (2) Is the transfemoral approach superior to the transapical approach with regard to mortality and periprocedural complications? Against this background we examined the mortality and morbidity of all patients who received an isolated conventional, transapical or transforaminal valve implantation in accordance with the criteria of the Valve Academic Research Consortium (VARC)-2.

Conclusion: Platelet size and bleeding following transcatheater aortic valve implantation (TAVI) is an established method without substantial complications. Platelet size and bleeding following TAVI is a well-known risk factor for the development of complications. However, the mechanism of platelet size and bleeding following TAVI is not fully understood. We hypothesized that platelet size and bleeding following TAVI is a marker of the extent of injury to the heart and other organs. To test this hypothesis, we performed a retrospective analysis of the data from a large cohort of patients who underwent TAVI.

Methods: We retrospectively evaluated all first-time TAVIs performed for predominant aortic stenosis using the balloon-expandable Edwards Sapien XT and Sapien 3 devices from March 2012 to July 2014. SAPIEN 3 was used for the entire study period.

Results: We analyzed data from 110 consecutive patients who underwent TAVI. Of these patients, 76 had undergone transfemoral implantation (Group 1) and 78 had undergone transapical implantation (Group 2). There was no difference in the rate of post deployment balloon dilatation (2.6% in Group 1 and 2.6% in Group 2). In three cases there was difficulty in crossing the valve without BAV, partial inflation of the distal balloon tip within the TAVI valve enabled crossing of the native aortic valve without subsequent deployment problems. There was a significant reduction in total procedure time in patients in Group 2 vs Group 1 (104.9 ± 125.5 min, p=0.012) and fluoroscopic time (12.9 ± 18.4 min, p<0.001). There were no differences between the 2 groups in terms of the number of solid, gaseous or total emboli on TCD (all p>0.05).

Conclusion: Balloon-expandable TAVI valves can be implanted transfemorally without BAV, with no reduction in VARC-2 defined success or safety. Without performing a TAVI there is a significant reduction in the total procedure time and fluoroscopic time. There is no significant difference in the rate of embolisation on TCD.
tients with abnormal hs-cTnT values (n=85), interventricular septal wall thickness (IVSWT) and maximum LV wall thickness (MLVWT) at baseline were thicker than in patients with normal hs-cTnT values. On the other hand, age at evaluation, LV end-diastolic diameter (LVEDD) and fractional shortening were not different between the two groups. During follow-up periods of 6.4±2.8 and 6.1±2.8 years in the abnormal hs-cTnT group and in the normal hs-cTnT group, respectively (p=0.482), IVSWT and MLVWT became significantly thinner (IVSWT: 16.7±4.6 mm to 15.6±4.0 mm, p=0.001; MLVWT: 20.9±4.5 mm to 19.0±4.1 mm, p=0.001) and LVEDD became larger (46.7±7.4 mm to 46.6±8.0 mm, p=0.001) in the abnormal vs the normal hs-cTnT group. On the other hand, IVSWT, MLVWT and LVEDD did not change significantly in the normal hs-cTnT group. Furthermore, patients with progression into end-stage phase of HCM characterized by LV systolic dysfunction were more frequently seen in the abnormal hs-cTnT group than in the normal hs-cTnT group (19.5% versus 2.5%, p=0.009).

Conclusions: An abnormal serum concentration of hs-cTnT was related to progression of LV remodeling in patients with HCM.

P1620 | BEDSIDE
The course of cardiac sarcoidosis with delayed vs early steroid therapy in patients with atioventricular block as the first clinical manifestation

R. Kandolin, J. Lehtonen, M. Kupari. Helsinki University Central Hospital, Heart and Lung Center, Helsinki, Finland

Introduction: Atrioventricular block (AVB) is the most common form of presentation in cardiac sarcoidosis (CS). AVB being the solitary manifestation, the underlying CS may remain undiagnosed and untreated for variable periods.

Purpose: We set out to study the progress of CS in patients receiving a PM for AVB but initially missing steroid therapy due to delayed diagnosis of CS.

Methods: In a nationwide 25-year CS study in Finland, a PM was implanted in 45 patients due to AVB as the first manifestative CS symptom. Follow-up from PM implantation to CS diagnosis and start of steroid therapy varied from 0 to 129 months. The delay was ≥3 months in 27 patients (=late steroid treatment group) and <2 months in 18 patients (=early steroid treatment group). Adverse cardiac events were recorded until 1 start of steroids in the late treatment group and 2/4/2014 in all.

Results: In the late steroid treatment group (N=27), the median time from PM implantation to start of steroids was 22 (3–129) months. During the steroid-free period, representing the natural course of CS, 1 patient died, 1 underwent transplantation, 2 had suVT and 7 developed new systolic LV dysfunction. Event free Kaplan-Meier survival was 89% at 1 year and 61% at 5 years. There was no difference in age, gender or EF between the early and late steroid treatment groups. During the entire follow-up until 2014, 9/18 patients receiving steroids early had an adverse event vs 17/27 patients receiving steroids late (i.e. after a median delay of nearly 2 years). There was no difference in the outcome between the two groups (Figure, log rank p=0.821).

Conclusions: The natural course of CS presenting with AVB is characterized by frequent progression to LV dysfunction and arrhythmic events. Starting steroids early vs late appears not to influence the outcome.

Acknowledgement/Funding: Finnish government study grant

P1621 | BEDSIDE
Early arrhythmic events in idiopathic dilated cardiomyopathy

P. Losurdo1, D. Stolfi1, G. Barbati1, M. Gobbo1, M. Gigli1, B. Pinamonti1, M. Zecchin1, G. Finocchiaro2, M. Merlo1, G.F. Sinagra1.

1 University Hospital Rinuitt, Department of Cardiology, Trieste, Italy; 2 St George’s University Hospital, London, United Kingdom

Background: Dilated cardiomyopathy (DCM) generally affects young individuals and is characterized by an unpredictable prognosis with a not negligible risk of sudden cardiac death/major ventricular arrhythmias (SCD/MVAs) also in the first period after diagnosis.

Purpose: The aims of the study were to provide an insight into the prevalence and characterization of patients with early SCD/MVAs and to identify possible reliable indicators of early SCD/MVAs in a large cohort of DCMs.

Methods and results: From 1988 to 2014 952 patients with DCM were consecutively included in the Heart Muscle Disease Registry of Trieste. Globally, 20 patients (2.1% of the overall population) experienced SCD/MVAs within the first 6 months after enrollment (primary end-point). At baseline, they showed a worse functional class (NYHA II-IV 42% vs 22%, p<0.038), a longer QRS complex duration (127±14 ms vs 108±33 ms, p=0.013) and a greater indexed left ventricular end-systolic volume (LVESVI) (22±49 ml/m² vs 67±34 ml/m², p=0.049). The rate of betablockers administration was significantly lower compared to patients without early SCD/MVAs (59% vs 83%, p=0.008), mostly due to hemodynamic intolerance. At multivariate analysis, LVESVI (OR 1.01, 95% CI 1.00–1.02, p=0.043) and QRS complexity (OR 1.01, 95% CI 1.00–1.03, p=0.015) were significantly associated with the primary end-point, whereas betablockers demonstrated a protective effect (OR 0.69, CI 0.48–0.93, p=0.006).

Conclusions: In patients with DCM, the risk of major arrhythmic events in the first phase of the disease is not negligible. Baseline LVESVI, QRS duration and intolerance to betablockers therapy might be useful tools in the arrhythmic early risk assessment of DCM patients.

P1622 | BEDSIDE
Secondary forms of Takotsubo Cardiomyopathy, a whole different prognosis

I. Nunez-Gil1, M. Almendro Delia2, M. Andres3, A. Sionis4, A. Martin5, T. Bastante6, J.G. Cordoba Soriano7, J.A. Linares Vicence8, S. Gonzalez Sucarrats8, O. Fabregat Andres5,1, Hospital Clinico San Carlos, Madrid; 2Hospital Virgen de la Macarena, Sevilla; 3University Hospital Vall d’Hebron, Barcelona; 4Hospital de la Santa Creu i Sant Pau, Barcelona; 5Hospital Clinico Universitario, Salamanca; 6University Hospital De La Princesa, Madrid; 7 Albacete University Hospital, Albacete; 8Clinical University Hospital Lozano Blesa, Zaragoza; 9Hospital Arnau de Vilanova, Leida; 10University General Hospital of Valencia, Valencia, Spain

Background: Takotsubo syndrome (TKS) usually mimics an acute coronary syndrome. However, several clinical forms have been reported. Our aim was to assess if different stressful triggers had prognostic influence on TKS, and to establish a working classification.

Methods: We performed an analysis including patients with TKS between 2003 and 2013 from our prospective local database and the National Registry (RE-TAKO), fulfilling Mayo criteria. Patients were divided in two groups regarding their potential triggers: 1) None/pyschic stress as “primary forms” and 2) Physical factors (asthma, surgery, trauma, etc.), as “secondary forms”.

Results: Finally, 328 patients were included, 90.2% women, mean age of 69.7 years. Patients were divided, as primary-TKS (n=265) and 63 secondary-TKS. Age, gender, previous functional class and cardiovascular risk profile displayed no differences between groups, before admission. However, primary-TKS suffered as main complaint chest pain (89.4% Vs. 50.7%, p<0.001) and is characterized by an unpredictable prognosis with a not negligible risk of sudden cardiac death/major ventricular arrhythmias (SCD/MVAs) also in the first period after diagnosis.

Conclusion: Secondary Takotsubo syndrome could present or mark worse short and long term prognosis in terms of mortality, recurrences and readmissions. We propose a simple working-nomenclature on TKS.

P1623 | BEDSIDE
High prevalence of N271I founder mutation in TNNT2 gene detected by NGS in a galician cohort cause hypertrophic cardiomyopathy associated with a benign course


1 A Coruña Biomedical Research Institute, A Coruña, Spain; 2 University Hospital Complex A Coruña, A Coruña, Spain; 3 Health in Code, A Coruña, Spain

Background: Hypertrophic Cardiomyopathy (HCM) is a genetically heteroge-
neous disease. N271I missense mutation in TNNT2 is highly prevalent in Galicia (Spain).

**Purpose:** To define the clinical spectrum of N271I mutation, and its prognosis compared with similar mutations in TNNT2 gene.

**Methods:** HCM probands were screened by NGS with a panel of 12 main genes related to the disease. A common haplotype was found, suggesting a founder effect, and supporting the hypothesis of a common ancestor. The penetration of HCM in carriers of N271I was near 80%, but dependent on age. The degree of hypertrophy was moderate (mean 17.76 mm) and none of the patients had severe hypertrophy (range 13–27 mm). Survival curves showed a clear better prognosis of N271I compared with other pathogenic missense mutations in TNNT2 (log rank test p < 0.001).

**Conclusion:** N271I mutation in TNNT2 gene is highly prevalent in Galician population, having a founder effect in this region. The clinical course of HCM is relatively benign, in contrast with other missense mutations in TNNT2. This illustrates the importance of evaluating every mutation one by one, and the need to be cautious when trying to generalize prognostic issues in a particular gene.

---

**P1625 | BEDSIDE**

**Expression of neural cell adhesion molecule (NCAM) in dilated cardiomyopathy is associated with inflammation and cardiomyocyte hypertrophy**

M. Noutsias1, H.P. Schultheiss2, K. Ostermann2.

1 University Hospital Jena, Department of Cardiology, KIMI, Jena, Germany; 2 Charite - University Medicine, Campus Benjamin Franklin, Berlin, Germany

**Background:** Intramyocardial inflammation is linked to the pathogenesis of dilated cardiomyopathy (DCM). NCAM (neural cell adhesion molecule) is expressed during cardiac organogenesis, but is absent in healthy adult cardiomyocytes. Inflammation can induce hypertrophy and re-expression of embryologically confined genes. We investigated NCAM expression in DCM hearts, and its association with inflammatory infiltrates (CD18, LFA-1, Mac-1, CD3, TNFα), adhesion molecules linked to inflammation: ICAM-1 and CD29), and hypertrophy in endomyocardial biopsies (EMB) from DCM patients.

**Methods:** EMB from DCM patients (n=85; LVEF < 45%) and controls (n=17) were immunostained. Immunostaining was scored by digital image analysis.

**Results:** The autotopic controls did not reveal any NCAM immunoreactivity. In contrast, NCAM expression on the intercalated discs and the sarcolemma was identified in n=46 (54%) of the DCM EMBs. The DIA quantified area fraction (AF) of NCAM was quantified by digital image analysis.

**Figure:** NCAM expression correlated with infiltrates (CD18, LFA-1, Mac-1, CD3, TNFα), with the expression of CD29 and ICAM-1, and the MCD (Spearman rho: 0.52, p < 0.001; Figure).

**Conclusion:** NCAM is de novo expressed in 54% of DCM hearts, and is associated with inflammation and the MCD. These data indicate that inflammation might be involved in the induction of the embryologically confined NCAM, and of cardiomyocyte hypertrophy in DCM. Thus, NCAM might be a useful marker in EMB evaluation indicating both inflammatory and hypertrophy pathways.

**Acknowledgement/Funding:** This study was supported by the Deutsche Forschungsgemeinschaft through the SFB TR19 "Inflammatory Cardiomyopathy" (SFB TR19).

---

**P1626 | BEDSIDE**

**Arrhythmic risk assessment in family members with arrhythmogenic cardiomyopathy associated desmosomal mutations**


1 Department of Cardiology, A. Protonotarios Medical Center of Naxos, Naxos, Greece; 2 University of Athens Medical School, 1st Department of Cardiology, Athens, Greece; 3 University College London and The Heart Hospital, University College London Hospitals Trust, Institute of Cardiovascular Science, London, United Kingdom; 4 Nicosia General Hospital, Department of Cardiology, Nicosia, Cyprus

**Purpose:** Arrhythmogenic Cardiomyopathy (ACM) is a genetically determined disorder, mostly caused by mutations in genes encoding desmosomal proteins. Following the identification of the causal gene mutation in the proband, cascade genetic screening of the family members commences, leading to the identification of mutation carriers. Arrhythmic risk assessment of these individuals is less well studied but crucial for clinical decision making. We aimed to identify characteristics associated with increased arrhythmic risk among family members in a cohort of consecutive ACM families harboring desmosomal mutations.

**Methods:** Thirty-nine consecutive ACM families harboring desmosomal mutations were studied. The families were 13 of PKP2, 14 of JUP, 6 of DSC2, and 6 of DSP; one of the DSP families presented digenic heterozygosity with PKP2 mutation. Cascade genetic screening identified 66 family members carrying the causal mutation. A clinical work-up including history, physical examination, 12-lead ECG was performed. The arrhythmic outcome was defined as the first event during cardiac organogenesis, but is absent in healthy adult cardiomyocytes. Inflammation can induce hypertrophy and re-expression of embryologically confined genes. We investigated NCAM expression in DCM hearts, and its association with inflammatory infiltrates (CD18, LFA-1, Mac-1, CD3, TNFα), adhesion molecules linked to inflammation: ICAM-1 and CD29), and hypertrophy in endomyocardial biopsies (EMB) from DCM patients.

**Results:** The autotopic controls did not reveal any NCAM immunoreactivity. In contrast, NCAM expression on the intercalated discs and the sarcolemma was identified in n=46 (54%) of the DCM EMBs. The DIA quantified area fraction (AF) of NCAM was quantified by digital image analysis.

**Figure:** NCAM expression correlated with infiltrates (CD18, LFA-1, Mac-1, CD3, TNFα), with the expression of CD29 and ICAM-1, and the MCD (Spearman rho: 0.52, p < 0.001; Figure).

**Conclusion:** NCAM is de novo expressed in 54% of DCM hearts, and is associated with inflammation and the MCD. These data indicate that inflammation might be involved in the induction of the embryologically confined NCAM, and of cardiomyocyte hypertrophy in DCM. Thus, NCAM might be a useful marker in EMB evaluation indicating both inflammatory and hypertrophy pathways.

**Acknowledgement/Funding:** This study was supported by the Deutsche Forschungsgemeinschaft through the SFB TR19 “Inflammatory Cardiomyopathy” (SFB TR19).

---

**P1627 | BEDSIDE**

**Prognosis of left ventricular non-compaction cardiomyopathy - a multicentre study**

D.A. Moreira1, J. Almeida2, K. Domingues2, N. Marques2, I. Cruz2, L. Teles4, B. Picarra5, S. Leao5, R. Faria5, O. Azedo5 on behalf of SUNSHINE group.

1 Hospital Sao Teotonio, Viseu, Portugal; 2 Hospital Center of Vila Nova de Gaia-Espinho, Vila Nova de Gaia, Portugal; 3 Hospital of Santarem, Santarem, Portugal; 4 Faro Hospital, Faro, Portugal; 5 Hospital Garcia de Orta, Almada, Portugal; 6 Hospital Espirito Santo de Evora, Evora, Portugal; 7 Hospital Center of Tras-os-Montes and Alto Douro, Vila Real, Portugal; 8 Alto Ave Hospital Center, Guimarães, Portugal

**Introduction:** Left ventricular non-compaction cardiomyopathy (LVNC) may lead to left ventricular (LV) systolic dysfunction. Previous studies show that heart failure is one of the main clinical manifestations of LVNC, along with embolic events and arrhythmias. However, natural history of LVNC is not clearly established and current knowledge come from small series.

**Aim:** To characterize a Portuguese population of patients with LVNC and to determine the prognosis in the medium term follow-up.

**Methods:** Portuguese multicentre study involving 11 hospital centers and including all patients diagnosed with LVNC. We evaluated the clinical, electrocardio-
graphic, echocardiographic and cardiac MRI data. We evaluated the medium term prognosis in terms of heart failure, ejection, arrhythmias and death.

Results: We included 81 patients with LVNC, 58% males, with mean age 46±20 years. Symptoms were present in 48% of patients, and dyspnea (37%) and palpitations (27%) were the most common symptoms. Diagnosis of LVNC was established by echocardiography in 90% of patients. The average LV ejection fraction was 47±16%. Mitral regurgitation was detected in 15% of cases. Most patients were in sinus rhythm (89%). A history of atrial fibrillation was present in 10% of the patients and non-sustained ventricular tachycardia in 11% of the cases. Delayed gadolinium enhancement on cardiac MRI was found in 31% of patients submitted to cardiac MRI. Family history of LVNC was identified in 7% of cases. In the medium term follow-up (mean follow up of 4 years), patients with LVNC presented heart failure in 33.3%, arrhythmia in 14.8%, ejection in 7.4% and mortality in 0.4% of cases.

Conclusions: In this Portuguese population of patients with LVNC the prognosis was generally good with only 2.4% mortality at 4 years. Heart failure was present in one third of the cases and was the most frequent clinical complication in the medium term follow up.

P1627 | BEDSIDE

Predictors of left ventricular systolic function recovery in the first 15 days after hospital admission in takotsubo cardiomyopathy - a Portuguese multicenter study

K. Domingues 1, C. Lourenco 2, O. Azevedo 3, S. Leao 4, B. Marmelo 5, I. Cruz 6, J. Almeida 7, L. Telles 8, B. Picarra 9, N. Marques 10 on behalf of Grupo SUNSHINE. 1 Hospital of Santarem, Santarem; 2 Hospital Centre do Tâmega e Sousa, Penafiel; 3 Alto Ave Hospital Center, Guimarães; 4 Hospital Center of Trás-os-Montes and Alto Douro, Vila Real; 5 Hospital Sao Teotônio, Viseu; 6 Hospital Garcia de Orta, Almada; 7 Hospital Center of Vila Nova de Gaia/Espinho, Vila Nova de Gaia; 8 University Hospitals of Coimbra, Coimbra; 9 Hospital Espírito Santo de Evora, Evora; 10 Faro Hospital, Faro, Portugal

Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction. The speed of recovery of LV dysfunction is variable. There are not studies determining the predictors of recovery of LV systolic function.

Aim: To identify predictors of LV systolic function recovery in the first 15 days after hospital admission with TC.

Methods: A multicentre study involving inclusion of all patients diagnosed with TC in the last 10 years. Demographic, clinical, electrocardiographic and echocardiographic data were analyzed to found which factors are associated with LV systolic function recovery in the first 15 days after hospital admission of TC patients. Multivariate analysis was performed to establish the independent predictors of early recovery of LV systolic function in patients with TC.

Results: We included 165 patients with TC, predominantly women (89.1%). The mean age was 66±14 years. At hospital discharge, 44.8% of patients have had complete recovery of LV systolic function and complete recovery had occurred in 50.9% of cases at 15 days after hospital admission.

In patients with TC in the first 15 days after admission, the following factors are associated with LV systolic function recovery in the first 15 days after admission: absence of a history of angina (97.6% vs 81.5%, p=0.001), the presence of a physical precipitating factor (23.8% vs 11.1%, p=0.032), the absence of ST-segment depression (96.4% vs 87.7%, p=0.036) and the absence of Q-waves in the initial ECG (88.1% vs 74.1%, p=0.032), the absence of Q-waves in the initial ECG (88.1% vs 74.1%, p=0.032), the absence of ST-segment depression (96.4% vs 87.7%, p=0.036) and the absence of Q-waves in the initial ECG (88.1% vs 74.1%, p=0.032), the absence of ST-segment depression (96.4% vs 87.7%, p=0.036). At hospital discharge, 44.8% of patients have had complete recovery of LV systolic function.

Conclusion: Complete LV systolic function recovery in TC patients occurs in half of the cases up to 15 days after hospital admission. This study revealed that the absence of a history of angina was an independent predictor of LV systolic function recovery in the first 15 days after hospital admission with TC.

P1628 | BEDSIDE

Ethnic variation in hypertrophic cardiomyopathy

O. Watkinson, C. Guttman, C. O'Mahoney, M. Torne, P. Elliott. The Heart Hospital, Inherited Cardiovascular Disease, London, United Kingdom

Hypertrophic cardiomyopathy (HCM) is a genetic disorder with significant variability defined by echocardiogram in 90% of patients. Clinical studies to date have enrolled predominantly Caucasian patients, but racial background may have an important effect on the disease course. In this study we have used a large single centre population to examine the effect of racial group on clinical phenotype at presentation and their long term outcomes. Further work is required to try and understand the different genetic and social factors which lead to these different disease patterns.

P1629 | BEDSIDE

Phenotypic variation of hypertrophic cardiomyopathy caused by the 3330+2T>G mutation in myosin binding protein-C in 303 Amish individuals

M. Muggenthaler1, K. Zakhia2, H. Lever3, M. Desai2, B.A. Chioza4, H. Cross5, E.R. Behr1, S. Sharma1, A.H. Crosby3,1 St George's University of London, London, United Kingdom; 2 Cleveland Clinic Foundation, Cleveland, United States of America; 3 Peninsula Medical School, Exeter, United Kingdom; 4 University of Arizona, Tucson, United States of America

Previous studies describing disease expression in hypertrophic cardiomyopathy (HCM) have been characterized by small sample size and number of individuals with identical mutations. The Amish communities in North America are of Western European descent and form a closed founder population with homogeneous lifestyle, large families and extensive genealogical records which make them conducive to the investigation of genetic disorders. We identified a frame-shift founder mutation in MYBPC3 (3330+2T>G) responsible for HCM occurring at very high frequency amongst the Amish. The aim of this study was to investigate disease expression in this unique population.

We identified 303 carriers of the MYBPC3 mutation 3330+2T>G via cascade screening in affected families. All 303 carriers interlink into one extensive pedigree. Carriers were assessed with Electrocardiogram and Echocardiogram and a subset also with 24 hour holter monitors. Of the cohort, data of 170 mutation carriers (50% [n=85] male) has been analyzed as of 2014. Mean age was 43±17.4 (range: 18-80) years in males and 41.5±15.9 (range 18-80) years in females. 24.7% of the male [n=21] and 9.4% of the female [n=8] individuals had known HCM prior to participating in our study. 11.7% [n=20] of individuals had a history of sudden cardiac death in a first degree relative. Different types of HCM were observed (n=50) more likely to receive a pacemaker (Annual rate >1%/year). We also observed a trend to fewer ICDs (Annual rate W 0.4%, B 0.4%, A 0.2%, p=0.2), but there were no significant differences in a secondary combined end-point of sudden cardiac death, aborted sudden death, and appropriate ICD therapy (Annual rates W 3.5%, B 2.5%, A 4.3% p=0.18). Rates of septal reduction therapy were similar across groups (Annual rates W 3.0%, B 3.1%, A 2.2% p=0.2).

In this large single centre study of hypertrophic cardiomyopathy, there were significant differences between racial groups in terms of their clinical phenotype at presentation and their long term outcomes. Further work is required to try and understand the different genetic and social factors which lead to these different disease patterns.

P1630 | BEDSIDE

Arrhythmias in patients with hypertrophic cardiomyopathy with apical hypertrophy

M. Rosca1, A. Calin1, A. Mateescu1, P. Varga1, C.C. Beladan1, M. Gurzun1, E.R. Behr1, S. Sharma1, A.H. Crosby3,1 St George's University of London, London, United Kingdom; 2 Cleveland Clinic Foundation, Cleveland, United States of America; 3 Peninsula Medical School, Exeter, United Kingdom; 4 University of Arizona, Tucson, United States of America

In this DNA analysis, we identified the heterogeneity and high frequency amongst the Amish. The aim of this study was to investigate disease expression in this unique population.

We identified 303 carriers of the MYBPC3 mutation 3330+2T>G via cascade and interlink into one extensive pedigree. Carriers were assessed with Electrocardiogram and Echocardiogram and a subset also with 24 hour holter monitors. Of the cohort, data of 170 mutation carriers (50% [n=85] male) has been analyzed as of 2014. Mean age was 43±17.4 (range: 18-80) years in males and 41.5±15.9 (range 18-80) years in females. 24.7% of the male [n=21] and 9.4% of the female [n=8] individuals had known HCM prior to participating in our study. 11.7% [n=20] of individuals had a history of sudden cardiac death in a first degree relative. Different types of HCM were observed (n=50) more likely to receive a pacemaker (Annual rate >1%/year). We also observed a trend to fewer ICDs (Annual rate W 0.4%, B 0.4%, A 0.2%, p=0.2), but there were no significant differences in a secondary combined end-point of sudden cardiac death, aborted sudden death, and appropriate ICD therapy (Annual rates W 3.5%, B 2.5%, A 4.3% p=0.18). Rates of septal reduction therapy were similar across groups (Annual rates W 3.0%, B 3.1%, A 2.2% p=0.2).

In this large single centre study of hypertrophic cardiomyopathy, there were significant differences between racial groups in terms of their clinical phenotype at presentation and their long term outcomes. Further work is required to try and understand the different genetic and social factors which lead to these different disease patterns.

CARDIOMYOPATHIES II

P1631 | BEDSIDE

Right ventricular wall thickness as a correlate of malignant ventricular arrhythmias in patients with hypertrophic cardiomyopathy

M. Rosca1, A. Calin1, A. Mateescu1, P. Varga1, C.C. Beladan1, M. Gurzun1, E.R. Behr1, S. Sharma1, A.H. Crosby3,1 St George's University of London, London, United Kingdom; 2 Cleveland Clinic Foundation, Cleveland, United States of America; 3 Peninsula Medical School, Exeter, United Kingdom; 4 University of Arizona, Tucson, United States of America

Background: Sudden cardiac death (SCD), the most feared complication in pa-
Purpose: To identify independent predictors of ventricular arrhythmias and to assess their relationship with the newly recommended HCM Risk-SCD Score.

Methods: We have prospectively enrolled 91 pts (52±17 years, 39 men) with HCM: 15 pts with non-sustained ventricular tachycardia during ambulatory 24 hours ECG monitoring (NSVT-) and 76 pts without (NSVT+). A comprehensive echocardiogram was performed in all pts, including measurement of maximum LV wall thickness (LWVT) and RV free wall thickness (RWVT). Global longitudinal LV strain (GLS) was assessed by speckle tracking echocardiography. HCM Risk-SCD Score was calculated based on the ESC 2014 guidelines on HCM.

Results: Pts carrying frameshift mutations had significantly higher values of LWVT (23.6±6.5 vs 19.8±4.1 mm, p=0.005) and RWVT (8.4±2.6 vs 6.0±1.5 mm, p<0.001), lower values of GLS (-12.6±2.8 vs -14.4±3.2%, p=0.04), and tended to be younger (46±21 vs 54±16 years, p=0.1) than pts NSVT-. There were no significant differences between NSVT+ and NSVT- pts regarding: sex distribution, indexed LV mass (1855±46 vs 172±64 mm²), indexed LA volume (58±16 vs 61±29 ml/m²), E/E' ratio (15±1.66 vs 16±3.65), systolic and diastolic myocardial velocities, severity of dynamic obstruction, cardiovascular risk factors (p>0.05 for all). At multivariable logistic regression analysis, RWVT emerged as the only correlate of NSVT (OR=2.2, 95% CI 1.36 to 3.77, p=0.002). Mean value of Risk-SCD Score was 3.3±2.3% (limits 0.83–15.90%). Twelve pts had an intermediate calculated 5-year risk of SCD (between 4 and 6%) and 9 pts had a high calculated 5-year risk of SCD (>6%). RWVT correlated with HCM Risk-SCD score independently of the parameters included in the risk score calculation (p=0.33, 95% CI 0.21 to 0.61, p<0.001).

Conclusions: In this cohort, RWVT was independently related to the presence of malignant ventricular arrhythmias and increased calculated SCD risk score. Considering these findings, a closer and more careful follow-up of HCM pts with RV hypertrophy seems warranted.

Acknowledgement/Funding: SOPHRD, contract number POSDRU 141531 and Programme Projects Young Scientists 2012, contract number 28329/04.11.2013.
The in-hospital mortality was significantly higher in the p-QRS group than the n-QRS group (22.5% vs 4.2%, log-rank test p<0.0001). Similarly, heart failure (50.0% vs. 24.7%, p<0.001), atrio-ventricular block (14.7% vs. 3.3%, p=0.0011), and ventricular tachycardia or fibrillation (13.9% vs. 1.7%, p<0.0001) were significantly higher in the p-QRS group.

On multivariate Cox proportional hazard model analysis, p-QRSsd was independent predictor of in-hospital mortality (hazard ratio, 3.599–29.433, p<0.001). Aggressive intervention may be required to prevent further deterioration of clinical course in TC admitted with p-QRSsd.

P1634 | BEDSIDE
Cardiovascular impact of tafamidis in familial amyloidotic polyneuropathy: experience of a center

Introduction: The prevalence of transthyretin-familial amyloidotic polyneuropathy (TTR-FAP) in Portugal is estimated to be superior to 1 to 5 individuals and all the cardiovascular structures can be affected by amyloid infiltration. Liver transplantation (LT) is still the standard of care in symptomatic patients, but recently a new oral drug, tafamidis, that acts as a TTR stabilizing agent has shown promising results. LT besides being much more invasive, is not always available and doesn’t effectively prevent the development of cardiac involvement.

Our aim was to evaluate the cardiovascular (CV) impact of tafamidis in patients with FAP.

Methods and results: We performed a retrospective study enrolling 700 patients with FAP from our center, 162 of which (23.1%) mediated with tafamidis. 51.2% were female with a mean age of 37.8±11 years and the mutation Val30Met predominated (98.1%).

Clinical presentation was, in the majority, with neurological (75%) symptoms and only 3% presented with cardiac signs or symptoms. The mean age of symptoms onset was 34.7±10.5 years and the drug was initiated, on average, 2.8±3.3 years after symptoms onset.

Before treatment, 29% had CV symptoms and 91% were in sinus rhythm (atrial fibrillation was found in 2%). The prevalence of rhythm disorders was: first-degree atrioventricular (AV) block in 20%; Mobitz I second-degree AV block in 2.5%; Mobitz II second-degree AV block and complete AV block in 1.2%. Left anterior fascicular block was found in 12%; left bundle branch block in 2% and right bundle branch block in 1.2%; finally poor R-wave progression was present in 10%, low QRS voltage in 14%, pseudo-infarct Q waves in 8% and left ventricular hypertrophy pattern in 2%.

The median follow-up under tafamidis was 12 months (IQR 6–15) with a survival rate of 99% (one death; two drop-outs, one for liver transplantation and one with end-stage kidney failure). After 1 year of treatment CV symptoms improved in 9% patients and deteriorated in 3%; 87% remained unchanged. AV conduction was, in the majority, with FAP.

Conclusion: There were no major cardiovascular changes after 1 year treatment with tafamidis. This data supports the safety of tafamidis, particularly in those with known genes for RCM and aimed to identify and validate a novel cause of the disease.

Methods: Cardiovascular assessment was done in all available family members after the index case was diagnosed with RCM leading to heart transplantation.

Genetic studies via next generation sequencing (NGS) have been performed in the index case followed by segregation analysis in affected family members. Explanted heart tissue has been evaluated by histology and immunohistochemistry.

Functional analysis of mutant FLNC protein was carried out in cultured cells and analyzed by immunocytochemistry and western blot analysis.

Results: The index case, a 13 year old female presented with heart failure requiring heart transplantation at the age of 14 years. Echocardiography confirmed restrictive cardiomyopathy showing a severely impaired diastolic filling pattern, enlarged atria, normal systolic LV-function and wall thicknesses. Subsequently three other family members were diagnosed with signs of RCM including her 2 year old daughter who also required heart transplantation. Genetic studies via NGS found a unique variant in FLNC (p.S1624L) segregating with the disease. Histopathology identified minimal myofiber disarray and cytoplasmic inclusions in muscle fibers. Western blot analysis of mutant FLNC protein revealed reduced amounts of mutant soluble protein compared to wild-type. Finding of a second mutation in a different family with RCM confirmed the involvement of FLNC in the genetic aetiology of RCM.

Conclusion: Mutations in FLNC are a novel cause of familial autosomal dominant RCM. It demonstrates the powerful strategy of NGS to uncover novel genetic causes for familial diseases.

P1636 | BEDSIDE
Filamin C is a novel disease gene for familial restrictive cardiomyopathy
A. Brodehl1, R. Ferrier2, S.C. Greenway1, M.-A. Brundler3, W. Yu3, N. Alvarez1, M. Giuffre1, B. Gerull 1, 1Libin Cardiovascular Institute of Alberta - University of Calgary, Calgary, Canada; 2University of Calgary, Calgary, Canada; 3University of Medical Genetics, Calgary, Canada; Alberta Health Services, Calgary, Canada

Background: Restrictive cardiomyopathy (RCM) is characterized by increased stiffness of the ventricles, impaired diastolic filling with preserved systolic function or both. RCM is a rare condition and caused by mutations in sarcomeric proteins and desmin - genes that have been also associated with other types of cardiomyopathies.

Purpose: In a family with autosomal dominant inherited RCM we excluded mutations in known genes for RCM and aimed to identify and validate a novel cause of the disease.

Methods: Cardiovascular assessment was done in all available family members after the index case was diagnosed with RCM leading to heart transplantation.

Genetic studies via next generation sequencing (NGS) have been performed in the index case followed by segregation analysis in affected family members. Explanted heart tissue has been evaluated by histology and immunohistochemistry. Functional analysis of mutant FLNC protein was carried out in cultured cells and analyzed by immunocytochemistry and western blot analysis.

Results: The index case, a 13 year old female presented with heart failure requiring heart transplantation at the age of 14 years. Echocardiography confirmed restrictive cardiomyopathy showing a severely impaired diastolic filling pattern, enlarged atria, normal systolic LV-function and wall thicknesses. Subsequently three other family members were diagnosed with signs of RCM including her 2 year old daughter who also required heart transplantation. Genetic studies via NGS found a unique variant in FLNC (p.S1624L) segregating with the disease. Histopathology identified minimal myofiber disarray and cytoplasmic inclusions in muscle fibers. Western blot analysis of mutant FLNC protein revealed reduced amounts of mutant soluble protein compared to wild-type. Finding of a second mutation in a different family with RCM confirmed the involvement of FLNC in the genetic aetiology of RCM.

Conclusion: Mutations in FLNC are a novel cause of familial autosomal dominant RCM. It demonstrates the powerful strategy of NGS to uncover novel genetic causes for familial diseases.

P1637 | BEDSIDE
Ventricular Tachycardia is a Significant Prognostic Factor in Patients with Cardiac Sarcoidosis Regardless of Corticosteroid Therapy
N. Serizawa, A. Nomura, Y. Inagaki, A. Yoshida, H. Hattori, N. Kikuchi, A. Suzuki, T. Suzuki, T. Shiga, N. Hagawa. Tokyo Women's Medical University, Department of Cardiology, Tokyo, Japan

Background: Fatal ventricular arrhythmia (VA) is an independent predictor of mortality in cardiac sarcoidosis (CS). However, clinical effects of corticosteroid therapy in such cases are still uncertain.

Methods: From a tertiary center between 1993 and 2014, we examined 102 patients with CS. Patients were followed-up to determine adverse outcomes (sustained ventricular tachycardia (VT), appropriate ICD therapy, or all-cause death).

Results: We enrolled 78 patients who underwent corticosteroid therapy in the present study. Forty four patients (56%) had nonsustained VT and/or sustained VT at diagnosis. During follow-up period of 4.8±5.0 years, 17 patients had fatal VAs and 7 patients died. There was a significant difference in the left ventricular ejection fraction (LVEF) between patients with and without VAs (p<0.01). In group 1 (mean 48 month (from 172 to 72 month)) was 64.7±5.6 mm Hg (p<0.005). In group 2 (mean 94 month (from 172 to 8 month)) was 32.7±5.3 mm Hg (p<0.01). In group 3 (mean 34 month (from 48 to 2 month)) was 28.7±4.6 mm Hg (p<0.01).

Conclusion: Short-term results of DDD pacing, alcohol ablation and surgical myotomy-myectomy are comparable. But hemodynamic results of alcohol septal ablation and surgical myotomy-myectomy have an advantage in long-term period.

D D D pacing didn't show significantly good, stable long-term results.

Cardiomyopathies II 275
justing for LVEF (HR 11.1, 95% CI 2.19–201.4, p=0.001). The median value of LVEF was 43%; 39 patients were classified as preserved EF (>43%) (mean EF 53%), and 39 patients were classified as reduced EF (<43%) (mean EF 32%). The presence of VAs at diagnosis was a significantly worse prognostic factor in patients with reduced EF (log-rank p=0.011), but not in those with preserved EF (Figure).

Conclusions: Ventricular tachyarrhythmia at diagnosis was an independent strong prognostic factor in CS patients with reduced EF after treatment of corticosteroid therapy. A patient with VA and reduced EF should be considered an aggressive anti-arrhythmic therapy such as ICD implantation and/or catheter ablation regardless of corticosteroid therapy.

P1639 | BEDSIDE
Pericutaneous coronary artery interventions in paediatric population: a 15-years experience
Z. Jala1, J.F. Piechaud2, S. Malekzadeh Milano1, Y. Boujdjemline1, M3C Necker, Pediatric cardiology, Paris, France; 2Institut Hospitalier Jacques Cartier, Massy, France
Background: Percutaneous coronary interventions (PCI) are generally performed in adult patients and have provided satisfactory results. However, reported experience in paediatric population is limited.

Purpose: To report indications, interventional techniques and procedural outcomes of PCI in children treated in 2 French institutions.

Methods: Medical records of all children in whom a PCI was attempted since 1998 were systematically reviewed. Diagnostic procedures including coronary angiograms were excluded.

Results: A total of 23 PCI were attempted in 20 patients (mean age 6.6±1.1 years, range 6 days – 17 years). Most common underlying disease was transposition of the great arteries (n=9). Heart failure was the most common symptom leading to coronary intervention (n=8). Thirteen procedures (57%) were performed in emergency. Abnormal electrocardiogram was found in 10 patients. A total of 17/23 coronary obstructions were successfully treated with no immediate residual postintervention stenosis. Initial balloon angioplasty was performed for all lesions (mean balloon size 2.4±0.8-mm), with subsequent stent placement in 11 of 17 lesions (average stent diameter 2.7±0.3 mm). There were 3 peri-procedural deaths. After mean follow-up of 34 months (1 week - 9.6 years) 3 late deaths occurred.

Conclusion: PCI can be used in the paediatric population to restore normal coronary blood flow in a wide range of anatomic conditions and revascularization indications. It may be safe and effective in selected patients with coronary artery stenosis and/or occlusion, but remains technically challenging.

P1640 | BENCH
Selective propensity of bovine jugular vein to bacterial adhesion and impact of percutaneous pulmonary valve implantation procedural steps in genesis of infective endocarditis: an in-vitro study
Z. Jala1, L.G. Galmiche1, D.L. Lebeaux2, O. Villemain1, G. Brugada1, J.M. Ghigo2, C. Beloin2, Y. Boujdjemline1, M3C Necker, Pediatric cardiology, Paris, France; 2Institut Pasteur, Paris, France

Purpose: To assess the impact of PPVI procedural steps on valvular histology, selective bacterial adhesion and leaflet mechanical behaviour.

Methods: Threevalved stents (BJV valved stent, homemade stents with bovine and porcine pericardium) were tested in-vitro in 4 conditions: I) control group, II) crimping, III) crimping + inflation of low-pressure balloon and IV) condition III + post dilatation (high-pressure balloon). For each condition, valvular leaflets (and venous wall sample for BJV stents) were taken for histological analysis, bacterial adhesion using S. aureus and S. sanguinis strains and mechanical uniaxial tests of leaflet valves.

Results: Among BJV valves, incidence of transverse fractures was significantly higher in traumatized samples compared with control group (p<0.05) whereas, incidence and depth of transverse fractures were not statistically different between the 4 conditions for bovine and porcine pericardial leaflets. Bacterial adhesion was higher on bovine jugular venous wall for S. aureus and on BJV valvular leaflets for S. sanguinis in control groups and significantly increased in traumatized BJV valvular leaflets with both bacteria (I vs IV, p<0.05). Bacterial adhesion was lower on bovine pericardial leaflets. Fig. 1 shows bacterial adhesion of S. sanguinis on Melody valve (white arrow).

Figure 1. S. sanguinis adhesion electron microscopy
Conclusion: Valved stent implantation procedural steps induce histological lesions on BJV valvular leaflets. Selective adhesion of S. aureus and S. sanguinis pathogenic strains to BJV tissue was noted at rest and procedural steps of implantation worsened it.

P1641 | BEDSIDE
Cardiac troponin I release after transcatheter closure of the atrial septal defect are related with arrhythmias in the early follow-up
M. Komar, T. Przewlocki, B. Sobien, P. Wilkolek, L. Tomkiewicz-Pająk, P. Prochowicz, U. Gancarczyk, M. Oliszewska, P. Podolec. Jagiellonian University Medical College - John Paul II Hospital - Department of Cardiac & Vascular, Krakow, Poland
Cardiac troponin-I (cTnI) is a very specific and sensitive marker of myocardial injury. A significant increase of cTnI levels after percutaneous atrial septal defect (ASD) closure has been reported. The aim of the study was to identify cTnI rise after percutaneous ASD closure, to determine its prognostic significance and to assess the relationship between supraventricular ectopy (SVE) in early follow-up and procedural increase of cardiac markers.
Methods: Consecutive 295 patients (154 F; 141 M) with a mean age of 46.9±21.2 (16-72) years with ASD who underwent transcatheter closure, were analyzed. The troponin I (TnI) and CK-MB level was measured at 0, 8, 16 and 24 hours after procedure. Holter monitoring was performed on all pts before procedure, 1 and 6 months of follow-up.
Results: The device was successfully implanted in all patients (procedure time 35.1±9.2 (11–53) minutes, fluoroscopy time 11.6±8.0 (9–42) minutes). A significant increase in number of SVE premature beats/24 hours was noted 1 month after procedure: 1180.9±531 (45–9880) compared to baseline data 71.5±53 (0–651) (p<0.0001), after 6 month SVE decreased to 65.8±59 (4–391). In none of the pts TnI was elevated before the procedure. Periprocedurally, the increase of cardiac markers: TnI over 50% beyond reference level was observed in 61.7% of pts, and a two-folded increase of CK-MB levels in 3.4%. There was a significant correlation between SVE premature beats/24 hours 1 month after procedure and periprocedural increase of TnI (r=0.0001; r=91.121).
In addition, cTnI rise was significantly related with the procedure time (p<0.001), fluoroscopy time (p<0.001), and the device size (p<0.001). In multivariable analyzes (including 12 clinical, procedural and anatomical factors) number of SVE ectopy 1 month after ASD closure, procedural time and device size were independent risk factors for TnI rise.
Conclusions: The significant increase of cTnI is noted frequently after the transcatheter closure of ASD not connected with myocardial infection symptoms or other serious clinical complications. The independent risk factors for cTnI rise are: number of the peri-procedural supraventricular ectopy, elongated time of procedure and larger device size. Cardiac troponin release can be an expression of myocardium microdamages, which can also be responsible for the transient supraventricular arrhythmias after transcatheter ASD closure.

P1642 | BEDSIDE
Percutaneous occlusion of vascular malformations in pediatric and adult patients: 20-year experience of a single center
T. Silva1, J.D. Ferreira Martins2, L. Sousa1, A. Flarresga1, C. Trigo Pereira2, R. Cruz Ferreira1, F. Pinto2, Hospital Santa Marta, Department of Cardiology, Lisbon, Portugal, 2Hospital Santa Marta, Department of Pediatric Cardiology, Lisbon, Portugal
Introduction: Vascular malformations (VM) are a diverse group of cardiovascular diseases and percutaneous occlusion is usually the preferred treatment method. We present, to the best of our knowledge, the largest series on different VM in children and adults, using a variety of devices.
Methods: Retrospective analysis of all patients submitted to percutaneous occlusion of VM in our center from 1995 to 2014, excluding patent ductus arteriosus. Clinical and angiographic data including vessels characteristics, procedural details, implanted devices, complications and clinical outcome were analyzed. Procedural success was defined as effective device deployment with none or minimal residual flow. Predictors of procedural failure were determined by multivariate logistic regression.
Results: A total of 122 VM were intervened, corresponding to 71 procedures in a predominately pediatric sample of 46 patients: median (minimum-maximum) 13 years (25 days-74 years), 48 (1.9–80) kg, 57% female and 52% with structural heart disease. Overall, 111 (91%) VM were arterial and 11 (9%) were venous: 53 pulmonary arteriovenous fistulae, 41 aortopulmonary collaterals, 9 systemic veno-venous collaterals, 6 peripheral arteriovenous fistulae, 5 Blalock-Taussig shunts, 4 coronary fistulae, 2 Fontan fenestrations and 2 renal artery aneurisms. Median device size was 4.5 (2.0–16.0) mm. The 139 devices used (1:1±0.66 vessels) were selected according to the lesion anatomy and flow and included 75 vascular, 22 duct occluders, 22 duct occluders and 1 atrial septal defect occluder. Median device size/vehicle size was 1.4 (1.1–3.0) and fluoroscopy time was 16 (7–34) minutes. Success was achieved in 112 (92%) VM: 94 complete occlusion and 18 minimal flow. Of the remaining 10 (8%) a device was not deployed in 6 due to inappropriate support and in 4 the VM was not effectively occluded. Six (4.9%) procedural complications occurred, none resulting in permanent sequelae: two contained vascular tears of aortopulmonary collaterals, medically managed; two cases of inferior limb ischemia, reversed with parenteral anticoagulation; one case of macroscopic hematuria after uncontrolled Blalock-Taussig stent closure (it was occluded in a second procedure); and one coil embolization to the femoral artery (surgically removed). Lower body weight was independently associated with procedural failure (OR 1.05, 95% CI 1.01–1.09).
Conclusions: Percutaneous occlusion was safe and effective for the treatment of different VM in children and adults, using a variety of devices.

P1643 | BENCH
Controlled, uncontrolled, and zero antegrade pulmonary blood flow after bidirectional Glenn procedure: Real-world outcomes in a developing country
H. Zhang, T. Zhang, S.J. Li, S.S. Hu, Fuxi Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Department of Cardiac Surgery, Beijing, China, People’s Republic of China
Background: The low rate of Fontan completion, an agressive policy for maintaining antegrade pulmonary blood flow (AnPBF) during bidirectional Glenn procedure (BDG) was developed for the patients with functional single ventricle.
Purpose: This study investigated the outcomes of BDG and Fontan completion rate in a developing country.
Results: From 2008 to 2013, 368 patients who received a BDG were divided into 3 groups: Group 1 (uncontrolled AnPBF, n=270), Group 2 (controlled AnPBF, n=24) and Group 3 (zero AnPBF and patients with pulmonary atresia, n=74). All the additional systemic to pulmonary shunts were excluded before BDG. Pulmonary artery banding was performed owing to the high central venous pressure in Group 2.
Results: Mean pre-BDG pulmonary artery pressure was 15±3.7 (Group 1), 19±5.9 (Group 2) and 12±2.5 mmmHg (Group 3, respectively). Compared with Group 1 and 2, zero AnPBF resulted in the dramatically decreased pulmonary artery index and arterial oxygen saturation. Although no impaired heart function was observed, echocardiographic study revealed that increased ventricular end-diastolic diameter and aggravated atriovenricular valve regurgitation in Group 1 and 2. Logistic regression analysis revealed systemic right ventricle morphologic abnormality was a risk factor for aggravation of valve regurgitation. Fontan completion rate was 15.2% and the average interval time was 2.2±1.1 years.
Conclusions: Low Fontan-achievement rate was a critical issue in the developing country. Our aggressive strategy offered higher oxygen saturation and more growth of pulmonary artery. However, the uncontrolled AnPBF resulted in the ventricle enlargement and aggravation of valve regurgitation. Therefore, AnPBF should be controlled, especially for the univentricular heart with right ventricle morphology.

P1644 | BEDSIDE
The fetal intracardiac echogenic foci debate: is it over?
A. Doronzo, R. Piazza, L. Neglia, E. Cervesato, G.L. Nicolosi, M. Cassin. Santa Maria degli Angeli Hospital, Pordenone, Italy
Background: Intrauterine echogenic foci (IEF), echogenic images inside the fetal heart, are a sign of congenital heart disease, and often detectable in the second trimester of pregnancy. Several studies demonstrated their benignity, few ones their association with congenital heart diseases (CHD); nevertheless the question remains unclear and gynecologists keep requiring fetal echocardiography after IEF visualization.
Purpose: To evaluate if the identification of prenatal IEF is associated with the development of CHD both prenatally and postnatally.
Methods: 1272 consecutive women underwent fetal echocardiography at a median gestation age of 22±3 weeks. We described localization (left ventricle, right ventricle, biventricular) and number (isolated/double/multiple) of the diagnosed IEF. Infants with IEF during fetal life underwent transthoracic echocardiography (TTE) at a median follow-up of 12±4 months.
Results: Out of 1272 pregnant women 312 (16.6%) IEF were detected. 188 IEF were isolated or double (68%) and 244 multiple (>3). 85% were typically located near or within mitral papillary muscles, 2% within tricuspid subvalvular apparaatus, 5% close to the right ventricle apex and 8% biventricular (near mitral and tricuspid valve). Only 3 IEF cases (1.4%) were associated with CHD: 1 tetralogy of Fallot with pulmonary trunk hypoplasia showed an isolated IEF located near a mitral papillary muscle; 1 atrioventricular canal defect in a Down’s syndrome 3 IEF within mitral papillary muscles and 3 within tricuspid subvalvular apparaatus; 1 pulmonary valve stenosis an isolated IEF within tricuspid subvalvular apparaatus. The post-natal TTE demonstrated in all infants (except that affected by Down’s syndrome) a complete IEF regression within 12 months of life, in absence of residual morphofunctional anomalies.
Conclusions: We reported no significant difference in the prevalence of CHD in newborns with IEF and the ones without IEF (1.4% IEF and 6.6% no IEF group). In spite of the high diagnostic suspicion for CHD suggested by multiple IEF detection, their identification seems to be not associated with an increased risk for CHD in euploid fetuses. Hence, IEF could be explained by...
temporary abnormal processes of myocardial excavation and endocardial tissue fenestration, contributing to the formation of papillary muscles and chordae tendine.

In support of this thesis, ICEF disappear when cardiac structures develop—fenestration, contributing to the formation of papillary muscles and chordae tendine.

**P1646 | SPOTLIGHT**

**Diagnosis and prognosis in nine fetuses with idiopathic constriction of the ductus arteriosus using fetal echocardiography**

X. Gai, Y. He, Y.E. Zhang, X.W. Liu, J.C. Han. Beijing AnZhen Hospital affiliated to Capital Medical University, Department of Ultrasound, Beijing, China, People's Republic of

**Objective:** Most constriction of the ductus arteriosus (DA) in fetuses are secondary to medication or structural lesions. Idiopathic constriction of the DA is a rare finding, and experience with this defect is poor, but it is associated with right heart failure and fetal hydrops, leading in some cases to fetal loss. The aim of this study is to summarize the fetal echocardiography characteristic of idiopathic ductus arteriosus constriction and prognostic analysis.

**Method:** Nine fetal echocardiograms indicating idiopathic DA constriction were reviewed in a population 4441 pregnant from August 2010 to December 2013. All of them had thoracoscopic echocardiography postnatal. Ductus arteriosus constriction related to maternal use of cyclooxigenase inhibitors, ductus arteriosus stenosis caused by congenital heart disease or absent ductus arteriosus were excluded.

**Results:** The incidence of idiopathic DA constriction is 0.20%. Mean gestation age was 34.6±2.9 (33–37) weeks and maternal age was 31.2±7.6 (24–37) years. The narrowed middle diameter of DA was seen in 7 fetuses with mean diameter was 2.52±0.97mm; normal middle diameter of DA was seen in 2 fetuses with the diameter was 4.6mm, 5.3mm. A turbulence flow was seen in DA of all fetuses with color Doppler, and wave Doppler showed increased velocity both in systolic and diastolic phase. Mean systolic velocity in the ductus arteriosus was 2.33±0.47m/s, diastolic velocity 0.765±0.17m/s. And pulsatility index 1.23±0.61. Right heart diastolic diameter dilated was seen in 7 fetuses, normal proportion of left heart and right heart in 2 fetuses. The diameter of right atrium is 16.9±3.72mm, right ventricle is 17.8±0.33mm, pulmonary artery is 8.0±0.85mm and left atrium is 13.3±1.34mm, left ventricle is 12.9±1.35mm, aortic artery is 6.3±0.45mm. Other complication include tricuspid regurgitation in 2 fetuses, mild regurgitation in 2 fetuses, right heart dysfunction was seen in 2 fetuses, arrhythmia in 1 fetus, mild pericardial effusion in 1 fetus. All nine cases underwent transathocy echocardiography study postnatal one to six month and the results showed all ductus arteriosus closed with a normal proportion of left heart and right heart and a normal heart function, no tricuspid regurgitation or pericardial effusion.

**Conclusion:** The incidence of idiopathic constriction of the ductus arteriosus is very low. It usually occurred in late gestation and is associated with dilated right heart, tricuspid regurgitation, fetal heart failure and fetal hydrops, but had a good outcome after birth from this cohort.

**P1646 | BEDSIDE**

**Indications for fetal echocardiography: do they have a real predictive role?**

A. Donoro, R. Piazza, L. Neglia, E. Cereseto, G.L. Nicolosi, M. Cassin. Santa Maria degli Angeli Hospital, Pordenone, Italy

**Background:** Indications for fetal echocardiography (FE) are based on a variety of maternal and fetal risk factors for congenital heart diseases (CHD). However, most cases are not associated with known risk factors.

**Purpose:** To assess whether fetal and maternal risk factors, actually considered as indications for FE, have a real role in predicting CHD.

**Methods:** We did a retrospective analysis of indications and diagnosis of 1272 performed FE in the last 10 years at our department.

**Results:** 881 (69.2%) FE were requested in absence of risk factors: 24.2% for a suspected CHD, 27% for inadequate visualization of cardiac structures (increased maternal abdominal wall thickness: BMI≥26), 18% for intracardiac echogenic foci (‘golf balls’). The remaining 391 (30.8%) FE were performed in presence of risk factors, having validated risk factors: 6.8% for twin pregnancy, 1% for maternal rheumatological diseases, 2.1% for maternal infections, 3% for maternal diabetes, 2.8% for teratogen exposure, 3.9% for fetal arhythmias, 5.2% for familiar history (first-degree relatives) positive for CHD, 2% for abnormalities of amniotic fluid volume, 4% for fetal extracardiac and/or chromosomal anomalies, 15% of 271 diagnosed CHD, only 2 cases (ventricular septal defects) were associated with maternal infections, 1 case (ventricular septal defect) with cardiac gene expression, 2 (pulmonary valve stenosis) with abnormalities of amniotic fluid volume, 3 (2 tumors and 1 tetralogy of Fallot) with fetal arhythmias. In case of parental history of CHD, probability of CHD recurrence was around 2.8% and recurrent defects were aortic coarctation and ventricular septal defect. In 10 cases (cardiac rhabdomyomas, aortic coarctation, interrupted aortic arch, tetralogy of Fallot, common arterial trunk, transposition of the great arteries) chromosomal and extracardiac anomalies were present.

**Conclusions:** 85% of prenatally detected CHD were not associated with any identified risk factor, therefore the indication for a detailed fetal heart scan should be carefully taken into account also in “low risk” pregnancies. No significant difference existed in the prevalence of CHD between the twin and the singleton pregnancies. Chromosomal and extracardiac anomalies, if compared to other risk factors, seem to be the major predictors of CHD (14%; p<0.001) and, particularly, of complex CHD and CHD with an adverse prognosis. Moreover, most cases of CHD were the first clinical manifestation of chromosomal aneuploidies, thus suggesting the need for a further investigation on coexisting fetal multifetal and genetic disorders.

**P1647 | SPOTLIGHT**

**Long-term outcome of Ross procedure performed in childhood: a single centre cohort study in an adult congenital heart disease unit**

M.O. Mohamed1, P. Clift1, F. Umar1, D. Barron2, 1 Queen Elizabeth Hospital Birmingham, Cardiology, Birmingham, United Kingdom; 2Birmingham Children's Hospital, Birmingham, United Kingdom

**Purpose:** To assess long-term outcomes and complications of Ross procedure over a 15-year follow-up period at a regional adult congenital heart disease (ACHD) unit.

**Methods:** This retrospective study comprised of all adult survivors treated with Ross Procedure during childhood in a regional paediatric cardiothoracic centre between 1991 and 2000. We report follow up of 29 patients in our ACHD Unit. Indications for surgery: recoarctation of native aorta, tetralogy of Fallot, pulmonary regurgitant valve.

**Results:** 29 patients (86% males) with mean age at time of surgery of 10.5±3.3 yrs and median follow up of 14±3 yrs (range: 12 to 23 yrs) were reviewed. The mean age at latest follow up was 25±7±4 yrs. CMR findings revealed PV Vmax of 2.3±0.71 m/s, pulmonary regurgitant valve of 6.6±9.4 m/l pulmonary regurgitant fraction of 6.7±9.5%, left ventricular (end diastolic volume indexed [EDVI]: 91.1±23.3 m/l/m², end systolic volume indexed[ESVI]: 31.6±16 ml/m², ejection fraction[EF]: 63.7±4.4%), right ventricular (EDVI: 84.9±19.2 ml/m², ESVI: 34.1±12.6 ml/m², EF: 59.7±9%). Mean aortic root size measured at Sinus of Valsalva on CMR was 44.13 mm. CPET data (n=21, 72.4%) revealed mean VO2 of 74.1±12.4% predicted, mean RER 1.29±0.06, mean O2 pulse 73.8±12.9% predicted. Adequate blood pressure response was achieved in 18 patients (85%) with all patients achieving adequate heart rate response. The mean time to first intervention was 11.0±5.0 yrs, with a mean interval of 12.0±5.0 yrs for replacement of RV-PA conduit, and a mean interval of 11.9±6.8 yrs to first aortic valve replacement. 41.3% (n=12) required replacement of RV-PA conduit, and 44.8% (n=13) required autograft with root replacement. At least one surgical intervention was required in 16 patients (55%). No mortality or aortic dissection was observed. Only 10.9% (n=3) developed endocarditis, all of which occurred prior to any intervention succeeding Ross operation.

**Conclusion:** Over a period of 15 years, our data suggests an excellent survival rate for Ross procedure in medical records, although long-term outcome of preserved left ventricle was seen to adult life, this was at a cost of further surgical intervention in a notable proportion of patients.

**P1648 | SPOTLIGHT**

**Assessment of ventricular global longitudinal function in hypoplastic left heart syndrome using velocity vector imaging**

X.U. Yang, Y. He, Y. Zhao, Y.E. Zhang, J.C. Han, X. Gu, L. Sun. Beijing AnZhen Hospital affiliated to Capital Medical University, Department of Ultrasound, Beijing, China, People’s Republic of China

**Objective:** The aim of this study was to assess global and regional longitudinal peak systolic ventricular function in fetuses with hypoplastic left heart syndrome (HLHS), And to determine the influence of heart rate and gestational age on these strain parameters.

**Methods:** Twenty HLHS fetuses were enrolled during second and third trimester ultrasound (20–35w), the control group were 1:1 paired. Clips with high frame rates and two-dimensional grayscale images of apical or basal four-chamber views of both ventricles were used for offline analyses. Longitudinal strain, strain rate, strain time to peak and systolic velocity were measured in the left ventricular free wall, ventricular septum and right ventricular free wall. The correlation of above measurements with gestational weeks and heart rate was analyzed.

**Results:** The comparison of left or right ventricular global velocity, strain, strain rate and strain time to peak between HLHS and control group showed significant differences (p<0.05). The gestational age had no significant correlation with the velocity, strain, strain rate and strain time to peak of left or right ventricular of HLHS group (p>0.05).

**Conclusion:** HLHS fetal left ventricular myocardial global longitudinal function is reduced, because of long-term compensation. Right and left ventricular myocardial longitudinal motion function and gestational age has no relevance.
Congenital, foetal heart disease and intervention / Classical and new risk factors for cardiovascular disease

P1649 | BEDSIDE
Follow-up of 316 molecularly defined pediatric long QT syndrome patients - clinical course, beta blocker treatment and side effects
M. Koponen1, A. Marjamaa2, A. Hippiala3, J.M. Happonen3, K. Kontula4, H. Swan5, 1University of Helsinki, Helsinki, Finland; 2Helsinki University Central Hospital, Heart and Lung Center, Helsinki, Finland; 3Helsinki University Central Hospital, Children's Hospital, Helsinki, Finland

Background: Inherited long QT syndrome (LQTS) is associated with risk of sudden death. Previous follow-up studies on pediatric LQTS patients have mainly consisted of ungenotyped patients. We assessed the clinical course, and efficacy and side effects of β-blocker treatment in molecularly defined pediatric LQTS type 1 and 2 (LQT1 and type 2 LQT2) patients.

Methods: The study population was drawn from the Finnish Inherited Cardiac Disorder Research Registry comprising 4000 molecularly tested subjects. The inclusion criteria were 1) genetically confirmed KCNQ1 or KCNH2 mutation, and 2) age <16 years at enrollment. A questionnaire was sent to the study subjects or their parents. Data of all deaths were obtained from Statistics Finland. Kaplan-Meier graphs, the log-rank test and time-dependent Cox regression model were used to evaluate the contribution of risk factors to cardiac event.

Results: A total of 457 subjects fulfilled the inclusion criteria. Three of them died during the follow-up, and 313 (69%) responded to the inquiry. The study population (n=316) comprised 224 KCNQ1 and 85 KCNH2 mutation carriers, and 7 carriers with more than one mutation. The total follow-up time including the retrospectively collected data from birth was 12.0±5.5 years.

No arrhythmic deaths occurred during the follow-up. LQT1 Finnish founder (FF) mutation carriers had fewer cardiac events by the age of 18 years than other LQT1 patients (cumulative probability [CP]= 11% vs 26%, p=0.008, and hazard ratio [HR]=0.38, p=0.04). Similar trend was observed in LQT2 FF and non-FF patients (CP= 4% vs 43%, p=0.002, and HR=0.17, p=0.02). QTc interval <470 ms increased the risk of cardiac events compared to QTc >470 ms (HR=3.92, p=0.002) and QTc 470–499 ms (HR=2.76, p=0.03). Treatment with β-blocker medication was associated with reduced risk of first cardiac event (HR=0.27, p=0.005). Non-compliant LQT2 patients were more often symptomatic than compliant LQT2 patients (18% vs 0%, p=0.03). Side effects were encountered in 23% of β-blocker users.

Conclusions: Severe cardiac events are uncommon in molecularly defined and appropriately treated pediatric LQTS mutation carriers. β-blocker medication reduces the risk of cardiac events in this age group of LQTS patients.

P1650 | BEDSIDE
Results and long-term follow-up for double-outlet right ventricle with biventricular repair
O. Villemain1, E. Belli2, M. Ladouceur1, L. Houyé2, Z. Jala1, M. Ly2, R. Roussin2, P. Vouhé1, D. Bonnet1, 1MSci, Congenital and Pediatric Cardiology, Paris, France; 2Surgical Centre Marie Lannelongue, Pediatric Cardiac Surgery, Le Plessis Robinson, France

Background: The objective of this study was to review surgical results in children with double outlet right ventricle (DORV) undergoing biventricular repair and to assess risk factors for mortality and reoperation.

Methods and results: Between 1993 and 2011, 433 patients presenting with DORV and undergoing biventricular repair were included into the study. DORV were classified as DORV with subaortic (or doubly committed) ventricular septal defect (VSD) associated with right ventricular outflow tract obstruction (RVOTO) in 33% (n=141), with subaortic (or doubly committed) VSD without RVOTO in 30% (n=130), with subpulmonary VSD (Tausig-Bing Anomaly) in 32% (n=139), with non-committed VSD in 5% (n=23). Three types of repairs were performed: 1) intraventricular baffle repair (IVR), n=149 (34%); 2) IVR with RVOT enlargement, n=163 (38%); 3) IVR with arterial switch, n=121 (28%). 135 patients (31%) had undergone prior palliative procedures. Early mortality was 7.4% and early cardiac reoperation was 6%. Actuarial survival rate at 10 years was 86.2%, and freedom for reoperation at 10 years was 61.8%. Median follow-up was 5.7±1.1 years. In the long term, reoperation and mortality was significantly more frequent for DORV with ncVSD (p<0.01). In multivariate analyses, the factors that influenced reoperation were: left ventricular outflow tract obstruction (p=0.05), associated surgical procedures during main procedure (p=0.05), duration of cardiopulmonary bypass procedures (p=0.01). The factors that influenced survival were: restrictive VSD (p=0.01), coronary artery anomalies (p=0.05), duration of cardiopulmonary bypass procedures (p=0.01), early cardiac reoperation (p=0.01). The type of repair did not influence reoperation (p=0.20) or mortality (p=0.27).

Conclusions: Factors affecting the prognosis of DORV are anatomical and surgical factors. However, there is no difference between the main types of surgical strategy.
Results: Over a mean follow-up of 115 months and >10 million patient-years of follow-up, over 65,000 individuals had at least one AF event (incident AF rate 5.1% and 5.8% excluding or including prior CVD, respectively). Those who devel-
oped AF were older and had more risk factors for atherosclerosis. The mean eGFR of those who developed AF during follow-up in both cohorts was approxi-
mately 83 ml/min/1.73m² as compared to approximately 95 ml/min/1.73m² in those who did not develop AF. Adjusting for age, gender, hypertension and di-
abetes mellitus, a 10-unit increase in eGFR was independently associated with a mean decrease in incident AF of 1.4% and 2.3% in the cohorts excluding or includ-
ing prior CVD, respectively (p<0.001 for both), with a sharp decline in AF
events in the eGFR−100 ml/min/1.73m² range (Figure). The association between eGFR and incident AF was more significant in middle aged (41–60 y) or elderly (>61 y), as compared to youngers (22–40 y) (p<interaction<0.001).
Conclusions: The minor allele in the normal or milder impaired range is inde-
pendently associated with lesser incident non-valvular AF in adults with and without prior CVD.

P1655 | BEDSIDE
A cardiometabolic protective phenotype associated with the ANP genetic variant rs5068 in African Americans: the Multi-ethnic Study of Atherosclerosis (MESA)

V. Canonne1, P.A. Deckers2, N.B. Larson3, C.G. Scott3, W. Palmas3, K.D. Taylor4, S. Bielinski5, J. Kanazawa University6, J. Ku1, Mayo Clinic7, Rochester, United States of America; 2 Mayo Clinic, Division of Biostatistics, Rochester, United States of America; 3 Columbia University, Department of Medicine Columbia University College of Physicians and Surgeons, New York, United States of America; 4 Harbor-UCLA Medical Center, Los Angeles Biomedical Research Institute (LA BioMed), Torrance, CA, United States of America

Introduction: Atrial natriuretic peptide (ANP) possesses cardiovascular and renal properties including vasodilation, natriuresis and aldosterone suppression. Impor-
tantly, ANP also exerts a metabolic action inducing lipolysis in vitro and in vivo. Previous genome-wide association studies showed that the NPPA genetic vari-
ant rs5068 is associated with increased plasma ANP levels, lower blood pressure and reduced risk of hypertension in European whites. We recently reported that in two separate community-based cohorts of whites the minor allele of rs5068 was associated with higher HDL-cholesterol plasma levels, lower body mass index (BMI) and waist circumference, reduced prevalence of obesity and metabolic syndrome.

Purpose: We characterized the cardiovascular and metabolic phenotype associated with rs5068 genotype in a general population cohort of African Americans from five different regions in the USA.

Methods: We genotyped 1628 African Americans for rs5068. Differences be-
tween genotype groups were tested via logistic or linear regression. Continuous variables were rank transformed, if necessary.

Results: Genotype frequencies of rs5068 were AA (N=1518) 93%, AG (N=109) + GG (N=1) 7%. All subsequent analyses were done by combining AG and GG and comparing to AA. After adjusting for age and sex, the G allele was associated with lower prevalence of metabolic syndrome (24% vs 36%, p=0.003). After fur-
ther adjustment for BMI, the minor allele was associated with lower prevalence of diabetes mellitus (8% vs 17%, p=0.02), lower plasma values of triglycerides (78 vs 91 mg/dl, p=0.02) and higher HDL-cholesterol levels (54 vs 50 mg/dl, p=0.01). Additionally, carriers of the G allele had significantly lower fasting glucose levels (54 vs 91 mg/dl, p=0.04). Genotype was not associated with blood pressure values or BMI.

Conclusions: The association between the minor allele of rs5068 and a favor-
able cardiometabolic phenotype that was previously reported in whites is now shown in a cohort of African Americans. The rs5068 G allele is associated with lower prevalence of metabolic syndrome, diabetes, and levels of fasting glucose.

The G allele carriers have a healthier lipid phenotype, characterized by higher HDL-cholesterol levels and lower triglycerides values. Our findings suggest that ANP plays an important role in determining the cardiovascular and metabolic phe-
notype. These studies may also support a novel strategy of cardiometabolic risk assessment and importantly, lay the foundation for future development of an ANP or ANP-like therapy for metabolic syndrome.

P1654 | BEDSIDE
Unexpected High Prevalence of Possible and Probable FH in Clinical Practice - Results of DYSIS I

A.K. Gitt1, D. Lautsch2, M. Horack3, B.M. Ambegaonkar4, P. Bruidl1, J. Ferrieres5

1 Heart Attack Research Center at the University of Heidelberg, Ludwigshafen am Rhein, Germany; 2 Merck, Vienna, Austria; 3 Institut I. Herzinfarktforschung Ludwigshafen, Ludwigshafen am Rhein, Germany; 4 Merck, Whitehouse Station, United States of America; 5 Toulouse Rangueil University Hospital (CHU), Toulouse, France

Background: The recent EAS consensus paper on familial hypercholesterolemia (FH) indicates a higher prevalence of elevated low density lipoprotein cholesterol (LDL-C) due to genetic reasons than previously estimated. On the basis of the DYSIS I registry we aimed to determine the % of patients with very high LDL-C levels.

Methods: The cross-sectional, observational study DYSIS I examined lipid goal attainment among statin-treated patients in Canada, Europe, the Middle East, Egypt and South Africa. We identified patients with possible genetic background for high LDL-cholesterol using 3 approaches: [1] prevalence of LDL-C >190mg/dl despite statin therapy, [2] Dutch Advanced method for the identification of patients with inherited hypercholesterolemia (using prevalence of cardiovascular disease, age, gender, LDL-C levels and family history of premature CVD) [2.1] prevalence of possible FH and [2.2] prevalence of probable FH. However, 3 variables used in the Dutch score “first degree relative cholesterol”, “xanthomas”, “arcs corneals” were not recorded in DYSIS I and therefore this aggregate method might under-
estimate the % of patients with FH.

Results: A total of 35.451 patients with chronic statin treatment were included, of whom 2.9% (range 0.4–8.6% per country) had LDL-C >190 mg/dl despite statin therapy, 6.0% (1.7–16.7%) had possible FH and 0.3% (0.0–1.4%) had probable FH with large variations between the countries (see figure).

Conclusions: In DYSIS I, the prevalence of LDL-C >190mg/dl despite statin treat-
ment was 2.9%, in some countries even nearly 9%. Genetic causes may explain the very high LDL levels. As not all parameters of the Dutch score were collected in DYSIS I, this might be an even too conservative estimate of the prevalence of familial hypercholesterolemia in clinical practice.

Acknowledgement/Funding: MSD

P1655 | BEDSIDE
Lipoprotein(a) in familial hypercholesterolemia with proprotein convertase subtilisin kexin type 9 gain-of-function mutations: Implication of residual risk in statin-era

H. Tada, M. Kawashiri, A. Nohara, A. Inazu, H. Mabuchi, M. Yamagishi, Kanazawa University, Kanazawa, Japan

Background: Lipoprotein(a) [Lp(a)] is an established residual risk factor for car-
diovascular disease. Proprotein convertase subtilisin kexin type 9 (PCSK9) in-
hibitors have been reported to reduce Lp(a) up to ~30%, the mechanism of which
remains unclear. In addition, few data exist regarding the Lp(a) levels in patients
with familial hypercholesterolemia (FH) exhibiting gain-of-function PCSK9 muta-
tions, which could provide us an insight into the mechanism of reduction of Lp(a)
by PCSK9 inhibitor.

Objective: We aimed to determine whether the patients with FH due to the gain-
of-function mutations in PCSK9 gene exhibit higher Lp(a) level as well as higher
incidents of cardiovascular disease compared to those in patients with LDL re-
ceptor mutation or to those in normal controls.

Methods and results: Nineteen mutation-determined heterozygous FH pa-

tients with gain-of-function PCSK9 mutation (FH-PCSK9, mean age = 38yr, male = 9, mean LDL cholesterol=284±85mg/dl), 68 mutation-determined heterozygous
FH patients with LDLR mutations (FH-LDLR, mean age=40yr, male=37, mean LDL cholesterol = 245mg/dl), and 34 controls (CONTROLS, mean age=62yr, male=20, mean LDL cholesterol = 108mg/dl) were evaluated. We assessed their total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol, the presence of coronary artery disease, and Lp(a) levels. There were no significant differ-
ences of Lp(a) levels of among those 3 groups (FH-PCSK9, FH-LDLR, and CONTROLS, median Lp(a)=20.7mg/dl [IQR: 11.0–37.6], 23.4 mg/dl [IQR: 15.1–40.0], 21.0mg/dl [IQR: 13.2–31.3], respectively, Mann–Whitney U test). Also there was no difference between the presence of coronary artery disease in FH-PCSK9 and that of FH-LDLR (15.8% vs. 17.6%, Chi-square test).

Conclusion: These data suggest that the mechanism of reduction in Lp(a)
through PCSK9 inhibitor might be independent of LDL receptor. Such unknown pathway(s) could be new therapeutic target(s) for the residual risk in this statin-
era.
P1656 | BEDSIDE
The association between serum apolipoprotein B and acute myocardial infarction is modified by plasma glycine
G.F.T. Svingen1, E.K.R. Pedersen1, Y. Ding2, P.M. Ueland1, H. Schartum-Hansen2, R. Seifert3, O.K. Nygaard1. 1University of Bergen, Department of Clinical Science, Bergen, Norway; 2Haukeland University Hospital, Department of Heart Disease, Bergen, Norway

Background: Hepatic cholesterol uptake and VLDL excretion depend on the availability of free fatty acid.

Purpose: We investigated whether plasma glycine levels modified the relationship between serum apoB and risk of acute myocardial infarction (AMI) among 4154 patients with suspected stable angina pectoris, of whom 80.1% received statins.

Methods: Survival analyses were carried out by Cox regression models adjusted for age, gender and fasting status, and additionally adjusted for smoking, hypertension, diabetes, hs-cTnT, BMI, statin therapy and folate status. Interactions were tested according to low (< median) and high (≥ median) plasma glycine.

Results: Median (IQR) serum apoB was 87 (73-104) mg/dL, and slightly higher among patients with low glycine levels. After median 4.6 years, 344 patients (8.3%) experienced an AMI, with equal incidence rates in strata of glycine levels. In analyses adjusted for age, gender and fasting status, the hazard ratio (HR) (95% confidence interval (CI)) per 1 SD serum apoB in the whole cohort was 1.19 (1.07–1.31). However, the relationship between apoB and AMI was confined to patients with low glycine levels (Figure 1; P for interaction = 0.003). A similar effect modification was seen in multivariate analyses.

Conclusion: Serum apoB was a particularly strong predictor of incident AMI among patients with low plasma glycine. This suggests that the relationship between circulating apoB and cardiovascular risk might be influenced by decreased hepatic clearance, rather than increased secretion, of circulating apoB containing lipoproteins. Impaired turnover of VLDL remnant particles between the systemic and hepatic compartments may increase the life-span of circulating atherogenic lipoproteins, and making them more prone to oxidative damage.

P1657 | BEDSIDE
A variant in FLT1 is associated with long-term cardiovascular events in high-risk patients: replication of genome-wide association data
C.J. Lee, J.-Y. Lee, S. Park, S.-M. Kang, D. Choi, Y. Jang, S.-H. Lee. Yonsei University College of Medicine, Cardiology, Internal Medicine, Seoul, Korea, Republic of

Background: Association between dozens of genetic variants and coronary artery disease has been discovered lately. However, replication of the association by long-term clinical follow-up is very limited, especially in Asian populations.

Purpose: To evaluate temporal trends of CAD severity in a rural population in developed countries.

Methods: Twenty-five years trends in coronary artery disease in coronary artery disease revealed by first cardiac catheterization decreased significantly over time: In 1986, 41% of females and 46% of males had multivessel disease and females (from 143/100000 inh. in 1986 to 439/100000 inh.). Yet, the severity (from 343/100000 to 69/100000 inh.) and females (from 143/100000 inh. to 439/100000 inh.) decreased 5 fold both in females (from 343/100000 to 69/100000 inh.) and in males (from 1032/100000 to 210/100000 inh. aged 35–74 years). Over the same period, the number of diagnostic coronary angiographic procedures performed increased steadily and significantly, both in males (ie from 510 to 1072/100000 inh, p<0.01) and females (from 143/100000 inh. in 1986 to 439/100000 inh.,). Yet, the severity of coronary artery disease revealed by first cardiac catheterization decreased progressively over time and the proportion of normal exams increased: In 1986, only 13% of first coronary angiograms performed in males and 32% in females were free of significant coronary disease, in 2011 these proportions increased to 42% and 66% in males and females respectively. Also, the proportion of patients having multivessel disease on their first angiogram decreased significantly over time: In 1986, 41% of females and 46% of males had multivessel disease revealed by their first angiogram. This decreased to 20% of females and 30% of proportional hazard model. Genotype of rs1333049 did not have association with the events in Kaplan-Meier analysis.

Conclusion: The association between GWAS-driven rs9508025 in FLT1 gene and cardiovascular risk was replicated in Koreans with long-term follow-up.
males in 2011. Consequence, the incidence of patients diagnosed with significant new CAD on first angiograms decreased from 592/100000 to 393/100000 male inh. from 1995 until 2011 and 171/100000 to 108/100000 female inh. aged 34–75 years. Also, rates of first revascularization by either PCI or CABG remained stable in females at about 125/100000 inh. aged 35–74 years, while it decreased significantly in males from a peak of 426/100000 inh. aged 34–75 years in 1996 to 358/100000 inh. in 2011. The proportion of first coronary angiograms resulting in revascularization decreased in females from 43% in 1995 to 30% in 2011 and remained stable in males around 48–53% since 1995.

**Methods and results:** The impact of single nucleotide polymorphism of superoxide dismutase on cardiovascular and all-cause mortality in the general population.

Y. Otaki, T. Watanabe, G. Yamaura, H. Takahashi, T. Arimoto, T. Shishido, T. Miyamoto, I. Kubota. Yamagata University, Yamagata, Japan

**Background:** Oxidative stress is a major cause of cardiovascular disease. Superoxide dismutases (SOD) are antioxidant enzymes which keep cellular reactive oxygen species homeostasis against oxidative stress. Single nucleotide polymorphisms (SNP) within SOD genes were reported to be associated with the development of cardiovascular disease. However, it remains to be determined the impact of SNPs within SOD on cardiovascular and all-cause mortality in general population.

**Methods and results:** This longitudinal cohort study included 2611 subjects who participated in a community-based health checkup, with 8-year follow-up. We genotyped 7 SNPs within the SOD genes (rs2070424, rs4998557, rs1041740, rs4817420 and rs17880487 within SOD1; rs4880 within SOD2; rs1799885 within SOD3) and found that rs1041740 was related to clinical outcomes. There were 147 deaths during the follow-up period, including 42 cardiovascular deaths. The homozygous T-allele, heterozygous and homozygous C-allele carriers of rs1041740 were identified in 286 (11%), 1179 (45%), and 1164 (44%), respectively. The homozygous T-allele of rs1041740 carriers showed elevated brain natriuretic peptide levels and kidney dysfunction. Multivariate Cox proportional hazard-regression analysis revealed that the homozygous T-allele of rs1041740 was associated with all-cause and cardiovascular deaths after adjustments for confounding factors. Net reclassification index was significantly increased by addition of rs1041740 to conventional cardiovascular risk factors. Kaplan-Meier analysis demonstrated that homozygous T-allele carriers had higher rate of all-cause and cardiovascular deaths compared to those without.

**Results:** Over 25 years’ time, our data demonstrate significant decrease of acute infarcts and of chronic CAD incidence, severity, and revascularization rates in a population aged 35–74 years, likely reflecting better control of CAD risk factors.

**Conclusions:** Whole exome sequencing identified deleterious variants in ABCA6 and ABCA10 genes possibly associated with hyper HDL-cholesterolemia. These results provide new insights into the novel pharmacological target for ABCA6 and ABCA10.

**P1660 | BEDSIDE**

The impact of single nucleotide polymorphism of superoxide dismutase on cardiovascular and all-cause mortality in the general population.

Y. Otaki, T. Watanabe, G. Yamaura, H. Takahashi, T. Arimoto, T. Shishido, T. Miyamoto, I. Kubota. Yamagata University, Yamagata, Japan

**Background:** Oxidative stress is a major cause of cardiovascular disease. Superoxide dismutases (SOD) are antioxidant enzymes which keep cellular reactive oxygen species homeostasis against oxidative stress. Single nucleotide polymorphisms (SNP) within SOD genes were reported to be associated with the development of cardiovascular disease. However, it remains to be determined the impact of SNPs within SOD on cardiovascular and all-cause mortality in general population.

**Methods and results:** This longitudinal cohort study included 2611 subjects who participated in a community-based health checkup, with 8-year follow-up. We genotyped 7 SNPs within the SOD genes (rs2070424, rs4998557, rs1041740, rs4817420 and rs17880487 within SOD1; rs4880 within SOD2; rs1799885 within SOD3) and found that rs1041740 was related to clinical outcomes. There were 147 deaths during the follow-up period, including 42 cardiovascular deaths. The homozygous T-allele, heterozygous and homozygous C-allele carriers of rs1041740 were identified in 286 (11%), 1179 (45%), and 1164 (44%), respectively. The homozygous T-allele of rs1041740 carriers showed elevated brain natriuretic peptide levels and kidney dysfunction. Multivariate Cox proportional hazard-regression analysis revealed that the homozygous T-allele of rs1041740 was associated with all-cause and cardiovascular deaths after adjustments for confounding factors. Net reclassification index was significantly increased by addition of rs1041740 to conventional cardiovascular risk factors. Kaplan-Meier analysis demonstrated that homozygous T-allele carriers had higher rate of all-cause and cardiovascular deaths compared to those without.

**Results:** Over 25 years’ time, our data demonstrate significant decrease of acute infarcts and of chronic CAD incidence, severity, and revascularization rates in a population aged 35–74 years, likely reflecting better control of CAD risk factors.

**Conclusions:** Whole exome sequencing identified deleterious variants in ABCA6 and ABCA10 genes possibly associated with hyper HDL-cholesterolemia. These results provide new insights into the novel pharmacological target for ABCA6 and ABCA10.

**P1662 | BEDSIDE**

Serum apoB level is superior to non-HDL-C and LDL-C in the severity prediction assessed by Gensini Score among un-treated patients undergoing coronary angiography.

Y. Zhang, S. Li, Y-L. Guo, C.-G. Zhu, N.-Q. Wu, G. Liu, Q. Dong, J.J. Li. Fu Wai Hospital, Division of Dyslipidemia, Beijing, China, People’s Republic of

**Background:** Cardiovascular risk assessment commonly incorporates measurements of atherogenic lipids such as low density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (NHDL-C), and apolipoprotein B (apoB). However, which is most closely related to the severity of coronary atherosclerosis has not been assessed yet.

**Methods:** We studied 1763 consecutive subjects undergoing coronary angiography who were not receiving any lipid-lowering therapy. LDL-C was measured directly, NHDL-C was calculated, apoB was measured with immunoassay. The severity of coronary stenosis was determined using the Gensini Score (GS) system.

**Results:** In patients with coronary atherosclerosis (n=1103), apoB (OR=0.138, p<0.001) and NHDL-C (OR=0.134, p<0.001) were more closely related to GS than LDL-C (OR=0.110, p<0.001) tested by Spearman correlation analysis. In the overall population, LDL-C, NHDL-C, and apoB were all dramatically increased according to the quartiles of GS (p<0.001, all). Multivariate logistic analysis suggested that apoB (OR=2.384, 95% CI 1.597–3.560, p<0.001) was superior to NHDL-C (OR=1.323, 95% CI 1.163–1.505, p<0.001) and LDL-C (OR=1.285, 95% CI 1.129–1.462, p<0.001) in predicting high GS after adjusting for potential confounders. To exclude the potential confounder induced by diabetes mellitus (DM), we performed a subgroup analysis and found that apoB (OR=2.912, 95% CI 1.344–6.308, p=0.007) was more strongly associated with high GS than NHDL-C (OR=1.337, 95% CI 1.050–1.702, p=0.018), while LDL-C (OR=1.224, 95% CI 0.955–1.569, p=0.110) could not predict high GS in patients with DM.

**Conclusion:** Our results demonstrated that apoB was superior to non-HDL-C and LDL-C in predicting the severity of coronary atherosclerosis, especially in patients with DM.

**Conclusions:** Serum apoB level is superior to non-HDL-C and LDL-C in the severity prediction assessed by Gensini Score among untreated patients undergoing coronary angiography.

**P1863 | BEDSIDE**

Validity and reliability of the HeartQoL questionnaire based on the EUROASPIRE IV study.

D. De Smedt1, E. Clays1, S. Hofer2, N. Oldridge3, K. Kotseva4, D. De Bacquer1

1 Ghent University, Department of Public Health, Ghent, Belgium; 2 Innsbruck Medical University, Department of Medical Psychology, Innsbruck, Austria; 3 University of Wisconsin, College of Health Sciences, Wisconsin, United States of America; 4 Imperial College London, National Heart and Lung Institute (NHLI), London, United Kingdom

**Background:** Recently, the HeartQoL, a core health-related quality of life (HRQL)
instrument in patients with coronary heart disease (CHD), was developed for making between-diagnosis comparisons possible and to assess the change in HRQoL after treatment. The HeartQoL consists of 14 items; 10 items focusing on physical HRQoL and 4 items on emotional HRQoL together providing a global scale. The HeartQoL has been validated in the original HeartQoL sample of coronary patients.

Purpose: The aim of the current study was to confirm the reliability and validity of the instrument in an independent large European sample of patients with CHD.

Methods: Analyses are based on the recently performed EUROASPIRE IV (EUROpean Action on Secondary and Primary Prevention through Intervention to Reduce Events) survey (2012–2013). 7449 patients between 18 and 80 years, with stable CHD who had been hospitalised for a first or recurrent coronary event, completed the HeartQoL questionnaire. Psychometric analyses assessing the reliability and construct validity of the HeartQoL, instrument were performed.

Results: The mean global score was 2.18 (0.66), the mean physical and emotional subscale scores were 2.13 (0.72) and 2.30 (0.72) respectively. No floor effects were observed, but small ceiling effects were seen on the global scale (8.1%) and physical subscale (11.1%) with moderate ceiling effects on the emotional subscale (28.7%). Overall, excellent internal consistency was found on the global scale (α=0.92) and the physical subscale (α=0.91), and good internal consistency was seen on the emotional scale (α=0.87). Factor analyses confirmed the two-dimensional construct with factor loadings >0.5 with potential allocation problems on one item and fit indices which resulted in inconsistent outcomes. On country specific level, Bosnia scored poorly, probably due to a mistranslation of the questionnaire. Discriminative validity was confirmed with females reporting poorer global, physical and emotional scores, older patients reporting poorer global and lower educated patients reporting poorer global, physical and emotional scores. Likewise convergent validity was confirmed with moderate to strong correlations among hypothesized constructs.

Conclusion: Overall, psychometric analyses of the HeartQoL instrument in a population of CHD patients showed good reliability and validity both at the European as well as on country-specific level. Further research should focus on respective language-translational issues, construct validity and the ceiling effect of the emotional subscale.

P1664 | BEDSIDE
Prevalence, predictors and protective factors of job-related distress in a nationwide cardiologists sample. The IANUS-ItaliaN cardiologist’s Undetected distress Study-Survey

G. Russo, G. Majani, R. De Maria, A. Giardini, M. Marin, M. Milli, C. Raineri, R. Maestri, N. Aspromonte, G. Di Tano, C. Cardiovascular Center, A.A.S.1 Trieste, Trieste, Italy; 2Salvatore Maugeri Foundation IRCSS, Pavia, Italy; 3CNR Clinical Physiologic Institute, CardioThorasic and Vascular Department, Niguarda Hospital, Milan, Italy; 4University Hospital Rubini of Ancona, Ancona, Italy; 5Hospital of Santa Maria Nuova, Florence, Italy; 6Polliconic Foundation San Matteo IRCSS, Pavia, Italy; 7San Filippo Neri Hospital, Rome, Italy; 8Hospital of Cremona, Cremona, Italy

Background: The shift from acute to chronic care, with the attending need for additional skills and competences to manage chronicity and end-of-life, has characterized the cardiological practice in the last years. Especially in the presence of numerous new demandings that may engender stress and affect work satisfaction. Physician distress impacts on the frequency of medical errors, patients’ compliance and health care costs. The IANUS survey was designed to determine the prevalence of job distress in a nationwide cardiologists sample and to assess the relationship between personal-professional characteristics and positive and negative experiences in cardiological practice.

Methods: Out of 7393 cardiologists of a national scientific cardiology society, 1064 completed a web-survey consisting in socio-demographics data collection and a 15-item questionnaire on distress and work satisfaction. The study sample was representative of the invited population for age, sex, geographic area of work, practice setting and job position.

Results: Organizational problems and worries about medical legal controversies were reported by 71% and 49% respectively; more than 33% cardiology issues of lack of enthusiasm, helplessness, work-life imbalance and lack of control over work. On the other hand, 86% felt competent at work, 67% were rewarded by the medical staff, 57% felt that work and 52% were satisfied with their job. Factor analysis revealed a meaningful underlying structure consisting in four factors characterized as personal-professional imbalance, positive emotional, emotional fatigue and relational difficulties. Subjects working in interventional areas reported significantly higher positive meaning than those in clinical cardiologists and outpatient with stable CHD showed good reliability and validity both at the European as well as on country-specific level. Further research should focus on respective language-translational issues, construct validity and the ceiling effect of the emotional subscale.

P1665 | BEDSIDE
Psycho-social consequences of venous thromboembolism in youth. Results from a mixed methods study

A.A. Hojen, A. Gorst-Rasmussen, G.Y.H. Lip, D.A. Lane, L.H. Rasmussen, E.E. Sorensen, P. Dreyer, T.B. Larsen, 1 Aalborg University Hospital, Aalborg Thrombosis Research Unit and Clinical Nursing Research Unit, Aalborg, Denmark; 2 Aalborg University Hospital, Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Aalborg, Denmark; 3University of Birmingham, Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom; 4 Aalborg University Hospital, Clinical Nursing Research Unit, Aalborg University Hospital Science and Innovation Center, Aalborg, Denmark; 5Aarhus University Hospital, Department of Anaesthesiology, Aarhus, Denmark

Background: Chronic medical illness in youth can lead to psychosocial problems, including psychiatric disorders. Although venous thromboembolism (VTE) is a life-threatening and long-term disease, psychosocial consequences of venous thromboembolism in youth have received limited attention.

Purpose: To explore the psychosocial consequences of VTE in youth

Materials: A mixed methods approach was adopted. Using Danish nationwide health registries, we compared the mental health prognosis of 13–33 year-old incident VTE patients with that of sex and age matched controls.Psychotropic medication purchase was used as a proxy measure for poor mental health. Additionally, semi-structured interviews were conducted with twelve young VTE patients to explore individual experiences of the psychosocial impact of VTE.

Results: The 1-year and 5-year risk of psychotropic drug purchase among the 4,132 VTE cases was 7.1% and 22.1% which was substantially higher than among the population controls (1- and 5-year risk differences relative to the control group were 4.7% and 18.3%, respectively; 95% confidence interval 3.9% to 5.5%; respectively;10.8%, 95% confidence interval 9.4% to 12.3%). Four main themes relating to the psychosocial impact of a VTE in youth was identified in the interview data 1) To be different and alone 2) Raising a red flag 3) Living with uncertainty and 4) To be serious about serious issues.

Conclusion: A VTE diagnosis in youth is associated with a poorer mental health prognosis: more than one in five patients will experience mental health issues requiring psychotropic medication within 5 years. A VTE diagnosis is accompanied by a perception of being different and alone, worry from realizing that life is not endless, fear of recurrence, and fear of not being taken seriously by the health care system. Long-term follow-up with a focus on mental health may be necessary in this patient group.
This study reinforces the need of raising awareness of ACS symptoms as well as
women were more likely to have more intense and non-focal chest pain.

**Conclusion:**

Regression analysis showed that pain irradiation, chest pain severity and type of transverse chest pain were more often referred by women (83.4% vs. 69.9%, p = 0.009). There were no differences between sexes in type of transverse chest pain. Sex differences in symptoms presentation and health care-seeking behaviour may influence an early diagnosis of acute coronary syndrome (ACS).

**Methods:** We included 820 patients with ACS, who were consecutively recruited from the cardiology departments of two tertiary hospitals, in Portugal, between August 2013 and December 2014. Patients were interviewed by trained researchers to assess sociodemographic characteristics, clinical history, symptoms onset, healthcare-seeking, and transports utilization. Univariate analysis was performed using chi-square test, Mann-Whitney test, and t-test, as appropriate, as well as linear and logistic regression models.

**Results:** Three-quarters of patients were male (73.3%) with a mean age of 63.9 ± 13.2 years. The final diagnosis was non-ST elevation AMI in 45.6%, ST-elevation AMI in 40.3% of patients, and unstable angina in 9.3%. Women died with a higher risk of death (40.5% vs. 33.4%, p < 0.001; 70.1% vs. 57.9%, p = 0.002; respectively).

**Conclusion:** The effects of occupational activities on CVD depend not only on the types of occupational tasks but also on the balance of activities at work and the compensatory effects of other activities. Cardiovascular prevention strategies should include a range of occupational physical activities.

**Background and aims:** Heart failure (HF) prevalence is growing in high-income countries. Comorbid depression is common in HF and may impact adversely on outcomes. Thus screening becomes more and more important. We studied the comparative potential of the shorter 2-item Patient Health Questionnaire (PHQ-2) versus that of the 9-item version (PHQ-9) to predict death or re-hospitalization in participants of the Interdisciplinary Network for Heart Failure Study program.

**Methods and results:** Patients were eligible, if hospitalized for cardiac decompensation and if left ventricular ejection fraction (echocardiography) was <40% before discharge. Patients were selected when they had completed the PHQ-9 at baseline. PHQ-2 scores were extracted from the first 2 questions. To analyze associations of PHQ-2 and PHQ-9 with death and re-hospitalization, univariable Cox regression models were employed. The sample consisted of 852 patients, (67.6±12.1 years, 27.7% female, 42.3% New York Heart Association class III/IV). Follow-up was 18 months (100% complete). Both PHQ-2 and PHQ-9 predicted death in univariable analysis (hazard ratio [HR] 1.19, 95% confidence interval [CI] 1.09–1.29, p = 0.001, and HR 1.07, 95% CI 1.04–1.09, p < 0.001). They also predicted re-hospitalization in univariable analysis (HR 1.07, 95% CI 1.01 to 1.21, p = 0.02 and HR 1.03, 95% CI 1.01 to 1.04, p = 0.001). These results were confirmed by c-statistics.

**Predictive value of PHQ-2 and PHQ-9:**

**Conclusions:** In univariable models and confirmed by c-statistics the predictive potential of both PHQ-2 and PHQ-9 proved comparable. In clinical practice, PHQ-2 screening seems reliable and more feasible than the time consuming PHQ-9 to identify patients at risk of adverse outcomes.
more of the maximal heart rate for age in 80% of the patients. Supra ventricu-
lar ectopic beats and paroxaymal atrial fibrillations were observed in 10 subjects
(9.8%). In bivariate analysis, goals, faults, supported team’s victory or defeat, relative
importance of the event and higher scale of passion were positively associated
with average heart rate during matches and with cardiac events (all p < 0.05) (all
p < 0.05).

Conclusions: During football competitions in World cup, supporters experience
abrupt increases in heart rate, which compare to changes expected in maximal
treadmill exercise tests, what should be taken into account, especially for those
with overt cardiac diseases, or high global cardiovascular risk.

P1671 | BEDSIDE
Spirituality and depression in patients with coronary artery disease
F. Malafaia, G. Nishida, G. Barreto, V.L. Amato, A. Avezum. Dante Pazzanese
Institute of Cardiology, São Paulo, Brazil

Introduction: Psychosocial factors have been associated with an increased risk
of myocardial infarction (MI) and depression is diagnosed in about two-thirds of
post-MI patients, predicting poor cardiovascular outcome. There is a growing in-
terest to evaluate spirituality in the context of coronary artery disease (CAD).

Purpose: Evaluate spirituality and depression in CAD patients.

Methods: Cross-sectional, single-center study including 507 patients, aged ≥18
years, with CAD diagnosed by means of coronary angiography in a tertiary hos-
pital. All patients answered a self-administered questionnaire about depression
(Dimension, Anxiety and Stress Scales 21-items - DASS-21) and spirituality
(Functional Assessment of Chronic Illness Therapy – spiritual well being – FACIT-
spiritualwell being – FACIT-SP).

For statistical analysis, 2 groups of depression were defined: Group A (no
or mild) and B (moderate, severe or very severe).

Results: 507 patients were enrolled, 66% male gender and median age of 63 years.
CAD management was 32.7% CABG, 32% PCI, 11.8% both and 23.5% optimal medical
treatment only. Concerning depression, we found 68.8% of patients in group A
and 31.2% in group B. Patients were categorized for spirituality in quintiles as
follows: quintile 1 (sp1): 20.3%, quintile 2 (sp2): 20.3%, quintile 3 (sp3): 24.9%,
quintile 4 (sp4): 19.7%, quintile 5: 14.8% (sp5; most spiritualized group).

The prevalence of moderate to very severe depression was higher in spirituality
lower quintiles patients (p-value 0.018).

Conclusion: Lower scores of spirituality were associated with higher severity of
depressive symptoms. Results should be seen as hypothesis-generating and fur-
ther studies should be conducted to test association of spirituality and depression
and its impact on cardiovascular outcomes.

P1672 | BEDSIDE
Influence of cognitive decline on 30-day outcomes in hospitalized
patients with acute heart failure
H. Kawanishi1, M. Oguri1, K. Yasuda1, T. Katagiri1, M. Shimano1, H. Kajiyama1, H. Ishii2, T. Murohara2. 1Japanese Red Cross Nagoya First Hospital, Department of Cardiology, Nagoya, Japan; 2Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan

Background: Previous reports have shown that contribution of social factors to
the prognosis of heart failure is increasing. However, the effect of cognitive decline
in 30-day outcomes have remained largely unknown.

Purpose: The purpose of the present study was to examine the association be-
 tween cognitive decline and outcomes in hospitalized patients with acute heart
failure.

Methods: A total of 734 consecutive patients who were admitted to our hospital
with acute heart failure from January 2011 to May 2014. We assessed the effects of
cognitive decline including mild cognitive impairment and previously diagnosed
dementia on the incidence of 30-day outcomes (all-cause mortality or readmis-
sion due to heart failure) and hospital length of stay. The nutrition status was
assessed using the Controlling Nutritional Status (CONUT) score taking into ac-
count including serum albumin, total cholesterol level and total lymphocyte count,
and poor nutrition status was defined as the score ≥5. Cox proportional hazard
analysis was used.

Results: The prevalence of cognitive decline was 13.7%. Overall 30-day out-
comes was 8.6% and median length of stay was 17 days (interquartile range
11–26). Age, female gender, the prevalence of poor nutrition status, anemia, and
stroke were greater, whereas the prevalence of smoking, diabetes mellitus, and
dyslipidemia were lower in patients with cognitive decline than those with nor-
cognitive function. In hospital treatments, including intravenous diuretics or
vasodilators, and non-invasive positive pressure ventilation, were similar between
the two groups. The incidence of 30-day outcomes was significantly greater in pa-
tients with cognitive decline (15.8% vs. 7.4%, P=0.005). The hospital length of
stay was not different between the two groups (P=0.5813). Univariate cox propor-
tional hazard analysis revealed that age, poor nutrition status, cardiogenic shock,
hypoxenemia (serum sodium concentration <136 mEq/L), chronic kidney disease
(eGFR< 60 ml/min/1.73 m²), etiology of acute myocardial infarction, and cognitive
decline significantly (P<0.05) associated with 30-day outcomes. In multivariate cox
proportional hazard analysis with adjustments for covariates, cognitive de-
cline significantly and independently associated with 30-day outcomes (hazard
ratio 1.419, 95% confidence interval 1.01–1.91, P=0.040)

Conclusions: This study suggested that cognitive decline conferred a significant
increase in the occurrence of 30-day outcomes in hospitalized patients with acute
heart failure.

TREATMENT STRATEGIES AND ADHERENCE: CAN WE DECREASE RISK?

P1673 | BEDSIDE
Plant sterol supplementation on top of lipid-lowering therapies in
familial hypercholesterolemia
M.C. Izar, V.A. Machado, H.A. Fonseca, F.A. Fonseca. Federal University of Sao
Paulo, Sao Paulo, Brazil

Background: Familial hypercholesterolemia (FH) is the most common inherited
disorder of lipid metabolism, resulting in very high levels of LDL-cholesterol (LDL-
C) and increased risk of premature coronary disease. Underdiagnosed and
under-treated, this condition often requires combined lipid-lowering therapy (LLT),
with room for further interventions. Plant sterols (PS) supplementation, by reduc-
ing intestinal cholesterol absorption, can further lower LDL-cholesterol in 10%, but
the combination of high-dose statin, ezetimibe and PS has not been additively
yet in FH individuals. We tested the effects of plant sterols on top of two intensive
LLT on LDL-C, sterols synthesis and absorption markers.

Methods and results: Forty-two individuals of both genders with confirmed
diagnosis of FH, aged 49–60 years were prospectively included. Study design
was PROBE (randomized, open label, with parallel arms and blinded endpoints).
After a 4-week washout period of previous LLT, eligible subjects were random-
ized to receive simvastatin 80mg or simvastatin 80mg plus ezetimibe 10mg in a
blinded fashion for 12 weeks. After this period, 2g of phytosterols, as free sterols
were given in 500ml capsules with meals for additional 12 weeks. Both LLTs
reduced total- and LDL-C, triglycerides and ApoB, while addition of phytosterols
further reduced LDL-cholesterol only in the group receiving simvastatin/ezetimibe
(P=0.031). Simvastatin increased campesterol, decreased desmosterol, while
combined therapy reduced absorption markers and reduced desmosterol plasma
levels (P<0.05 vs baseline, for all).

Conclusions: This study has shown that PS supplementation in FH benefited
those individuals treated with simvastatin plus ezetimibe, but not those receiving
treatment alone. In addition to ezetimibe, PS can counterbalance the increased
sterol absorption besides improving lipid profile. Our study confirms the re-
levance of a more intensive blockade of cholesterol absorption and the validity
of phytosterol supplementation for patients with FH.

Acknowledgement/Funding: FAPESP (Foundation for Research of the State
of Sao Paulo, Brazil), INCT-Fox (National Institute of Science and Technology
Complex Fluids, Brazil)
The present project is a follow-up to the Observa-
lowering healthcare costs
the management of dyslipidemia with a decrease in coronary heart disease and
Salut, Health Department,
tory of Innovation Experiences in ICTs and Health in Catalonia (Fundació Tic-
Conclusion:
and 7.4% in males and between 1.8% and 2.0% among women and a decrease
The widespread use in Spain of HTE-DLP would mean in 2020 a reduction in fatal
cases and use was described as comfortable in 85% of cases. Assessing users
HTE-DLP by Questionnaire QoE for applications in health

Acknowledgement/Funding: The present project is a follow-up to the Observa-

P1675 | BEDSIDE
Are coronary patients on lipid-lowering therapy in Europe achieving the recommended LDL-C target? Results from the Dyslipidemia International Study (DYSIS) II Europe

Introduction: More than 40% of patients using statins discontinue therapy due to
higher cardiovascular risk aged
18 years old with LDL-cholesterol (LDL-C) ≥100 mg/dl. Included patients were randomly distributed into the intervention or control
group by a computer program. HTE-DLP was blocked automatically if a patient
was assigned to the control group. Physicians used HTE-DLP in the “real-clinic-
world” during 3 months. It was assessed the theoretical impact on the frequency
of coronary artery disease with the CASSANDRA-REGICOR methodology. Research-
sters were asked to evaluate HTE-DLP with questionnaire QoE for applica-
tions in health.

Results: Use HTE-DLP meant additional lowering of LDL-C of 20.5%. When experts in vascular risk using HTA-DLP number of high vascular risk patients reaching lipid targets of LDL-C <70 mg/dl increased by 4.4 times. In general practitioners would increase 5.8 times. Use of HTE-DLP reduced direct costs of lipid lowering therapy per patient, 19% less per mg of LDL descended. Physicians expressed good agreement with the 1st HTE-DLP recommendation in 86.1% of cases and use was described as comfortable in 85% of cases. Assessing users HTE-DLP by Questionnaire QoE for applications in health was positive (3.89/5).

Conclusion(s): Three out of four coronary patients did not achieve the rec-
commended LDL-C target, even while being treated with LLT, primarily statin
therapy increases the risk of cardiovascular morbidity and mortality. Clinical guide-
delines lack consistent criteria for diagnosis and management of “statin intolerance” (SI).

P1676 | BEDSIDE
Identification and management of statin-intolerance: a survey of clinicians from 13 countries

Introduction: More than 40% of patients using statins discontinue therapy due to
the onset of side effects (also termed “statin intolerance”). Discontinuation of ther-
apy increases the risk of cardiovascular morbidity and mortality. Clinical guide-
delines lack consistent criteria for diagnosis and management of “statin intolerance” (SI).

Purpose: To understand how patients with SI are identified and managed in an
actual clinical practice. A multicountry, observational cross-sectional chart review
conducted in 257 sites throughout Belgium, France, Germany, Greece, Ireland, Italy, and Russia. Two distinct patient cohorts were enrolled: patients surviving an ACS event and patients diagnosed with stable CHD. Full lipid profiles were available and eligible patients and 0–12 months prior to their most recent hospital admission for ACS patients were included to enrollment for CHD patients. Patients were on lipid-lowering therapy (LLT) ≥3 months and not participating in clinical trials involving medication. Patient characteristics, risk factors, treatment patterns, and laboratory values were collected.

Conclusion(s): The results of the meta-analysis suggest a significant reduction of Lp(a) levels following tibolone therapy. Taking into account the limited num-
ber of Lp(a)-targeted drugs, tibolone might be an effective alternative for post-
menopausal women.

P1677 | BEDSIDE
Tibolone can decrease lipoprotein(a) concentrations in postmenopausal women: a systematic review and meta-analysis of controlled trials

Introduction: Many studies have shown that the synthetic oral steroid tibolone has many positive effects on climacteric symptoms in postmenopausal women, but evidence of the effects on Lp(a) remains underdetermined.

Purpose: To perform a meta-analysis to evaluate the efficacy of oral tibolone on Lp(a) concentrations in postmenopausal women.

Methods: The literature search included PUBMED, Cochrane Library, Scopus, and EMBASE up to January 29, 2015, to identify prospective studies investigating the effects of tibolone on Lp(a) concentrations in postmenopausal women.

Results: Overall, the impact of tibolone on plasma Lp(a) was reported in 12 trials with 1117 patients. The results suggested a significant reduction of Lp(a) levels following treatment with tibolone (WMD: −25.28%, 95% CI: −36.50, −14.06, p < 0.001). This result was robust in the sensitivity analysis. When the studies were categorized according to the tibolone dose, there were consistent significant re-
ductions in Lp(a) concentrations in the studies with doses −2.5 mg/day (WMD: −17.00%, 95% CI: −30.22, −3.77, p = 0.012) and ≥2.5 mg/day (WMD: −29.18%, 95% CI: −45.02, −13.33, p = 0.001). Likewise, there were similar reductions in the studies lasting either <24 months (WMD: −26.79%, 95% CI: −38.40, −15.17, p < 0.001) or ≥24 months (WMD: −23.10%, 95% CI: −40.17, −6.03, p = 0.008). The results did not suggest any significant association between the changes in plasma concentrations of Lp(a) with dose (slope: −6.07, 95% CI: −20.16–8.02, p = 0.399) and therapy duration (slope: −0.027, 95% CI: −0.53–1.38; p = 0.505).

Conclusions: The results of the meta-analysis suggest a significant reduction of Lp(a) levels following tibolone therapy. Taking into account the limited num-
ber of Lp(a)-targeted drugs, tibolone might be an effective alternative for post-
menopausal women.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475 by guest on 07 February 2019
with suspected SI presented with muscle-related symptoms (range across countries [RAC] 50–87%). In these patients, clinicians took a range of steps to establish SI, including 1) discontinuation of statin (average 59%; RAC 48–67%); 2) statin re-challenge (average 74%; RAC 60–85%); and 3) modification of statin regimen (average 76%; RAC 65–83%); some clinicians reported trying a combination of above steps. An average of 39% of clinicians (RAC 32–46%) performed all three steps prior to diagnosing SI. Eventually, 6% of hypercholesterolemia patients qualified as statin intolerant (RAC 2–12%). On average 52% of “confirmed” SI patients continued to receive low-dose statin, usually with other lipid-lowering therapies (LLT). Of the remaining 48%, 75% received alternative LLT only. An average of 11% of patients with confirmed SI received no LLT.

Conclusion: Current clinical practice in patients with statin intolerance lacks consistency for diagnosis and management. A structured work-up to identify SI patients, followed by a defined therapeutic algorithm, is expected to more satisfactorily address CV risk management in these patients.

Acknowledgement/Funding: This study was sponsored by Amgen Inc.

P1678 | BEDSIDE
Real life adherence data to clinical practice guidelines for lipid management in chronic kidney disease: a multicenter cross-sectional survey
M. Arici on behalf of Turkish Society of Nephrology Working Group on Cardiorenal Syndrome. Hacettepe University, Nephrology, Ankara, Turkey

Background: The recent “Clinical Practice Guideline for Lipid Management in CKD patients” by Kidney Disease: Improving Global Outcomes (KDIGO) management these are: 1) obtaining a lipid profile upon first presentation of a CKD patient, 2) establishing the indication of treatment based on clinical data and/or cardiovascular risk status, but not LDL level, and 3) treating with a “fire-and-forget” strategy without any tailoring to patients’ risk profile or repeat lipid-testing.

Purpose: In this study, “real-life” clinical practice of lipid management in 5 major nephrology centers was surveyed immediately after the release of the guidelines.

Methods: All eligible outpatient CKD patients were included. Data were collected from patient files and/or electronic health records. Data regarding diagnosis, comorbid diseases, lipid profile and frequency of measurement, drug use, history of CVD, cardiovascular interventions and outcomes, cardiovascular risk assessment, and scoring system were collected.

Results: 

- Patients aged <50 years with eGFR <60 ml/min/1.73 m² and GFR categories G1-G2 only (N=476 patients (age 53.3±15.98 years, 41.9% female, median CKD duration 4 years, 29.9% with diabetes) were included. Most patients (80.5%) were under regular follow-up, however 19.5% of the patients were first admissions. Mean serum Cre level was 3.39±1.01 mg/dl and mean proteinuria was 1676.23±2069.88 mg/day. Mean LDL level was 131.29±178.15 mg/dl and 44.2% of the patients had levels above normal (LDL ≥130 mg/dl). Lipid profile was assessed at first admission in only 32.6% of the group and the rest had regular lipid measurements at every 3 months. (30.9%), every 6 months (32.8%), every 12 months (19.8%) or at every clinical visit (14.2%). Patients with known cardiovascular disease comprised 21.8% of the group, but only 16.6% of the patients had regular annual cardiovascular risk assessment with a chosen risk chart. When lipid treatment state was checked according to age and CKD stages, in adults aged ≥50 years with eGFR <60 ml/min/1.73 m² and GFR categories G3a-G5 only also contribute to insulin resistance and atherogenic dyslipidemia. This ratio was 44.4% in adults aged ≥50 years with eGFR <60 ml/min/1.73 m² and GFR categories G1-G2 only 36.6% of the patients were receiving a statin. In adults aged 18–49 years with CKD, statin treatment was used by only 19.5% of the patients.

Conclusion: The study showed that although more than 95% of the patients had regular and frequent testing for lipid profile, most patients above age 50 were not receiving recommended statin treatment. Most patients had also regular cardiovascular assessment. The management of dyslipidemia in this cohort from “real-life” is far from the guideline recommendations.

P1679 | BEDSIDE
Icosapent ethyl (eicosapentaenoic acid ethyl ester): effects on apolipoprotein C-III in patients from the MARINE and ANCHOR studies
C.M. Ballantyne1, H.E. Bays 2, R.A. Braeckman 3, S. Philip 4, W.G. Stirtan 4, C.M. Ballantyne1, H.E. Bays 2, R.A. Braeckman 3, S. Philip 4, W.G. Stirtan 4

Background and introduction: Icosapent ethyl (eicosapentaenoic acid ethyl ester) inhibits lipoprotein hepcidin, and generally promotes hypertriglyceridemia. Its increased activity is due to increased production of apolipoprotein C-III in patients from the MARINE and ANCHOR studies.

Methods: Total ApoC-III levels were assessed in 148 (MARINE) and 612 (ANCHOR) patients. Compared with placebo, IPE statistically significantly reduced ApoC-III levels at 4 days (Table 2) and 2 days (14.3%, p=0.0154, MARINE, 8.5%, p=0.008, ANCHOR). ApoC-III levels in patients of the MARINE and ANCHOR studies (IPE 4 g/day and placebo groups only)

<table>
<thead>
<tr>
<th>ApoC-III</th>
<th>Median baseline value, mg/dL (IQR)</th>
<th>Median final value, mg/dL (IQR)</th>
<th>Median change from baseline, % (p value)</th>
<th>Median change from baseline, % (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MARINE IPE 4 g/day n=53</td>
<td>25.6 (11.6)</td>
<td>19.7 (10.5)</td>
<td>-10.1 (27.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MARINE Placebo n=208</td>
<td>26.6 (17.3)</td>
<td>32.7 (14.6)</td>
<td>-12.2 (24.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ANCHOR IPE 4 g/day n=208</td>
<td>15.2 (4.7)</td>
<td>13.7 (4.8)</td>
<td>-9.4 (25.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ANCHOR Placebo n=201</td>
<td>14.8 (4.4)</td>
<td>16.2 (5.5)</td>
<td>10.9 (30.0)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion: Compared with placebo, IPE significantly reduced ApoC-III levels in adult patients in the MARINE and ANCHOR studies, in which IPE also significantly lowered TG and apolipoprotein B without increasing LDL-C.

Acknowledgement/Funding: Funded by Amarin Pharma Inc.
**P1681 | BEDSIDE**

Prevalence of lipid abnormalities among coronary patients remains high in the Middle East/Africa region: the Dyslipidemia International Study (DYSII) II MEA results

S.N. Al Shri1, W. Al Mahmeed2, R. Azer3, M. Sobby4, A.K. Gitt5, M. Horack6, V. Ashton7, P. Brudi4, S. Ambegaonkar2, S. Wajih7 on behalf of DYSIS II Middle East/Africa Investigators. 1Al-Hada Military Hospital, Taif, Saudi Arabia; 2Heart and Vascular Institute, Cleveland Clinic, Abu Dhabi, United Arab Emirates; 3Hotel-Dieu de France Hospital, Beirut, Lebanon; 4International Cardiac Center Hospital, Alexandria, Egypt; 5Stiftung Institut fur Herzinfarktforschung, and Herzzentrum Ludwigshafen, Med. Klinik B, Cardiology, Ludwigshafen am Rhein, Germany; 6Stiftung Institut fur Herzinfarktforschung, Ludwigshafen am Rhein, Germany; 7Merck & Co., Inc., Kenilworth, United States of America

**Background:** Persistent lipid abnormalities among coronary patients increase the risk of future cardiovascular events. Current lipid guidelines recommend a low density lipoprotein cholesterol (LDL-C) target of <1.8mmol/l.

**Purpose:** DYSII II documents the prevalence of lipid abnormalities and real world lipid target achievement among acute coronary syndrome (ACS) and stable coronary heart disease (CHD) patients in the Middle East/Africa region.

**Methods:** DYSII II is a multicountry, observational cross-sectional study conducted in Egypt, Jordan, Lebanon, Saudi Arabia, and United Arab Emirates in 2013/2014. General practitioners, internists, cardiologists and endocrinologists from 18 sites enrolled patients surviving an ACS event and patients diagnosed with stable CHD. Full lipid profiles were available within 24 hours of hospital admission (ACS) or 0–12 months prior to enrollment (CHD). Patients were on lipid lowering therapy (LLT) ≤3 months or not at all and were not participating in clinical trials involving medication. Patient characteristics, treatment patterns, risk factors, and laboratory values were collected. LDL-C target achievement was assessed based on 2011 ESC/EAS guidelines.

**Results:** 671 ACS and 1054 CHD patients were enrolled in DYSII II, with 74.7% (n=501) and 97.8% (n=1031) being treated with LLT. Approximately 82% of treated ACS and 72% of treated CHD patients did not achieve the recommended LDL-C <1.8mmol/l target (mean LDL-C 2.8±1.1 mmol/l and 2.2±1.3 mmol/l respectively). Median distance to LDL-C target was 1.1 mmol/l (IQR 0.6, 1.8) for ACS and 0.5 mmoll/l (IQR 0.2, 0.9) for CHD patients. Table 1 provides patient characteristics and LLT details. High intensity statin (atorvastatin 40–80mg/day equivalent) was not administered to more than half the patients (68.9% ACS and 55.4% CHD patients).

<table>
<thead>
<tr>
<th>Treated patient characteristics and LLT</th>
<th>ACS patients</th>
<th>CHD patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>60.2±10.5</td>
<td>63.5±10.1</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>77.4%</td>
<td>75.8%</td>
</tr>
<tr>
<td><strong>Hypercholesterolemia</strong></td>
<td>81.1%</td>
<td>94.1%</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>66.5%</td>
<td>78.7%</td>
</tr>
<tr>
<td><strong>BMI &gt;30 kg/m2 (obese)</strong></td>
<td>54.0%</td>
<td>50.3%</td>
</tr>
<tr>
<td><strong>Type 2 diabetes mellitus</strong></td>
<td>52.1%</td>
<td>66.6%</td>
</tr>
<tr>
<td><strong>Current smoker</strong></td>
<td>35.9%</td>
<td>14.1%</td>
</tr>
<tr>
<td><strong>Prior myocardial infarction</strong></td>
<td>19.7%</td>
<td>65.5%</td>
</tr>
<tr>
<td><strong>Family history of CHD</strong></td>
<td>18.2%</td>
<td>30.4%</td>
</tr>
<tr>
<td><strong>Atorvastatin equivalent dose (mg/day)</strong></td>
<td>25±14</td>
<td>30±18</td>
</tr>
<tr>
<td><strong>Statin monotherapy</strong></td>
<td>93.0%</td>
<td>78.9%</td>
</tr>
<tr>
<td><strong>Statin + ezetimibe</strong></td>
<td>4.2%</td>
<td>14.6%</td>
</tr>
<tr>
<td><strong>Statin + other non-statin (fibates, omega 3 fatty acids)</strong></td>
<td>2.0%</td>
<td>5.0%</td>
</tr>
<tr>
<td><strong>Non-statin monotherapy</strong></td>
<td>0.8%</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

**Conclusion(s):** Even with LLT treatment, the majority of ACS and CHD patients in the MEA region did not achieve their recommended LDL-C target. More intensive LLT is needed to further reduce patients LDL-C.

**Acknowledgement/Funding:** This study was funded by Merck & Co., Inc.

---

**P1682 | BEDSIDE**

Predicators of failure to use of a high potency statin regimen after an acute coronary syndrome: insights from the SOLID-TIMI 52 trial

A. Eisen1, C.P. Cannon1, E. Braunwald1, D.L. Steen2, J. Zhou1, A.J. Dalby3, J. Spinario4, S. Daga5, M.A. Lukas5, M.L. O'Donoghue1. 1Brigham and Women’s Hospital, TIMI Study Group, Boston, United States of America; 2University of Cincinnati, Cincinnati, United States of America; 3Milpark Hospital, Johannesburg, South Africa; 4University Hospital Brno, Brno, Czech Republic; 5GSK, Philadelphia, United States of America

**Background:** A high potency statin regimen has been shown to reduce CV events after ACS, but remains underused in clinical practice. We examined predictors of failure to administer a high potency statin regimen in a large contemporary trial population after ACS.

**Methods:** The SOLID-TIMI 52 trial enrolled 13,026 patients stabilized within 30 days of hospitalization for an ACS. The use of guideline-recommended therapies was strongly encouraged and performance reports were sent to sites, but the decision to treat with a statin and the dose were at the discretion of the treating physician. A high potency statin regimen was defined as ≥40mg atorvastatin, ≥20mg rosuvastatin or 80mg simvastatin daily. A logistic regression model with forward selection was used to identify independent predictors associated with the failure to administer a high potency statin.

**Results:** Of patients enrolled, 95.4% were on a statin at baseline after ACS, but only 41.9% were on a high potency statin. Multiple independent predictors of the failure to treat with a high potency statin were identified including: age ≥75 years, non-white race, eGFR < 60 mL/min/1.73m2, higher baseline LDL and HDL cholesterol and heart failure during ACS. Positive predictors of high-potency statin use included elevated cardiac biomarkers, PCI for index event, diabetes mellitus, peripheral arterial disease and statin treatment prior to the index event (Figure).

**Conclusion:** Despite the widespread use of statins after ACS, only a minority of patients are initiated on a high potency statin regimen early after the event, including many patients at highest risk of recurrent events.

---

**P1683 | BEDSIDE**

Statin utilization and low-density lipoprotein cholesterol goal attainment in patients at very high cardiovascular risk: insights from a French general practice population

J. Ferrieres1, D.L. Steen2, R. Sanchez3, J. Chin4, K. Goryca5, I. Khan6. 1University Hospital of Toulouse - Rangueil Hospital, Toulouse, France; 2University of Cincinnati, Cincinnati, United States of America; 3Milpark Hospital, Johannesburg, South Africa; 4University Hospital Brno, Brno, Czech Republic; 5GSK, Philadelphia, United States of America

**Background:** The ESC/EAS cholesterol guidelines recommend lowering low density lipoprotein cholesterol (LDL-C) to <1.8 mmol/L (70mg/dL) for very high cardiovascular (CV) risk patients.

**Purpose:** To summarize lipid-lowering treatment (LLT) and achieved LDL-C levels in patients with established CV disease and/or diabetes from a general practice cohort in France.

**Methods:** This analysis included patients from the Cegedim general practice database in France meeting the following criteria: a valid LDL-C in 2013 (index date); ≥20 years of age; continuous representation in the database for ≥2 years; and ≥1 very high risk CV condition. Patients were restricted to patients in exclusive categories via the following hierarchy: acute coronary syndrome (ACS) within 12 months; other coronary heart disease (CHD); ischemic stroke; peripheral arterial disease (PAD); and type 2 diabetes mellitus. Patients were considered treated with a medication if covered by a filled LLT prescription on the index date (or within 30 days).

**Results:** A total of 29,565 patients met the inclusion criteria. Median age was 68 years, 61% were male, and the median LDL-C was 2.6 mmol/L (100 mg/dL). Overall, statin use was 57% with 13% of these patients treated with high-intensity statins. The use of statins in combination with non-statin LLT was low, 9% and 10% among high-intensity and moderate-to-low intensity statins, respectively. Additionally, 37% were not being treated with any LLT. Achievement of LDL-C <1.8 mmol/L was only 15% and was associated with LLT intensity.

**Conclusion:** In a large cohort of very high CV risk patients, overall statin use as well as non-statin LLT use was suboptimal, contributing to only 15% achieving the guideline-recommended LDL-C goal <1.8 mmol/L. Only 57% of patients were treated with statins suggesting better strategies are needed to increase appropriate use of statins.

**Acknowledgement/Funding:** Sanofi and Regeneron Pharmaceuticals, Inc.
Investigators. Our study documented real world lipid target attainment and the prevalence of dyslipidemias among patients with stable CHD and patients surviving an ACS event in Asia-Pacific.

Methods: DYSIS II is a multicountry, observational cross-sectional study conducted in 87 sites throughout Hong Kong, India, Indonesia, Philippines, South Korea, Singapore, Taiwan, Thailand, and Vietnam. General practitioners, internists, cardiologists and endocrinologists enrolled patients in two distinct study cohorts: patients surviving an ACS event and patients diagnosed with stable CHD. Full lipid profile was available within 24 hours of hospital admission (ACS) or 0–12 months prior to enrollment (CHD). Patients were on lipid-lowering therapy (LLT) ≥3 months or not at all and were not participating in clinical trials involving medications. Patient characteristics, risk factors, treatment patterns, and laboratory values were collected. Low density lipoprotein cholesterol (LDL-C) target attainment was assessed based on 2011 ESC/EAS guidelines.

Results: Overall 1803 ACS and 2802 CHD patients were enrolled in 2013/2014, with 63.3% (n=1142) and 91.7% (n=2570) currently on LLT respectively. Only 31.0% (n=354) of treated ACS and 32.6% (n=838) of treated CHD patients attained recommended LDL-C <1.8mmol/l, with median distance to target being 0.8 mmol/l (IQR 0.4, 1.4) and 0.6 mmol/l (IQR 0.3, 1.0) respectively. Mean atorvastatin equivalent dose was 22±18 mg/day for ACS and 20±14 mg/day for CHD patients. LLT regimens for ACS and CHD patients were respectively: statin monotherapy 91.6%, 86.3%; statin + ezetimibe 2.5%, 7.7%; statin + other non-atorvastatin equivalent dose was 22±18 mg/day for ACS and 20±14 mg/day for CHD patients. LLT regimens for ACS and CHD patients were respectively: statin monotherapy 91.6%, 86.3%; statin + ezetimibe 2.5%, 7.7%; statin + other non-atorvastatin 4.4%, 5.3%; and statin-monotherapy 1.6%, 0.8%.

Patient characteristics and mean lipids

<table>
<thead>
<tr>
<th></th>
<th>ACS treated patients (N=1142)</th>
<th>CHD treated patients (N=2570)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63.8±11.8</td>
<td>62.1±10.6</td>
</tr>
<tr>
<td>Males</td>
<td>70.8%</td>
<td>78.6%</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>56.0%</td>
<td>60.3%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>76.1%</td>
<td>69.2%</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>29.8%</td>
<td>46.7%</td>
</tr>
<tr>
<td>Family history of CHD</td>
<td>18.1%</td>
<td>23.5%</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td>4.3%</td>
<td>42.3%</td>
</tr>
<tr>
<td>Sedentary lifestyle</td>
<td>37.7%</td>
<td>30.3%</td>
</tr>
<tr>
<td>Current smoker</td>
<td>14.1%</td>
<td>11.2%</td>
</tr>
<tr>
<td>LDL-C (mmol/l)</td>
<td>2.4±1.0</td>
<td>2.2±0.8</td>
</tr>
<tr>
<td>Total Cholesterol (mmol/l)</td>
<td>4.2±1.3</td>
<td>4.0±1.0</td>
</tr>
<tr>
<td>Non-HDL-C (mmol/l)</td>
<td>3.1±1.2</td>
<td>2.8±0.9</td>
</tr>
</tbody>
</table>

Conclusion(s): More than two-thirds of LLT treated patients did not attain the recommended LDL-C target, primarily being on moderate statin dose. Higher intensity LLT should be provided to these high risk patients.

Acknowledgement/Funding: This study was funded by Merck & Co., Inc.

How does stress affect Cardiovascular Risk?

P1686 | BEDSIDE
Troponin T and brain natriuretic peptide (BNP) in patients with psychosis


Background: Cardiovascular disease (CVD) is the leading cause of death in patients with serious mental illness (SMI). These patients often complain of chest pain and or dyspnea. At the emergency department test with Troponin T and brain natriuretic peptide (BNP) is often taken. However, it is not known how often stable patients with psychosis have increased levels of these risk markers. To evaluate this there is a need to investigate large population-based schizophrenia patients without symptoms of chest pain or dyspnea. Previous studies have mostly included SMI patients admitted to the emergency department. These patients are likely to have a more severe illness and this might contribute to increased levels of these markers.

Objective: To determine the prevalence of increased BNP and Troponin T.

Material and methods: During 2005 to 2012 a total of 300 consecutive outpatients with psychosis were recruited from psychosis outpatient clinics in Stockholm County. Of the patients 54% had a schizophrenia diagnosis, 19% had another psychosis diagnosis (delusional disorder or psychosis NOS), 10% schizoaffective syndrome, and the remaining 17% other psychiatric diagnoses including bipolar disorder and ADHD.

Results: Mean age of the psychosis patients was 47 years, male 65%. The 99% CI for Troponin T in healthy controls is 14 ng/l. However, 9% of patients with psychosis had Troponin T values > 15 ng/l. The upper normal values for BNP is 150 ng/l. Studies at an emergency unit have indicated the patient with BNP > 100 ng/l has a positive predictive value for detection of heart failure. Our results showed that 19% of all patients with psychosis had BNP > 100. The levels of BNP and Troponin T was significantly but weakly related (r=0.21, p.<0.01).

Conclusion: A surprisingly high percentage of stable patients with psychotic disease have high levels of risk markers (Troponin T and BNP). The reason for this increase in cardiovascular markers is not clear but could be a future markers to detect subgroup of patients with high risk of CVD death.

P1686 | BEDSIDE
Clinical impact of psychological interventions to quality of life in Japanese patients with implantable cardioverter defibrillator

K. Miyazawa1, M. Ueda1, Y. Kondo2, M. Ishimura1, T. Kajiyama1, N. Hashiguchi1, T. Kanaeda2, Y. Kobayashi3,1 University of Tokyo Graduate School of Medicine, Department of Cardiovascular Medicine, Chiba, Japan; 2University of Bonn, Bonn, Germany; 3Kinki University School of Medicine, Osaka, Japan

Background: The implantable cardioverter-defibrillator (ICD) prevents sudden cardiac death and improves quality of life (QOL) in patients with high risk of life-threatening arrhythmias. However little is known about the psychological influence of ICD therapy in Japan. All patients completed the Florida Shock Anxiety Scale (FSAS), which was a tool designed to provide a quantitative measure of ICD shock-related distress. High FSAS scores reflect a patient’s individual anxiety. In the DEF-Chiba study, all patients were followed-up without psychological interventions. On the other hand, in the DEF-Chiba2 study, all patients underwent interventions by psychiatrists before and after ICD implantation.

Methods: We analysed the data of 2 studies (DEF-Chiba and DEF-Chiba2), which were prospective multicenter-studies investigating the psychological influence of ICD therapy in Japan. All patients completed the Florida Shock Anxiety Scale (FSAS), which was a tool designed to provide a quantitative measure of ICD shock-related distress. High FSAS scores reflect a patient’s individual anxiety. In the DEF-Chiba study, all patients were followed-up without psychological interventions. On the other hand, in the DEF-Chiba2 study, all patients underwent interventions by psychiatrists before and after ICD implantation.

Results: A total of 256 patients were enrolled in these studies. Table demonstrates the scores of FSAS with and without psychological interventions 12months after ICD implantation. The FSAS score at 12 months was significantly lower in DEF-Chiba2 study than in DEF-Chiba study (7.16±8.5 vs 14.3±5.0, P=0.001).

Conclusion: Psychological interventions were effective in patients with ICD. Female, experience of shock therapy and secondary indication influenced psychological QOL. Therefore, these population should be considered to aggressive interventions by psychiatrists.

P1687 | BEDSIDE
Trigger and consequence of shock therapy in Japanese patients with implantable cardioverter defibrillator

Y. Kondo1, M. Ueda1, T. Kurita1, T. Kanaeda1, M. Nakano1, N. Hashiguchi1, T. Kajiyama1, K. Miyazawa1, Y. Kobayashi3,1 University of Tokyo Graduate School of Medicine, Department of Cardiovascular Medicine, Chiba, Japan; 2University of Bonn, Department of Medicine-Cardiology, Bonn, Germany; 3Chiba University Graduate School of Medicine, Department of Cardiovascular Medicine, Chiba, Japan; 4Kinki University Faculty of Medicine, Department of Internal Medicine, Division of Cardiology, Osaka, Japan

Introduction: Shock-related anxiety is particularly relevant to psychological condition and quality of life for the implantable cardioverter defibrillator (ICD) population. Recently, the Florida Shock Anxiety Scale (FSAS), which was designed to provide a quantitative measure of ICD shock-related distress, has established trigger factors of device firing (e.g., feeling sexual activity) and consequence factors.
How does stress affect cardiovascular risk?

P1688 | BEDSIDE
The effect of synthetic cannabinoids on P-wave dispersion: an observational study

M. Sunbul1, A.E. Sunbul2, A. Terzi2, S. Cali2, E. Koca2, R. Bilici3, S. Cıtkaz2.
1Marmara University, Faculty of Medicine, Department of Cardiology, İstanbul, Turkey; 2El ENTERNO RUH SINIR HASTALIKLARI Hastanesesi, Psychiatry, İstanbul, Turkey

Purpose: Synthetic cannabinoids (SC) consumption has become widespread, despite law enforcement and regulatory control measures. SC is cheaper and easily available than other cannabinoids and its popularity has been increased due to intense psychoactive effects and lack of detectability in routine urine drug tests nowadays. Previous studies have shown that SC may lead to increased risk of cardiovascular disease (CVD). P wave dispersion (PD), defined as the time difference between the maximum and minimum of the P wave on 12-lead electrocardiography (ECG), is an non-invasive marker of disorganized atrial repolarization, and was proposed to be used as a predictor of the increased risk of CVD. The aim of the present study is to investigate the effect of SC on PD in patients with SC consumption.

Methods: The study population included 40 patients with SC consumption and 20 age and sex matched healthy controls. The severity of addiction was detected by using addiction profile index (BAPI). BAPI score >12 was defined as low level of addiction. BAPI score 12-14 was defined as moderate level of addiction and BAPI score > 14 was defined as high level of addiction. PD was measured through 12-lead ECG obtained during the admission of patients.

Results: Age and sex distribution were similar between two groups (26.9±7.3 years vs 26.2±6.4 years and 39 male vs 19 male, p=0.687, 0.611, respectively). Mean duration of SC consumption was 1.8±0.7 years. Mean BAPI score of patients with SC consumption was 13.8±2.8. Our study population had moderate level of addiction according to BAPI score. Patients with SC consumption have significantly higher PD value than controls (41.2±13.8 ms vs 32.3±7.6, p=0.002). BAPI score was significantly correlated with PD value (r=0.528, p=0.003). Among PD value, age and heart rate that were included in the linear regression model, PD value was shown to be significantly and independently affecting BAPI score (r2 of the model = 0.528, p=0.003).

Conclusions: Patients with SC consumption have higher PD value than healthy controls. PD value was correlated with BASI score. PD was also independent predictor of BASI score in those patients. Our results demonstrated that SC consumption may lead to increased risk of CVD through prolonged PD. A simple and cheap ECG may help the clinician to assess cardiovascular risk in patients with SC consumption.

P1690 | BEDSIDE
A continuum in cocaine cardiotoxicity. From myocardial strain alteration to left ventricular dysfunction. A cardiovascular magnetic resonance strain/stRAIN study

A.M. Macieza Gonzalez1, L. Tuset2, C. Ripoll3, J. Cosin-Sales4, B. Igual4, J. Salazar5, V. Belloch1. 1Cardiac Imaging Unit - ERESA, Valencia, Spain; 2Catedra ERESA-University of Valencia, Valencia, Spain; 3Hospital La Fe, Addictions treatment Unit, Valencia, Spain; 4University Hospital Arnau de Vilanova, Dept. of Cardiology, Valencia, Spain; 5University General Hospital of Valencia, Dept. of Psychiatry. CIBERSAM, Valencia, Spain

Background: Cocaine is a highly addictive drug with potentially cardiovascular lethal effects. We have previously shown with cardiovascular magnetic resonance (CMR) decreased left ventricular ejection fraction (LVEF) in 35% of asymptomatic cocaine addicts, though preclinical myocardial dysfunction might appear earlier. New analysis softwares allow for the accurate and reproducible measurement of myocardial strain and strain rate with CMR. We aimed to measure with CMR at 3T global myocardial strain and strain rate in cocaine addicts with normal vs decreased LVEF.

Methods: 20 cocaine addicts with decreased LVEF (D) and 20 with preserved LVEF (P), as well as 20 healthy controls (H), were included. All of them underwent a CMR protocol at 3T that included cine sequences in usual views as well as short axis series with typically 40 phases for each acquisition, administration of gadolinium-DTPA (0.1mM/kg) and late gadolinium sequences in the same views as the cines. LV parameters were measured. A dedicated software was employed to analyse 2D global longitudinal, circumferential and radial strain and strain rate. The statistical analysis was done with ANOVA and Tukey post-hoc test when applicable.

Results: All the subjects included were males and no differences were found in age. Years of regular cocaine use were 12.5±9. Significant differences were found in young patients (≤ 24 years) vs older patients (> 24 years) in global longitudinal and radial strain rate (GLSR, GRSR), all showing a significant and progressive decrease along the groups (H vs P vs D).

Conclusion: Cocaine addicts with preserved ejection fraction already show decreased global longitudinal and radial strain and strain rate, as well as global circumferential strain, with intermediate values between healthy controls and cocaine addicts with overt decreased ejection fraction. CMR strain-analysis can

tors of device firing (e.g., creating a scene). The aim of this study was to examine these factors in Japanese patients with ICD.

Methods: We analysed the data of DEF-Chiba study, investigating the relationship between inappropriate shock therapies and psychological distress, which reflects a multi-center prospective study in Japan. All patients completed FSAS. High FSAS scores reflect a patient’s individual anxiety. We examined the relationship between experience of appropriate shock therapy and the scores of trigger and consequence factors using the FSAS.

Results: Two hundred and fourteen patients were enrolled in this study. The score of trigger factors was significantly higher in the “appropriate shock group” (patients who have experienced shock therapies) compared to the “no shock group” (patients who have never experienced shock therapies), as demonstrated in Table. The score of consequence factors was not significantly different between two groups.

Conclusions: Experience of appropriate shock therapy reflects an important determinant of anxieties about triggering device shock in Japanese patients with ICD. Therefore, the main goal to reduce distress in patients with ICD is to reduce shock delivery by programming the ICD properly, i.e. activating antitachycardia pacing and SVT discriminators, and change detection settings according to recent trials.

Acknowledgement/Funding: None

2 Iberoamuturam Prevention Society, Madrid, Spain; 3 Hospital Universitari Virgen de la Victoria, Málaga, Spain

Background: The incorporation of routine electrocardiograms in healthy populations, such as the working population, is still controversial. In some European countries, screenings of competitive athletes or other young people have been developed, but results of these studies cannot be extrapolated to other wider populations.

The knowledge of the prevalence of electrocardiographic (ECG) abnormalities in working population might be interesting in order to design screening programmes. In spite of this, prevalence of most ECG patterns remains unclear for this kind of population.

Purpose: Our aim was to evaluate the prevalence of ECG abnormalities in a large sample of Spanish workers of both genders and from every different employment sector.

Methods: Between May 2008 and November 2010, 13,495 consecutive 12-lead resting electrocardiograms were obtained during health examinations of working adults aged 18 to 65 years, in five cities in different regions of Spain. 13,179 electrocardiograms that were suitable for interpretation were included in this study. All tracings were read and classified by the same cardiologist according to the Minnesota code criteria.

Results: Mean age of the sample was 40 years (39.8–40.1), and 73.4% were male. Only 6.1% of participants had a moderate or high cardiovascular risk using the Framingham Risk Score. 22.8% had at least one ECG abnormality. The prevalence of incomplete right bundle branch block, complete right bundle branch block, complete left bundle branch block and left ventricular hypertrophy were 5.7%, 1.1%, 0.2% and 3.6%, respectively. Major Q wave abnormalities were observed in 1.7% of subjects, minor Q wave abnormalities in 0.7%, T wave abnormalities in 0.7%, atrial fibrillation in 0.08% of workers, atrial flutter in 0.02%, WPW pattern in 0.2%, and second degree atroventricular block in 0.02%. Third degree atroventricular block pattern was not seen.

Conclusions: In a large sample of Spanish workers, the prevalence of many ECG patterns related to structural heart disease and/or adverse prognosis (mainly left ventricular hypertrophy, complete left bundle branch block, T wave abnormalities, ST segment abnormalities and atrial fibrillation) was low. Hence, this suggests that the Spanish working population could have a profile of low risk of heart disease.

290 How does stress affect cardiovascular risk?
detect cocaine-related myocardial disease at an earlier stage than conventional CMR studies.

P1691 | BEDSIDE
Factors associated with improvement of depression after acute coronary syndromes
D. Nanchen1, R. Auer1, B. Gencer2, O. Muller2, P. Jun4, C.M. Matter3, S. Windeker4, T.F. Luschser5, F. Mach2, N. Rodondi4, D. Department of Ambulatory Care and Community Medicine, Lausanne, Switzerland; 2University Hospital of Geneva, Department of Cardiology, Geneva, Switzerland; 3University Hospital Centre Vaudois (CHUV), Lausanne, Switzerland; 4Bern University Hospital, Bern, Switzerland; 5University Hospital Zurich, Zurich, Switzerland

Background: Depression increases the risk of recurrence and mortality by two-fold after acute coronary syndromes (ACS). However, less is known about clinical and behavioral factors associated with improvement of depression after ACS, as compared to persistent or new depression during follow-up.

Methods: Patients were part of the Swiss ACS cohort, a large prospective multicenter study of patients with ACS in Switzerland. We used a validated self-assessed questionnaire, the 20-items Center for Epidemiologic Studies Depression Scale (CES-D), to screen for depression (score ≥ 16) during hospitalization, and one year after discharge. Complete depression improvement was defined as the presence of depression at baseline only, 2) persistent or new depression when present both at baseline and after one year, or after one-year only. In a multivariate logistic model we assessed whether one-year: 1) ideal cholesterol management (defined as LDL-cholesterol below 1.8 mmol/l or 50% decrease or use of high-intensity statins (atorvastatin 40 mg or rosuvastatin 20 mg or higher); 2) ideal blood pressure control, defined as below 140/90 mmHg; 3) smoking cessation for smokers; 4) reduction of alcohol consumption for those with more than 14 drinks per week (intensification of physical activity 6) reporting using drugs according to guidelines, defined as the concomitant use of aspirin, statin and either angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, or beta-blockers; were associated with improvement of depression.

Results: Between 2009 and 2013, 1,164 patients with ACS were screened for depression both at baseline and at one-year follow-up. Overall, 444 (38.1%) patients had depression; 129 (11.1%) had improved depression at one-year, and 315 (27.1%) had persistent or new depression. Patients with depression were less frequently married (p<0.015), had more diabetes (p<0.03), were more frequently smokers (p<0.001) and anti- depressive drug users (p<0.001) than patients without depression. At one year, factors associated with improvement of depression were intensification of physical activity with multivariate-adjusted odds ratio (OR): 1.96, 95% confidence interval (CI): 1.25–3.06, and smoking cessation for smokers (OR 2.30, 95% CI: 1.10–4.78). Rates of ideal cholesterol or blood pressure management, alcohol reduction for at-risk users, and adherence to recommended drugs were similar between improved or persistent/new depression.

Conclusion: Intensification of physical activity and smoking cessation were associated with improvement of depression after ACS.

Acknowledgement/Funding: Supported by the Swiss National Scientific Foundation

P1692 | BEDSIDE
Electrophysiological features in chronic alcoholics in their relation to the echocardiographic and clinical data
A. Gorbonova, S.Y.U. Leviashov, South-Ural State Medical University, Chelyabinsk, Russian Federation

Objective: To determine electrophysiological features in chronic alcoholics in their relation to the echocardiographic and clinical data.

Methods: A cross-sectional study, including 3 groups of men: 1- chronic alcoholics, aged 35–55 years during alcohol withdrawal (n=115), 2 – chronic alcoholics in abstinence for 3–6 months (n=30), 3 – healthy controls of the same age (n=50).

Patients underwent clinical examination, biochemical tests, ECG, first ECG derivative, Holter ECG monitoring. In 1 group Holter ECG monitoring traces were satisfactory for diagnostic purposes in 35 patients. Echocardiography was used in groups 2 and 3. First ECG derivative represents velocity parameters of cardiac electrical activity and changes significantly in cases, associated with electrical heterogeneity. Quantitative parameter of first ECG derivative - ventricular activation rate (VAR) was used in analysis. Collected data were analyzed by one way ANOVA, Post hoc test for independent samples, linear regression analyses using SPSS software version 19.

Results: There was a significant difference between groups in VAR as determined by one way ANOVA F(2,16)=3.12, p=0.047. Dunnett’s T3 test for post hoc revealed that VAR in alcoholic patients during withdrawal was similar to euglycemic controls (38.8±2.2sec-1 vs. 39.7±2, p=0.002). Echocardiographic data didn’t reveal significant abnormalities in chronic alcoholics in comparison with controls: EF 61±5 vs. 68±5%, p=0.001, LV mass/BSA 115±12 vs. 112±7 g/m², NS; PWT 0.99±0.1 vs 0.99±0.1 cm, NS; LVEDd 4.9±0.2 vs 4.9±0.2, NS. In alcoholicholics different types of cardiac arrhythmias were detected with Holter ECG monitoring: atrial fibrillation in 5 (14%), atrial ectopics in 8 (23%), high grade ventricular arrhythmias, including non-sustained ventricular tachycardia, in 19 patients (54%). Linear regression analyses demonstrated significant relationship between VAR and ventricular arrhythmias in alcoholics (adjusted R square=0.78, β=−0.887, p<0.001).

Conclusions: Electrophysiologic remodeling of heart in alcohol heart disease precedes morphological changes. In alcoholics with normal echocardiographic parameters alcohol consumption provokes electrical heterogeneity of heart, which may be diagnosed using ECG and first ECG derivative, and results in cardiac arrhythmias. First ECG derivative demonstrates early stage of electrophysiological remodeling, results are consistent in alcoholics during withdrawal and abstinence and help to identify alcoholics at highest cardiovascular risk.

P1693 | SKYRIOT
Dramatic and specific differences in cardiovascular disease risk factors between homeless people and general population - a representative survey
E. Naszydlowska1, T. Zdrojewski2, S. Gluszek3, A. Jegier4. 1The Jan Kochanowski University (JKU), The Faculty of Health Science, Kielce, Poland; 2Medical University of Gdansk, Department of Prevention and Education, Department of Hypertension and Diabetology, Gdansk, Poland; 3The Jan Kochanowski University, The Faculty of Health Sciences, The Institute of Nursing and Obstetrics, Kielce, Poland; 4Medical University of Lodz, Department of Social and Preventive Medicine, Department of Sports Medicine, Lodz, Poland

Introduction: Cardiovascular diseases (CVD) in the homeless represent a serious medical, social and economic problem. However, in the socially-deprived group of people, knowledge is still limited.

Purpose: The aim of the study was to assess prevalence and control of cardiovascular risk factors in homeless people and to compare them with general population.

Methods: The study included a representative group of 614 homeless people (104 females[F] aged 21–79, mean age 49.0±13.6 years; 501 males[M] aged 18–79, mean age 53.7±11.6 years) at Polish shelters and hostels. The participants BMI, blood pressure, fasting serum lipids concentration, C-reactive protein (CRP), glucose, creatinine were determined. The occurrence of smoking and depression was assessed with questionnaire. The results were compared with the ones obtained in a representative age-matched group of adults (NATPOL, 2011).

Results: Hypertension was identified far more often in the homeless than in NATPOL study subjects. (54.9% & 64.3% M vs 27.9% F & 34.8% M respectively; p<0.05). The homeless subjects were much less often aware of their hypertension (F:69.5% & M:83.8% vs 22.9% & 33.1% respectively; p<0.05) and fewer were treated for their hypertension (F:25.3% & M:10.8% vs 72.3% & 55.4% respectively; p<0.005). Total cholesterol and LDL levels were significantly higher in homeless men (209±12 mg/dl vs 197±17±mg/dl and 133±22 mg/dl vs 123±14mg/dl respectively). CRP concentration was also higher in homeless subjects, F:5.6±1.5mg/l, M:6.0±0.6mg/l vs F:2.0±0.1mg/l, M:1.8±0.1mg/l, than in general population. Glucose concentration in homeless men was higher compared to general population but the difference was not statistically significant (100.9±2.2mg/dl vs 95.9±0.9mg/dl respectively). There are more smokers in the homeless group than in general population (F:73.3% & M:79.6% vs F:37.8% & M:49.7% respectively; p<0.05). Depressive symptoms according to Beck’s Depression Scale were observed more often in homeless people (M:55.4% & F:54.6% M vs 25.1% F & 17.6% M respectively; p<0.05). Obesity wasn’t dominant in the homeless.

Conclusions: CVD risk factors are more increased in the homeless group, especially homeless males, than in general population. The study is congruent with European Platform Against Poverty. The results may be applied in preventive programs, reduction of social inequalities.

Acknowledgement/Funding: The grand of Ministry of Science and Higher Education, Poland

P1694 | BEDSIDE
Endothelial cell examination-related metabolic abnormalities in new university students: cross-sectional and follow-up analyses
T. Konno1, M. Ikeda2, M. Shimizu2, T. Yoshimuta3, H. Yoshikawa2, J. Koizumi2, T. Okada3, A. Suzuki4, M. Yamagishi1, 1Kanazawa University Hospital, Division of Cardiovascular Medicine, Kanazawa, Japan, 2Kanazawa University Health Service Center, Kanazawa, Japan, 3Ikishika Prefectural Hospital, Division of Gastroenterology, Kanazawa, Japan, 4Duke University Medical Center, Division of Gastroenterology, Durham, United States of America

Objective: In Japan, high-school graduates who failed to pass the university entrance examination mostly attend full-time cram schools to devote themselves to another try for a year(s). These full-time cram school students, called ‘Ronin samurai’ in Japanese, could be at risk for development of metabolic abnormalities because they live sedentary lifestyle under persistent examination stress until they pass the entrance examination.

Methods: We assessed whether the Ronin-samurai period before entering university has detrimental metabolic effects in new university students.

Results: The cross-sectional study in 1777 new university students revealed that the Ronin-samurai group (n=319, 19.9±1.3 years) showed higher BMI (21.6±4.0 vs. 20.8±2.7 kg/m²; p<0.001), systolic blood pressure (123.5±12.1 vs. 121.2±11.7 mmHg; p<0.001), total cholesterol levels

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475/1/163/434475 on 07 February 2019
IU/L, n=94) demonstrated a drastic and spontaneous decrease of ALT values.

Touloise, France; Hospital Saint-Antoine, Paris, France

early myocardial infarction (MI). The prevalence of FH, which is estimated to be

Department of Cardiology, DIJON, France; European Hospital Georges

J. Ferrieres6, T. Simon7, Y. Cottin3, N. Danchin 4 on behalf of RICO and

M. Zeller1, M. Farnier 2, C. Touzery3, E. Puymirat 4, F. Schiele5, J.C. Beer3,

With acute myocardial infarction: an algorithm-based approach

P1696 | BEDSIDE

Marker of periodontitis as an independent predictor of cardiovascular outcome: a longitudinal population-based study

N. Kanjanahattakij 1, T. Yingchoncharoen 1, R. Mahanonda 2, N. Kanjanahattakij 1, T. Yingchoncharoen 1, R. Mahanonda 2,

Data were obtained from Electrical Generating Authority of Thailand study. A total of 1613 participants were enrolled in 2002. Baseline characteristics, outcomes and periodontal parameters [pocket depth (PD), clinical attachment level (CAL), and tooth loss] were recorded. Patients were followed for 11.7±2.4 years for cardiovascular outcomes and all-cause mortality. A multivariable Cox regression was performed to identify associations with events.

Results: Total outcome occurred in 190 participants (11.8%), of these 88 (46.3%) were cardiovascular events. There were 60 patients with myocardial infarction (MI) and 28 with stroke (31.6% and 14.7% of total outcome respectively). Mean PD were 2.44±0.68mm. There were 244 subjects (15%) with PD ≥ 5 mm. Mean PD was significantly higher in male patients (p < 0.001) compared to the non-Ronin-samurai group (p = 0.0001) irrespective of the Ronin-samurai period although no lifestyle intervention was performed during the time period.

Conclusions: These findings suggest that prolonged entrance examination-stress, represented by the Ronin-samurai period, may have detrimental metabolic effects in new university students. Further studies are warranted to clarify whether this “entrance examination-related metabolic abnormalities” could be observed not only in new university students, but also in new high-school students or even in new junior high-school students, if they passed the competitive entrance examination.

P1695 | BEDSIDE

Remnant cholesterol predicts cardiovascular event risk in patients with type 2 diabetes independently from the baseline coronary artery disease state

C.H. Saely1, D. Zanolli2, P. Rein3, A. Vonbank4, A. Leherer5, A. Muehlen6, H. Drexel7,1,2,3,4,

1 Academic Teaching Hospital, Department of Medicine and Cardiology, Feldkirch, Austria; 2 Private University of the Principality of Liechtenstein, Triesen, Liechtenstein; 3 VIVIT Institute, Feldkirch, Austria; 4 Drexel University College of Medicine, Philadelphia, United States of America

Background and introduction: Remnant cholesterol, which is calculated as total cholesterol minus LDL cholesterol minus HDL cholesterol recently has attracted interest as a marker of cardiovascular risk.

Purpose: Whether remnant cholesterol has the power to predict cardiovascular events in patients with type 2 diabetes (T2DM) as well as in non-diabetic patients in whom the baseline coronary artery disease (CAD) state was verified angiographically is still unclear and was therefore addressed in this study.

Methods: We enrolled 1774 consecutive patients undergoing coronary angiography for the evaluation of established or suspected stable CAD. Prospectively, cardiovascular events were recorded over a mean follow-up period of 7.5±2.9 years. Diabetes was diagnosed according to ADA criteria.

Results: During follow-up, 32.5% of our patients suffered cardiovascular events; the event rate was significantly higher in patients with T2DM (n=513) than in nondiabetic subjects (40.5 vs. 29.3%; p < 0.001). Remnant cholesterol significantly predicted cardiovascular events in the total study population, among patients with T2DM as well as among non-diabetic patients (HR 1.15 [1.07–1.24], p=0.001; 1.20 [1.05–1.38], p=0.008 and 1.19 [1.09–1.30], p < 0.001, respectively) and after multivariate adjustment including presence as well as extent of baseline CAD (HR 1.15 [1.07–1.24], p=0.001; 1.20 [1.05–1.38], p=0.008 and 1.15 [1.05–1.25], p=0.002, respectively).

Conclusion: From our data we conclude that remnant cholesterol predicts cardiovascular event risk in patients with type 2 diabetes as well as in non-diabetic patients independently from the baseline CAD state.

P1696 | BEDSIDE

Increased plant sterol deposition in vascular tissue characterizes patients with severe aortic stenosis and concomitant coronary artery disease

O. Weingaertner1, A. Luister2, H. F. Schott2, C. Huschef2, H. J. Schaefers2,1,2,3,4,5,6,7,8,9,10

1 University of Burgundy, INSERM U866, Dijon, France; 2 Le Point Medical, Endocrinology, Dijon, France; 3 University Hospital, Dijon, France; 4 European Hospital Georges Pompidou, Paris, France; 5 Regional University Hospital, Cardiovascular, Besançon, France; 6 Toulouse Rangueil University Hospital (CHU), Cardiology, Toulouse, France; 7 Hospital Saint-Antoine, Paris, France

Background and aim: Familial hypercholesterolemia (FH) is at very high risk of early myocardial infarction (MI). The prevalence of FH, which is estimated to be at least 1:500 in the general population, remains unclear in patients with acute MI. From databases of 3 French regional and nationwide registries of acute MI (RICO and FAST-MI 2005 and 2010, respectively), we aimed to determine FH prevalence by developing a specific algorithm.

Methods and results: Consecutive patients with AMI ≤48 hours of onset in January 1, 2005 to December 31, 2005 (RICO and FAST-MI 2005) and in January 1, 2010–December 31, 2010 (RICO: from January 2005–December 2013, were considered in the 3 databases. The algorithm was adapted from Dutch lipid clinic network criteria and build upon 4 variables (i.e. LDL level on admission and previous use of lipid lowering medications, premature and family cardiovascular (CV) history) to identify FH probability. The LDL level was adjusted on each type of lipid lowering drug (LLD) and the probability of FH was defined taking into account missing data. Among the 7484 included patients in the RICO registry, 31.6% had premature CV disease, 29.7% had familial history, 19.9% were under LLD and 9.7% had LDL ≥ 5 mmol/L. FH prevalence was calculated as unlikely (72.6%), possible (24.6%) and probable/definite (2.8%). From the 1957 patients from FAST-MI 2005 with all data available, 29.7% had premature CV disease, 23% had a family history, 26.6% were on LLDs, and 5.4% had LDL > 5 mmol/L. FH prevalence was calculated as unlikely (77.9%), possible (19.4%) and probable/definite (2.7%). In the 2223 patients from FAST-MI 2010, 32.2% had premature CV disease, 24.9% had a family history, 28.1% were on LLDs, and 5.0% had LDL ≥ 5 mmol/L. FH prevalence was calculated as unlikely (75.7%), possible (21.5%) and probable/definite (2.7%).

Conclusion: Our 4-variable algorithm yielded concordant results to determine FH probability in 3 different cohorts of MI patients. In this large population reflecting routine clinical practice in acute MI, a high prevalence of FH was found, suggesting the opportunity for prevention strategies for these high-risk patients.

Acknowledgement/Funding: PFIZER, Servier, CNAM-TS
synthesis) and oxysterols were determined in plasma and aortic valve tissue from 104 consecutive patients with severe aortic stenosis (n=68 statin treatment; n=36 no statin treatment) using gas chromatography-flame ionization and mass spectrometry. The extent of CAD was determined by coronary angiography prior to aortic valve replacement.

Results: Patients treated with statins were characterized by lower plasma cholesterol, cholesterol, and lathosterol concentrations. However, statin treatment did not affect the sterol concentrations in cardiovascular tissue. The ratio of campesterol-to-cholesterol was increased by 0.46±0.34 μg/ml (26.0%) in plasma of patients with CAD, and 0.22±0.12 μg/ml (11.7%) in the aortic valve cusps and oxidized solstivor-to-cholesterol ratios were increased by 0.35±0.20 μg/ml (22.7%) in the plasma of patients with CAD. Of note, neither cholesterol nor the ratio of cholesteral-to-cholesterol was associated with CAD.

Conclusions: Patients with concomitant CAD are characterized by increased deposition of plant sterols, but not cholesterol in aortic valve tissue. Moreover, patients with concomitant CAD were characterized by increased oxysterol concentrations in plasma and aortic valve cusps.

Acknowledgement/Funding: Netherlands Organisation for Scientific Research (Grant 014-012-010)

P1690 | BEDSIDE
Post-prandial remnant-like particles formation in abetalipoproteinemia: prediction of the effectiveness of microsomal triglyceride transfer protein inhibitor on post-prandial remnant-like particles
Kanazawa University, Kanazawa, Japan

Background: Abetalipoproteinemia (ABL) is an extremely rare autosomal recessive disorder, characterized by almost complete absence of apop-containing lipoproteins. This condition is caused by mutations in microsomal triglyceride transfer protein (MTP) gene, leading to prevent the formation of chylomicrons. It has been reported that MTP inhibitor was effective to reduce LDL-C even in patients with ABL, exhibiting complete absence of MTP. The purpose of this study was to investigate whether MTP inhibitor contributed to the reduction of the formation of post-prandial RLP by investigating the metabolism of them in ABL subject which exhibits complete absence of MTP.

Methods: ORFT cream (Jomo Shokuhin, Takasaki, Japan) 50 g was given per body surface area (m²), blood sampling was performed at 2 hours intervals up to 6 hours. Plasma lipoprotein and RLP fraction were determined by HPLC system in one ABL subject (age 46yr, LDL-C=1mg/dl, four heterozygous FH subjects (mean age=58±17 yr, mean LDL-C=240.5±26.3mg/dl), and four controls (mean age=61±8.6 yr, mean LDL-C=87±5.8mg/dl). Plasma lipoprotein and RLP fraction were determined by HPLC system. The area under curve (AUC) of TG, RLP-TG, and RLP-C levels were evaluated.

Results: After oral fat load, the AUC of TG, RLP-TG, and RLP-C levels were almost completely absent in the ABL subject (45mg/dl×hour, 49mg/dl×hour, 43mg/dl×hour, respectively), whereas, those of FH subjects were significantly higher than those of controls (441±87mg/dl×hour vs 316±13mg/dl×hour, 126±50mg/dl×hour vs 49±11mg/dl×hour, p<0.05, 34±8mg/dl×hour vs 23±12 mg/dl×hour, respectively).

Conclusions: Our results indicate that ABL appeared to have low levels of TG response and diminished remnant lipoprotein formation after fat-load, and that MTP inhibitor should contribute to the reduction of the formation of post-prandial RLP as well as that of LDL-C.

P1701 | BEDSIDE
Random blood glucose and incidence of cardiovascular disease among adults without diabetes: findings of the China Kadoorie Biobank
R. Peto1, Z. Chen1 on behalf of China Kadoorie Biobank Collaborative Group.

We analysed data from 467,508 men and women aged 35–79 years.

Methods:

Background:

Random blood glucose and incidence of cardiovascular disease (CVD) among apparently non-diabetic individuals, in both terms of the shape and strength of the relationship. The association is poorly documented in Chinese populations.

Results:

Conclusion:

P1702 | BEDSIDE
Harnessing publicly available genetic data to prioritize therapeutic targets for cardiovascular prevention
1 University of Oxford, Clinical Trial Service Unit & Epidemiological Studies Unit, Oxford, United Kingdom; 2 University Medical Center Utrecht, Department Heart & Lungs, Utrecht, Netherlands; 3 University College London, Institute of Cardiovascular Science, London, United Kingdom; 4 University of Pennsylvania, Department of Surgery, Philadelphia, United States of America

Background and introduction: LDL-cholesterol (LDL-C) reduction effectively reduces risk of coronary artery disease. However, statins (the most widely prescribed LDL-C lowering drugs) increase type 2 diabetes (T2D) risk.

Purpose: To identify potential therapeutic targets that alter LDL-C and CVD risk without causing dysglycemia.

Methods: We used publicly available genome data from genome-wide association studies (GWAS) including: Global Lipids Genetics Consortium (GLGC); Meta-Analyses of Glucose and Insulin-related traits Consortium ( MAGIC); DIAbetes Genetics Replication And Meta-analysis (DIAGRAM) consortium, and; Coronary Artery Disease Genome-Wide Replication And Meta Analysis (CARDIOGRAM) plus The Coronary Artery Disease (CAD) Genetics, collectively known as CARDIOGRAMplusC4D consortium. We used these data to investigate the shared association of LDL-C-related SNPs with CAD risk, T2D risk and fasting glucose. We conducted meta-GWAS analyses of glycemic traits and performed Mendelian randomization analyses to investigate causal relationships.

Results: A single standard deviation (SD) increase in LDL-C caused an increased odds ratio (OR) for CAD of 1.63 (95% confidence interval [CI]: 1.55, 1.71)
we identified heterozygous mutations in 4 families, and compound heterozygous mutations in 1 family within the coding region of PCSK9 gene, one of which was novel (c.1301G>A;p.Arg434Gln).

**Conclusion:** WES combined with integrated variant annotation prediction successfully identified causative mutations in patients with FHBL either with APOB coding semi-automated method and indexed by body surface. A multivariate analysis was utilized to assess for an independent association of EFV with coronary atherosclerotic burden. **Results:** Age, total cholesterol, LDL-C, HDL-C, apolipoprotein A-1, apolipoprotein B, biometric filtration rate and presence of Achilles tendon xanthomas were associated with atherosclerotic burden in univariate analysis. After adjusting for confounders and abdominal circumference (a marker of visceral fat), an independent association between EFV and presence of plaques, CAC > 0, CAC scores as a continuous variable and presence of coronary segments with plaques was found. For and increment in 10 m3 of ETV the odds ratios (95% confidence intervals) respectively for the presence of plaques, CAC > 0, CAC scores and number of coronary segments with plaques were respectively: 1.40 (1.02–1.93) p=0.041, 1.40 (1.02–1.91) p=0.035, 1.12 (1.11–1.14) p<0.001, and 1.16 (1.08–1.26) p<0.001.

**Conclusions:** EFV was independently associated with the presence and severity of atherosclerotic plaque burden in FH patients.

### P1705 | BEDSIDE

**Association between epidermal fat and subclinical atherosclerosis assessed by coronary computed tomographic angiography in familial hypercholesterolemia**

L.C. Mangili, M.H. Miname, L.M. Lima, C.E. Rochitte, R. Prado, R. Kalil, R.D. Santos. Heart Institute InCor University of Sao Paulo, Sao Paulo, Brazil

**Background:** Familial hypercholesterolemia (FH) is a common disorder resulting in severe elevations of blood cholesterol and increased prevalence of subclinical atherosclerosis and high risk of premature coronary heart disease. Pericardial fat, a visceral adipose tissue depot, has been associated with subclinical atherosclerosis in non-FH subjects.

**Purpose:** Evaluate the association of epicardial fat volume (EFV) in m3, defined as the fat volume inside the pericardial sac, with the presence and extent of subclinical atherosclerosis and high risk of premature coronary heart disease. **Methods:** 97 hypercholesterolemic FH subjects (35% male, age 45±13 years, LDL-C 281±56 mg/dL) underwent computed tomography angiography and coronary artery calcium (CAC) scoring. EFV was measured in non-contrast images using semi-automated method and indexed by body surface. A multivariate analysis was utilized to assess for an independent association of EFV with coronary atherosclerotic burden.

**Results:** Age, total cholesterol, LDL-C, HDL-C, apolipoprotein A-1, apolipoprotein B, biometric filtration rate and presence of Achilles tendon xanthomas were associated with atherosclerotic burden in univariate analysis. After adjusting for confounders and abdominal circumference (a marker of visceral fat), an independent association between EFV and presence of plaques, CAC > 0, CAC scores as a continuous variable and presence of coronary segments with plaques was found. For and increment in 10 m3 of ETV the odds ratios (95% confidence intervals) respectively for the presence of plaques, CAC > 0, CAC scores and number of coronary segments with plaques were respectively: 1.40 (1.02–1.93) p=0.041, 1.40 (1.02–1.91) p=0.035, 1.12 (1.11–1.14) p<0.001, and 1.16 (1.08–1.26) p<0.001.

**Conclusions:** EFV was independently associated with the presence and severity of atherosclerotic plaque burden in FH patients.

### Table 1

<table>
<thead>
<tr>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3350g</td>
<td>≥3350g</td>
<td>≥3350g</td>
<td>≥3350g</td>
</tr>
<tr>
<td>N</td>
<td>(n=441)</td>
<td>(n=446)</td>
<td>(n=442)</td>
</tr>
<tr>
<td>Fat mass</td>
<td>&lt;0.24 (&lt;0.71; 0.23)</td>
<td>&lt;0.33 (&lt;0.80; 0.14)</td>
<td>&lt;0.11 (&lt;0.49; 0.53)</td>
</tr>
<tr>
<td>BMI</td>
<td>−0.35 (&lt;0.78; 0.09)</td>
<td>−0.24 (&lt;0.49; 0.19)</td>
<td>0.001 (&lt;0.44; 0.44)</td>
</tr>
</tbody>
</table>

**Note:** Coefficients were adjusted for sex, age, BMI, eGFR, systolic blood pressure, LDL, HDL triglycerides, HbA1c, education level, alcohol consumption, vegetable/fruit consumption, physical activity, smoking (current or past).

### P1704 | BEDSIDE

**Birth relationship of weight body composition in young adulthood**

T. Koffer, M. Bossard, S. Aeschbach, A. Tabard, J. Rupert, Replidol, S. Van Der Leiy, S. Berger, M. Risch, L. Risch, D. Korens, University Hospital Basel, Internal Medicine, Basel, Switzerland, University Hospital Basel, Endocrinology Division, Basel, Switzerland, Labormedizinisches Zentrum Dr. Risch, Schaan, Liechtenstein

**Background:** Low birth weight has been associated with an increased risk of cardiovascular diseases and diabetes in epidemiological studies. However underlying mechanisms are poorly understood. We hypothesized that differences in body composition during adulthood could be a potential mediator for this inverse relationship. **Methods:** The "genetic and phenotypic determinants of blood pressure and other cardiovascular risk factors" (GAPP) study is a population based prospective cohort study in the Principality of Liechtenstein. Young and healthy adults aged 25-41 years without overt cardiovascular disease or diabetes and a body mass index ≤35 kg/m^2 were enrolled. Birth weight was assessed by self-report. Bioelectrical impedance analysis was used to assess body composition in all participants. Multivariable regression models adjusting for potential confounders were constructed to assess the relationship between birth weight and body composition during adulthood.

**Results:** Out of 1774 individuals with available information about birth weight, 53.4% were female. Median age was 37 years. Median and interquartile range of birth weight were 3350g (3050g; 3700g). The main results are shown in the table. Across quartiles of birth weight, there was a highly significant decrease in body
Y. Odaka1, J. Takahashi1, R. Tuburaya2, K. Nishimiya1, K. Hao1, Y. Matsumoto1, Y. Hirokawa1, H. Shimokawa1, 1Tohoku University Graduate School of Medicine, Cardiovascular Medicine, Sendai, Japan; 2Toosh Corporation, Bioscience Division, Kanagawa, Japan

Background: Coronary microvascular dysfunction (CMD) plays an important role in the pathogenesis of a wide range of ischemic heart disease (IHD), not only in microvascular angina but also in epicardial coronary artery disease (CAD), vasospastic angina (VSA) and acute coronary syndrome. However, useful biomarker for the presence of CMD remains to be developed.

Methods and results: We enrolled 198 consecutive patients (M/F 116/82, age 60.1±13.2 [SD] years) who underwent acetylcholine (ACh) provocation test (<12.7±2.7, n=109, P<0.05) and non-VSA (10.3±2.0, n=53) groups (P=0.142). However, when the 2 groups were further divided into 4 groups according to the presence or absence of CMD, including VSA with CMD, VSA without CMD, CMD alone, and non-HD (non-VSA and non-CMD) groups, serotonin levels were significantly higher in VSA with CMD (25.8±12.5, n=36) compared with VSA without CMD (12.7±2.7, n=109, P<0.05) and non-HD (5.4±0.6, n=23, P<0.01) groups, and trended to be higher in CMD alone group (13.8±3.4, n=30). Importantly, there was a positive correlation between plasma serotonin levels and baseline TIMI flow frame count (r=0.204, P<0.05), which is a marker of coronary vascular resistance. The classification and regression tree analysis for the presence of CMD revealed that the first discriminant was the cut-off value with plasma serotonin level of 9.5 μmol/L. Moreover, multiple logistic regression analysis showed that serotonin levels greater than the cut-off value was the sole and most powerful predictor for the presence of CMD [odds ratio (95% confidence interval) 2.45 (1.19–5.03), P<0.05].

Conclusions: These results suggest that plasma levels of serotonin are the novel biomarker for the presence of CMD in patients with angina

P1708 | BENCHMARK
Direct quantitative assessment of the peripheral artery collateral circulation: validation of collateral flow index
M. Stoller, H. Steck, R. Grossenbacher, C. Seiler. Bern University Hospital, Department of Cardiology, Bern, Switzerland

Background: The purpose of this study was to validate collateral flow index (CFI) as a reference method in the assessment of the peripheral artery collateral circulation.

Methods: Collateral function of the left superficial femoral artery was determined by CFI and regional perfusion index (RPI) during a 3-minute balloon occlusion. Mean proximal superficial femoral artery pressure (Pa), mean central venous pressure (CVP) and mean superficial femoral artery wedge pressure (Pw) were obtained to calculate CFI: (Pw – CVP)/(Pa – CVP). Transcutaneous oxygen tension was measured at the anteromedial calf (tcpO2a) and at a reference site at the lower left abdomen (tcpO2ref) to calculate minimal RPI (RPImin) during left superficial femoral artery occlusion: tcpO2a/tcpO2ref.

Results: 86 patients, 66 men (77%), mean age 71±12 years, underwent collateral function determination in the left superficial femoral artery. Mean CFI was 0.58±0.185, while mean RPImin was 0.512±0.144. Using linear regression analysis, CFI was significantly related to RPI (figure 1).

Conclusion: Direct quantitative assessment of the peripheral artery collateral circulation by CFI is well reflected in noninvasive measures of tissue oxygenation and should be considered as the reference method for assessment of the peripheral artery collateral circulation.

P1709 | BEDSIDE
The use of acute pd/pa drop after intracoronary nitroglycerin infusion to rule out significant FFR: CANICA (can intra-coronary nitroglycerin predict fractional flow reserve without adenosine?) study
R. Martin Reyes1, J.A. Franco Pelaez2, J.M. De La Torre3, R. Lopez Palop2, M. Larmarn4, A. Sanchez Recalde1, I. Lozano4, S. Brugalla1, F. Navarro1, F. Arfe1, F. Foundation Jimenez Diaz, Madrid, Spain; 2University Hospital Marques de Valdecilla, Santander, Spain; 3University Hospital San Juan de Alicante, Alicante, Spain; 4Donostia University Hospital, San Sebastian, Spain; 5University Hospital La Paz, Madrid, Spain; 6Hospital de Cabuenes, Gijon, Spain; 7Hospital Clinico de Barcelona, Barcelona, Spain

Introduction: Functional assessment of coronary artery stenosis is performed by measuring the fractional flow reserve (FFR) under hyperemic conditions (Adenosine). However the use of adenosine portends limitations.

Objective: We sought to investigate the relationship and correlation between FFR and the Pa/dPa value obtained just after the intra coronary infusion (acute drop) of intracoronary bolus of nitroglycerin (pd/Pa-NITG) and if this parameter enhances diagnostic accuracy for FFR prediction compared to the resting baseline pd/Pa measurement.

Methods: We conducted a multicenter study that prospectively included 338 consecutive patient with normal coronary angiographic lesion data were collected. Resting baseline pd/Pa, pd/Pa-NITG after coronary infusion of a 2 mcg bolus of nitroglycerin and FFR after continuous intracoronary (iv) adenosine infusion (140 mcg/kg/min) or after intracoronary (ic) adenosine infusion (>360 mcg in the left system and >90 mcg in the right coronary artery), were measured following a standard protocol in all the centers.

Results: Resting baseline pd/Pa value was 0.72 to 1.0 (0.93±0.04), pd/Pa-NITG was 0.60 to 1.0 (0.87±0.07) and FFR value after Adenosine iv or ic 0.55 to 1.0

Effect of different risk factors on the cardiovascular system / Physiology and coronary circulation 295

fat mass. In continuous analyses, the beta coefficient (95% confidence interval) per 100g increase in birth weight was −0.06 (−0.10; −0.03) and p<0.0001. There was no relationship between birth weight and muscle mass.

Conclusion: Among young and healthy adults, there was a highly significant inverse correlation between birth weight and body fat mass. This inverse association may at least in part mediate the adverse cardiovascular outcomes among individuals with low birth weight.

Acknowledgement/Funding: Schweizerischer Nationalfonds, Schweizerische Herzstiftung

PHYSIOLOGY AND CORONARY CIRCULATORY
P1711 | BEDSIDE
Serial changes in microvascular resistance associated with elective percutaneous coronary intervention and their relationships with lesion characteristics assessed by optical coherence tomography
T. Murali, T. Lee, Y. Kanaji, J. Matsuda, E. Usui, T. Nida, M. Isobe, T. Kakuta, T. Tsuchida, Kyoto Hospital, Tsuchita, Japan; Tokyo Medical and Dental University, Department of Cardiology, Tokyo, Japan

Background: The influence of elective percutaneous coronary intervention (PCI) on coronary microvascular function has not been fully elucidated.

Purpose: We investigated the serial changes of microvascular function associated with elective PCI in patients with stable angina pectoris and the impact of microvascular function on clinical outcomes after PCI. We also assessed the current clinical relevance of using OCT imaging for PCI.

Methods and results: The index of microcirculatory resistance (IMR) and fractional flow reserve (FFR) were measured at pre-PCI, post-PCI, and follow-up (10 months) in 48 patients treated with elective PCI (male 81.3%, age 66.4±8.5). All patients underwent OCT examination before PCI. The median IMR values at pre-PCI, post-PCI, and follow-up were 24.9 (interquartile range (IQR) 13.1–32.0), 15.7 (IQR 11.6–21.5), and 14.5 (IQR 11.3–19.8), respectively. IMR values significantly decreased immediately after PCI (P < 0.05), and showed no further significant change at follow-up. Greater improvement of FFR values by PCI was significantly associated with greater peri-procedural IMR reduction (P = 0.03) and the effect of FFR improvement on the IMR reduction was maintained up to follow-up (P = ns). Although there was no significant relationship between pre-PCI IMR values and epicardial stenosis severity represented by FFR, the presence of OCT-derived thin-cap fibroatheroma in the culprit lesion was associated with increased IMR values at all serial measurements (pre-PCI, post-PCI and follow up).

Conclusion: The removal of functional stenosis of epicardial coronary arteries by PCI was associated with a reduction of microvascular resistance. Increased pre-PCI IMR values in the target vessel were significantly associated with OCT-derived high-risk lesion characteristics, and post-PCI IMR values may help identify patients at high risk for target vessel revascularisation.

P1712 | BEDSIDE
Distribution of pressure gradients along left anterior descending artery in patients with angiographically normal arteries
K. Fuji, M.F. Fukunaga, T.I. Imakana, K.M. Miki, H.T. Tamura, T.H. Horimatsu, T.S. Sata, M.N. Nishimura, M.S. Shibuya, M.I. Ishihara, Hyogo College of Medicine, Nishinomiya, Japan

Background: In the clinical setting, some pressure gradient exists in the left anterior descending artery (LAD) even after successful coronary intervention despite the absence of vessel obstruction in patients with coronary artery disease.

Purpose: We validated the hypothesis that there is no decline of coronary pressure from the proximal to distal part in the LAD.

Methods: Two hundred and sixty patients with normal coronary angiogram in the LAD without signs of anterior wall ischemia were prospectively enrolled. A mean pressure ratio (PR: mean distal/proximal pressures at hyperemia) was measured in the LAD at each points: 12, 10, 7, 5 and 0cm distal to the ostium. Intravascular ultrasound (IVUS) was also performed, and blood sample was obtained from the aortic-root and the anterior interventricular vein to calculate myocardial oxygen uptake (MV02). The Romhilt-Estes score on electrocardiogram was calculated using scores of 4 points for the diagnosis of left ventricular hypertrophy (LVH).

Results: In all cases, the PR gradually decreases in proportion to distance from the ostium (average: 0.85±0.06 at 12 cm to distal ostium). No difference was identified in the degree of degradation of PR between patients with and without the evidence of minor plaque on IVUS (left figure). MV02, myocardial bridge, and ejection fraction did not correlate with the degree of degradation of the PR value. However, the degradation degree of the PR was significantly larger in LVH patients than in patients without LVH (right figure).

P1713 | BEDSIDE
Improvement of left ventricular function: an additional benefit of percutaneous revascularization for occluded coronary artery
M. Chimura, S. Yamada, Y. Yasaka, H. Kawai, Himeji Cardiovascular Center, Himeji, Japan

Background: Compared to significant stenosis without occlusions (non-CTO), chronic total occlusions (CTO) represent the more complex and challenging coronary revascularization (CVR) task. OCT findings and the relationship between the lesion characteristics and microvascular function.

Methods: Sixty four CTO (case) and target lesion matched non-CTO (control) patients who underwent successful PCI and evaluated by echocardiography before and 9 months after procedure were investigated. Echocardiography was performed before and 9 months after the procedure with conventional assessment including LV end diastolic and end systolic volume (LVEDV, LVESV), LV ejection fraction (LVEF), ratio of early to mid-diastolic flow to diastolic contraction (E/A ratio), deceleration time (DTc), and with 2DSTE analysis of GLS.

Results: There were no stent thromboses during follow-up. All patients showed relaxation abnormal pattern assessed by E/A ratio and DTc. GLS showed a significant improvement 9 months after in CTO group, whereas in non-CTO group GLS did not change significantly. Change of GLS (ΔGLS) was significantly greater in CTO group than in non-CTO group (P < 0.01), LVEF did not change significantly during follow-up in both groups.

Conclusion: In comparison with non-CTO, successful PCI for CTO improves left ventricular function assessed by LV GLS. Increased myocardial perfusion after treatment of CTO may improve the left ventricular function.

P1714 | BEDSIDE
Instantaneous wave-free ratio (iFR) provides the most robust measure of any resting physiological index: the effects of pressure drift and measurement variability on stenosis misclassification

Background: Pressure drift and measurement variability (real-time fluctuations in value during measurement) can result in stenosis misclassification if values cross treatment thresholds.

Purpose: We assessed these variables and investigated their effect on stenosis misclassification with FFR, iFR and whole cycle Po/Pa indices.
Methods: 447 stenoses were assessed (mean age 62.7 years ±10.1 years), 79% male. Data were analyzed to calculate physiological stenosis severity by FFR, iFR, and whole cycle Pd/Pa indices. Cutoff thresholds for a positive result for FFR, iFR and Pd/Pa were <0.80, <0.90 and <0.93 respectively. The effect of drift was analyzed by offsetting the distal intracoronary pressure trace by ±1mmHg (from −3mmHg to +3mmHg). FFR, iFR and whole cycle Pd/Pa values were recalculated and compared to their respective cutoffs. Measurement variation was analyzed by recalculating values with an offset of ±0.01 units (from −0.03 to +0.03 units). Values were compared to cutoff thresholds as previously described.

Drift and variability were plotted against stenosis misclassification (% of total cohort) across a range of −3mmHg to +3mmHg and ±0.03 to ±0.03 units respectively. The area under the curve was calculated to compare the diagnostic performance of FFR, iFR and whole cycle Pd/Pa. FFR and whole cycle Pd/Pa indices were compared to the current gold standard method (FFR). The misclassification rates across the three techniques were compared using the Chi squared test, and p-values for post-hoc comparisons were adjusted using the Bonferroni method.

Results: Mean FFR, iFR, and whole cycle Pd/Pa values for the cohort were 0.78 (±0.14), 0.85 (±0.16), and 0.90 (±0.12). Pressure drift across the range of ±3mmHg resulted in 43% (192/447), 55% (246/447) and 72% (322/447) of stenoses being reclassified with FFR, iFR and whole cycle Pd/Pa respectively. All ±0.03 units resulted in 35% (156/447), 47% (210/447) and 67% (299/447) of all stenoses being reclassified with FFR, iFR and whole cycle Pd/Pa respectively. All three groups were significantly different from each other (p<0.001).

Conclusion: FFR is more resistant to drift and measurement variability than whole cycle Pd/Pa by approximately 40% less stenoses misclassification using FFR across ±1mmHg range in contrast with whole cycle Pd/Pa, making FFR a far more clinically robust tool in the catheter laboratory. Acknowledgement/Funding: National Institute of Health Research

P1715 | BEDSIDE Prognostic value of the index of microcirculatory resistance after percutaneous coronary intervention in patients with non-ST-segment elevation acute coronary syndrome

T. Murali1, T. Lee1, Y. Kanaj1, J. Matsuda1, E. Uzu1, M. Araki1, T. Nishi1, M. Fuse1, T. Takakura1, T. Tsuchida Kyodo Hospital, Tsuchiura, Japan; 2Tokyo Medical and Dental University, Department of Cardiology, Tokyo, Japan

Background: The Index of microcirculatory resistance (IMR) is a readily available, wire-based method for invasively assessing coronary microvascular function in the catheterization laboratory. Previous study reported that increased IMR value (IMR >40) after primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) predicts a higher incidence of undergoing PCI after STEMI. The current study aimed to assess the prognostic role of the IMR in patients with non-ST-segment elevation acute coronary syndrome (NSTEMI) post PCI.

Purpose: We investigated the prognostic value of IMR after PCI in the setting of non-STEME elevation acute coronary syndrome (NSTEME-ACS) compared with fractional flow reserve (FFR) and coronary flow reserve (CFR).

Methods and results: Fifty-four hemodynamically stable patients (male: N=42, age: 64.4±10.6 years, unstable angina: N=22, NSTEMI: N=32; peak Troponin I (TnI): median 1.62ng/dL (interquartile range (IQR) 0.51–10.07 ng/dL)) underwent PCI with the use of a pressure wire to monitor intra-coronary pressure and temperature sensor. The median IMR value was 25.1 (IQR 11.1–38.6) and 12 patients (22.2%) showed IMR >40. IMR was significantly associated with peak TnI (p=0.01), patient’s age (p=0.02) and diabetes mellitus (p=0.02). Although there was no death or hospitalization for heart failure during the follow up (median 423 days; IQR 282–743 days), 2 patients were admitted with NSTEME-ACS and 7 other patients underwent PCI for angina (2 patients for in-stent restenosis of target lesions and 5 for new lesion progression). IMR and CFR values after PCI were significantly associated with coronary revascularisation (p=0.007 and p=0.03, respectively), although there was no significant relationship between FFR after PCI and adverse coronary events (p=NS). ROC curve analysis demonstrated the best cut-off value of IMR to predict coronary revascularisations was IMR =40 (AUC =0.78, p=0.007). Patients with higher post-PCI IMR values (>40) showed higher incidence of undergoing PCI than those with lower IMR values (<40) (6/12 (50.0%) VS 3/44 (7.1%), p<0.015). Multivariate logistic regression analysis revealed that IMR value <40 was the only positive predictor of coronary revascularisation (p=0.002).

Conclusion: Our results showed that the patients with NSTEME-ACS presented relatively high prevalence of high IMR value (>40) after uncomplicated PCI. Assesment of microvascular resistance after PCI in patients with NSTEME-ACS may help identify patients at high risk for adverse coronary events.

P1716 | BEDSIDE The randomized physiologic assessment of thrombus aspiration in patients with acute myocardial infarction with ST-segment elevation (PATA STEMI) trial: final results

D. Orlíč1, M. Ostojic2, B. Beleslin1, M. Tesic1, M. Borovic2, D. Sobic-Saranovic1, D. Milasinnovic1, S. Stjepovic1, M. Nedeljekovic1, G. Stankovic1 on behalf of PATA STEMI investigators. 1Clinical Center of Serbia, Belgrade, Serbia; 2Institute for Histology, Belgrade, Serbia

Background: Routine manual thrombus aspiration is superior to standard primary PCI (pPCI) in terms of improved myocardial perfusion in patients with acute myocardial infarction with ST-segment elevation (STEMI). However, myocardial perfusion after thrombus aspiration has not been assessed by an index of microvascular resistance (IMR) in a randomized fashion.

Methods: We performed a randomized, controlled clinical trial to evaluate impact of thrombus aspiration on microcirculatory resistance after pPCI in 128 patients with the first STEMI randomly assigned to thrombus aspiration or standard pPCI as a dependent variable, after adjusting for clinical, angiographic and procedural variables, thrombus aspiration was not an independent predictor of lower IMR (28.4% VS 95% CI, 24.7 to 32.8 U, VS 32.4% VS 95% CI, 28.1 to 37.4 U, p=0.077, 95% CI, 0.715–0.777, P=0.21).

Conclusions: Manual thrombus aspiration reduces microcirculatory resistance indicating better myocardial perfusion compared to conventional PCI in patients with STEMI. However, routine manual thrombus aspiration is not an independent predictor of reduced microcirculatory resistance. Reduction in microcirculatory resistance of 12.3% achieved by thrombus aspiration is not sufficient to allow echocardiographic improvement in STEMI patients at mid-term follow up.
change in resting physiology. Virtual-PCI could permit assessment of different stenting strategies in the lab and may advance trials in intervention.

Acknowledgement/Funding: Medical Research Council (UK) and British Heart Foundation

P1718 | BEDSIDE Impact of additional intracoronary nicorandil administration during fractional flow reserve measurement with intravenous ATP infusion


Background: Although adenosine triphosphate (ATP) is generally used as a hyperemic agent for fractional flow reserve (FFFR) measurement, it is uncertain whether ATP can produce maximal hyperemia in every patient. The aim of this study was to evaluate changes in FFR values with additional intracoronary nicorandil administration during intravenous ATP infusion.

Methods: We evaluated 86 coronary artery diseases (61 males, average age 71±9 years) with 112 lesions. All patients first received intravenous ATP infusion (180mcg/kg/min) for 3 minutes to measure FFR (ATP-FFR). After additional intracoronary nicorandil administration (2mg/30sec) during intravenous ATP infusion, FFR measured again (NIF-FFR). We assessed changes of FFR values and hemodynamics during FFR measurement. We also assessed baseline echocardiographic findings.

Results: In this study, 112 lesions consisted of 59 LADs, 23 LCXs and 30 RCAs. LAD lesions were significantly lower ATP-FFR and NIF-FFR than non-LAD lesions (p<0.0001). NIF-FFR was significantly lower than ATP-FFR (0.82±0.10 vs. 0.84±0.10, p<0.0001). In 14 lesions (13%), FFR values decreased more than 0.05 after intracoronary nicorandil administration. These patients with 14 lesions tend to have lower left ventricular mass index (LVM) than the others (p<0.009). Moreover, NIC-FFR decreased from deferral FFR range (≥0.8) to therapeutic FFR range (≥0.8) in 8 patients with 8 lesions. These patients were significantly lower LVM (p<0.05) and higher left ventricular ejection fraction (p<0.01) than the others.

Conclusions: Additional intracoronary nicorandil administration during FFR measurements might be useful to make sure maximal hyperemia during intravenous ATP infusion.

P1719 | BEDSIDE Efficacy of pressure-derived indices by contrast medium induced submaximal hyperemia in comparison with fractional flow reserve and hyperemic end-diastolic Pd/Pa ratio

Y. Kanaji, T. Lee, T. Murali, J. Matsuda, E. Usui, M. Araki, T. Nida, T. Kakuta. Tsushu University Hospital, Cardiovascular Department, Tsushu, Japan

Background: Instantaneous ECG-gated Pd/Pa ratio acquired at end-diastole of hyperemic state has been recently reported to show an improved correlation with Qs/On measured directly with flow-probe, and has been shown to be highly sensitive for detection of inducible myocardial ischemia compared with conventional FFR in animal model.

Purpose: We first evaluate if hyperemic ECG-gated end-diastolic Pd/Pa (H-ED-Pd/Pa) shows, as reported, good correlation with conventional FFR in humans.

Methods and results: Seventy-four intermediate stenosis in 68 patients were prospectively studied. The instantaneous wave-free ratio (IWR) was measured at the basal state. Then, C-ED-Pd/Pa obtained by 6ml/2sec intracoronary contrast medium injection was calculated. Subsequently, conventional adenosine-induced hyperemic FFR and H-ED-Pd/Pa at 60ms before R-wave of the ECG were measured. Obtained measures were 0.896 [0.857–0.938] (IWR), 0.796±0.117 (C-ED-Pd/Pa), 0.832±0.090 (conventional FFR), and 0.763±0.131 (H-ED-Pd/Pa), respectively. Correlation coefficient between hyperemic ED-Pd/Pa and conventional FFR was 0.85 (R2:0.001), and an area under the curve (AUC) was 0.95. Correlation coefficient between hyperemic ED-Pd/Pa and conventional FFR was 0.84±0.10, p<0.0001). NIC-FFR was significantly lower than ATP-FFR (0.82±0.10 vs. 0.84±0.10, p<0.0001). In 14 lesions (13%), FFR values decreased more than 0.05 after intracoronary nicorandil administration. These patients with 14 lesions tend to have lower left ventricular mass index (LVM) than the others (p<0.009). Moreover, NIC-FFR decreased from deferral FFR range (≥0.8) to therapeutic FFR range (≥0.8) in 8 patients with 8 lesions. These patients were significantly lower LVM (p<0.05) and higher left ventricular ejection fraction (p<0.01) than the others.

Conclusions: Additional intracoronary nicorandil administration during FFR measurements might be useful to make sure maximal hyperemia during intravenous ATP infusion.

P1720 | BEDSIDE The impact of elective percutaneous coronary intervention on coronary microvascular resistance

T. Murali1, T. Lee1, Y. Kanaji1, J. Matsuda1, E. Usui1, M. Araki1, T. Nida1, M. Isobe1, T. Kakuta1. 1.Tsushu University Hospital, Cardiovascular Department, 1.Tsushu, Japan; 2.Tokyo Medical and Dental University, Department of Cardiology, Tokyo, Japan

Background: The influence of elective percutaneous coronary intervention (PCI) variations on coronary microvascular function in patients with stable angina has not been fully elucidated. In order to diagnose and treat microvascular dysfunction, a better understanding of the interactions between epicardial lesion and microcirculation is important.

Purpose: We investigated serial changes of microvascular function in patients undergoing elective PCI.

Methods and results: The index of microcirculatory resistance (IMR) and fractional flow reserve (FFR) was measured before, after PCI, and at follow-up (10 months) in 72 patients treated with single vessel uncomplicated elective PCI (male: N=57 (78.2%), age 64±8.3y). The median IMR values before, after PCI, and at follow-up were 21.4 (interquartile range (IQR) 13.1–30.9), 16.2 (IQR 12.4–23.0), and 15.4 (IQR 11.8–20.7), respectively. IMR values significantly decreased after PCI (P<0.003), and showed no further significant change at follow-up. There was a negative correlation between delta IMR (post-pre IMR) values and PCI related cardiac troponin elevations that distributed in the range of (mean: 0.49 mg/ml, IQR 0.23–1.02 mg/ml). Periprocedural IMR decrease (Pre-Post) was inversely associated with pre-PCI FFR (P=0.009) and greater improvement of FFR values by PCI was significantly associated with greater reduction of IMR values at follow-up (P=0.007). To investigate the details of serial IMR change, lesions were divided into tertiles based on Pre-PCI IMR value (the lowest Pre-PCI IMR: 11.4 (IQR 9.1–13.4), the intermediate: 21.5 (17.9–24.7) and the highest: 36.8 (30.9–49.4)). In the intermediate and the highest tertiles, IMR values were significantly decreased at follow-up (P<0.03 and P<0.001, respectively). IMR values of the intermediate tertile were decreased to the same level of those of the lowest tertile at follow up. Whereas follow up IMR values of the highest tertile still remained higher than those of the lowest tertile, the highest tertile showed the greatest decrease of IMR values after PCI than those of other tertiles (the lowest IMR at follow up: 13.9 (IQR 10.9–15.7), the intermediate: 15.9 (12.4–19.0) and 19.7 (14.2–26.2), P<0.01).

Conclusions: Removal of physiologically significant epicardial stenosis leads to a decrease in microvascular resistance in patients with stable angina undergoing electively performed uncomplicated PCI and the effect was maintained up to 10 months. The baseline status of microvascular function is a significant determinant of post-PCI and follow-up microvascular function in these patients.

P1721 | BEDSIDE Influence of microvascular resistance on anatomical and functional severity of coronary artery stenosis

K.W. Seo, M.H. Yoon, S.J. Tahk, S.Y. Choi, B.J. Choi, H.S. Lim, H.M. Yang, J.H. Shin, G.S. Hwang, J.S. Park. Ajou University School of Medicine, Suwon, Korea, Republic of

Background: Coronary angiography has been standard diagnostic tool for assessing the anatomical severity of coronary artery disease. However, there are mismatching between anatomical and functional severity.

Purpose: The purpose of this study was to evaluate the influence of microvascular resistance on anatomical and functional severity of coronary artery stenosis.

Methods: We enrolled 85 patients (58 males, 63±10 year-old; who had 104 coronary lesions. Quantitative coronary angiography, fractional flow reserve (FFR) and hyperemic microvascular resistance index (hMVRI) were measured at all lesions using 0.014-inch intracoronary dual pressure doppler sensor-tipped guidewire. FFR was calculated as distal pressure (Pd) divided by proximal pressure (Pa). And hMVRI was calculated as distal pressure (Pd) divided by hyperemic APV. Lesions with diameter stenosis (DS) ≥50% and FFR ≥0.80 were defined as the mismatch group and lesions with DS ≥50% and FFR <0.80 were defined as the reverse mismatch group.

Results: There were 46 lesions (44%) of mismatching and 58 lesions of matching. In the mismatching lesions, 31 lesions (30%) were included in the mismatch group and 15 lesions (14%) were included in the reverse mismatch group. In all lesions, the mean FFR, diameter stenosis (%) and hMVRI were 0.79±0.11, 56.5±9.9 and 2.23±1.24. hMVRI was 2.03±1.03 in the match group (n=58), 2.96±1.53 in the mismatch group (n=31) and 1.50±0.31 in the reverse mismatch group (n=15). hMVRI was significantly higher in the mismatch group (p<0.01 by ANOVA). The reverse mismatch group had a tendency of lower hMVRI values. 13 lesions from among 15 reverse mismatch lesions were in left anterior descending artery.

Conclusions: There was a considerable mismatching between anatomical and functional severity. And functional physiologic assessment with microvascular function test should be required for percutaneous coronary intervention in myocardial ischemia-related lesions.
P1724 | BENCH
Influence of the side branch stenosis on the fractional flow reserve value of the main branch in a swine model
J.-H. Oh1, J.S.K. Kim2, J.H.C. Choi1, B.W.K. Kim1, J.S.P. Park1, H.W.L. Lee1, J.H.C. Choi1, H.C.L. Lee1, K.S.C. Cha1, T.J.H. Hong1, 1 Busan National University Hospital, Busan, Korea, Republic of; 2 Pusan National University Yangsan Hospital, Yangsan, Korea, Republic of

Background: The aim of this study was to evaluate the effect of side branch stenosis on the FFR of the main branch.

Methods and results: The proximal segments of the left anterior descending (LAD) and the left circumflex artery (LCX) were exposed through left lateral thoracotomy in eight swines (55 to 70 kg). Each proximal segment, no major branches in between them, was encircled with a Teflon pledge complex which was sutured and snared with a plastic tourniquet. Five degrees of stenosis (angiographic diameter stenosis of 0%, 25%, 50%, 75%, and 100%) were made by tightening up the pledgets. FFR values of the LAD and the LCX were obtained simultaneously with two pressure wires in each coronary artery. The association of FFR values of the LAD and the LCX was analyzed using mixed effect linear model. The FFR of the LAD was not affected by the FFR of the LCX (β estimate = 0.272, P = 0.276).

Conclusions: The FFR value of the main branch was not affected by the stenosis of the side branch significantly over the whole range of degrees.

P1725 | BEDSIDE
Hypermic flow velocity falls with worsening stenosis severity: the challenge for non-invasive predictors of coronary physiology
S.S. Nijjer1, G. De Waard2, S. Sen3, R. Petracco 1, T.P. Van De Hoef4, M. Echavarria-Pinto1, J. Escaned1, J. Piek1, J.E.R. Davies1, N. Van Royen2, 1 Imperial College Healthcare NHS Trust, London, United Kingdom; 2 Imperial College London, London, United Kingdom; 3 Academic Medical Center of Amsterdam, Amsterdam, Netherlands; 4 Hospital Clinic San Carlos, Madrid, Spain

Background: Previous descriptions of coronary physiological behaviour were performed in animal models using external constrictors to mimic stenoses. Human outcome data confirms the value of physiological assessment but there remains limited modern data using high fidelity techniques to describe the phasic physiological response to a stenosis. Simultaneously, computer-simulated physiological testing has gained interest but makes assumptions of a large and uniform increase in flow across all vessels to simulate a transtenotic pressure drop. Since clinical application requires robust models, we used combined intracoronary pressure and flow velocity measurements in a large clinical cohort to describe the response of the human coronary circulation to a stenosis.

Methods: 167 simultaneous intracoronary pressure and flow velocity assessments from 301 patients were analyzed for coronary flow velocity, transtenotic gradient (TG) and microvascular resistance (MVR). Measurements were made during basal conditions and during hyperemia. The whole cardiac cycle and the resting diastolic wave-free period was assessed. Linear regression, trend analysis and paired analysis was used, according to stenosis severity as determined objectively by fractional flow reserve (FFR).

Results: FFR values ranged from 0.28 to 1.0. With progressive worsening of stenoses, from unobstructed angiographically normal vessels to those with FFR≤0.50, hyperemic flow velocity over the whole cycle falls significantly from 45 to 19 cm/s, (-0.01) in a curvilinear pattern. In contrast, resting flow was unaffected by stenosis severity (R² 0.01) and was consistent across all strata of stenoses, with wave-free flow being significantly higher (whole cycle:18.05±0.5 cm/s wave-free: 24.50±0.7 cm/s, p<0.01). Resting resistance showed a decline with stenosis severity (-0.01), but was unchanged at hyperemia (2.3±1.1, P=0.19). Transtenotic gradient rose with stenosis severity, increasing from 1.7±0.3 to 46±3 mmHg at rest, and from 3.5 to 55 mmHg at hyperemia (P<0.01 for both). Both FFR and FFR were strongly related to transtenotic gradients (R² 0.96 and 0.93 respectively).

Conclusions: With progressive stenosis severity, transtenotic gradient increases alongside a worsening of pressure indices such as IFR and FFR. However, while hyperemic flow falls regrettably, resting coronary flow is maintained by compensatory reduction of microvascular resistance, demonstrating coronary auto-regulation. This data will assist in computer flow modeling such as CT-FFR and virtual-PCI systems potentially provide more credible estimates of human physiology.
**INVASIVE AND NON-INVASIVE FUNCTIONAL CORONARY IMAGING**

**P1726 | BEDSIDE**
Reduction of radiation exposure in diagnostic cardiac catheterization and PCI - results of a German coronary angiography and angioplasty registry

B. Levenson1, S. Goering2, W. Haerer3, N. Reifart4, G. Ringwald5, A. Albrecht1, 1Cardiac Catheterization Laboratory & Group Practice on St. Gertraudens Hospital, Berlin, Germany; 2Health Care Consulting, Weinheim, Germany; 3Heizklinik, Ulm, Germany; 4Main-Taunus-Hospital, Bad Nauheim, Germany; 5Friedrichsplatz Hospital, Bruchsal, Germany

Introduction: Exposure to radiation is a growing concern as there is an increasing number of CT scans, procedures in interventional radiology, and in intervention cardiology. It is unclear whether experienced interventionalists when using a system of quality control can still reduce radiation although cases have become more complex?

Methods: Since 1996 the Association of German Cardiologists in Private Practice has been continuously collecting data of diagnostic procedures PCI performed by contributing cath labs. The individual results of each cath lab and a comparison with the overall data are provided for each participant. Over 1.5 million procedures have been documented during a period of 20 years. We compared the values for radiation dose area product (DAP) as Gy * cm², fluoroscopy time (min) and contrast medium consumption (ml) from 2002 to 2013.

Results: In diagnostic procedures a reduction of DAP of over 20% was observed from 2002 to 2013, and a reduction of contrast medium by 28%. However, the fluoroscopy time did not change significantly. Similar were the results for percutaneous coronary interventions (PCI). The reduction of DAP was about 32%, and contrast medium consumption dropped by 37%. Fluoroscopy time was unchanged (table). Coronary multi-vessel-disease was the prominent indication for PCI with increasing complexity over the years.

DAP and fluoroscopy time in PCI

<table>
<thead>
<tr>
<th>Year</th>
<th>N</th>
<th>DAP (Gy cm²)</th>
<th>Fluoroscopy time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2002</td>
<td>18823</td>
<td>44.99</td>
<td>8.42</td>
</tr>
<tr>
<td>2006</td>
<td>23934</td>
<td>39.35</td>
<td>7.53</td>
</tr>
<tr>
<td>2011</td>
<td>21438</td>
<td>35.15</td>
<td>7.52</td>
</tr>
<tr>
<td>2011</td>
<td>21438</td>
<td>34.77</td>
<td>7.46</td>
</tr>
<tr>
<td>2011</td>
<td>21438</td>
<td>35.30</td>
<td>7.63</td>
</tr>
<tr>
<td>2011</td>
<td>21438</td>
<td>34.35</td>
<td>7.76</td>
</tr>
<tr>
<td>2011</td>
<td>21438</td>
<td>32.65</td>
<td>7.89</td>
</tr>
<tr>
<td>2011</td>
<td>21438</td>
<td>30.65</td>
<td>7.92</td>
</tr>
</tbody>
</table>

Conclusions: When using a system for quality control with regular feedback experienced interventionalists can further reduce radiation exposure and amount of contrast medium to achieve an angiographic diagnosis or a successful PCI result although there was an increasing complexity of cases over time.

**P1727 | BEDSIDE**
Comparison of first and second generation drug eluting stents (DES) - in-stent restenosis assessed by optical coherence tomography (OCT)

T. Kajiyama1, J. Takaoka2, K. Fukunaga3, R. Arima1, A. Miyamura4, N. Atsuci1, H. Yamaguchi2, M. Kannori1, M. Nakahara1, Y. Atsuci1, 1 Teyoukai Central Hospital, Department of Cardiology, Kagoshima, Japan; 2 Yamaguchi Hiroshi Clinic, Kagoshima, Japan

Background: In second generation DES era, in-stent restenosis (ISR) is not commonly seen but is still encountered occasionally. The pathophysiology and mechanism of ISR after second generation DES implantation have not been fully clarified.

Methods: Patients who underwent follow-up coronary angiography (CAG) after first (Cypher and Taxus) and second generation DES (Nobori, Promus Element, Resolute Integrity, and Xience) implantation were examined. ISR was defined as lesions more than 75% diameter stenosis at follow-up CAG. Optical coherence tomography (OCT) was performed at the time of revascularization to ISR. Then OCT imaging of second generation DES ISR were compared with first generation DES ISR, retrospectively.

Results: From April 2008 to January 2010, first generation DES were implanted in 805 lesions. From January 2011 to December 2014, second generation DES were implanted in 1269 lesions in our hospital. ISR rate were significantly lower in second generation DES (9.6% (N=177) vs 3.8% (N=48), p<0.05). In qualitative OCT assessment of second generation DES ISR, each ratio of homogeneous, layered, heterogeneous and lipid rich attenuation tissue morphologies were 63.2% and 18.4%, 13.2% and 5.3%, respectively. Compared with first generation DES ISR, heterogeneous morphology was significantly higher in second generation DES ISR (63.2% vs 36.0%, p<0.05).

Conclusions: Homogenous tissue morphology by OCT was more frequently found in second generation DES ISR than first generation DES ISR. This finding suggests that variety of mechanism is considered as cause of DES ISR, however neointimal hyperplasia is main mechanism in second generation DES ISR.

**P1728 | BEDSIDE**
Clinical characteristics and angiographic features of optical coherence tomography verified spontaneous coronary artery dissection in patients with acute coronary syndrome

T. Nishiguchi, A. Tanaka, A. Taruya, Y. Matsuo, Y. Ino, K. Hirata, T. Kubo, T. Hozumi, T. Akasaka, Wakayama Medical University, Department of Cardiovascular Medicine, Wakayama, Japan

Aims: Spontaneous coronary artery dissection (SCAD) is an increasingly recognized cause of acute coronary syndrome (ACS), however, it is still misdiagnosed and underestimated due to the limitation of coronary angiography. Moreover, it is difficult for most clinicians to speculate SCAD on angiography in the first place for the poor understanding of angiographic features of SCAD. Recently, we reported that optical coherence tomography (OCT) was able to diagnose SCAD that is undetectable on angiography. We proposed to reveal the angiographic features of SCAD.

Methods: This study consisted of 245 patients with ACS who underwent pre-intervention OCT to explore the entire culprit artery. All OCT images were analyzed by two expert OCT readers who were blind to the clinical data. Patients were divided into three groups; a SCAD group, a plaque rupture (PR) group, and a non-SCAD/non-PR (NR) group according to lesion morphologies. OCT criteria for SCAD was a separation of the different layers of the artery wall with the creation of a false lumen. Quantitative coronary analysis (QCA) including the minimum lumen diameter, reference vessel diameter, percent diameter stenosis, and lesion length was also measured.

Results: OCT revealed 9 SCADs, 146 PRs, and 109 NRs. There was a general increase in individual core clinical risk factors, while the prevalence of patients with more than 3 risk factors was lower in SCAD (11.1% vs. PR: 51.5% vs. NR: 56.6%, p<0.05). The proportion of male and female was different among the groups (Female: SCAD: 66.7% vs. PR: 20.0% vs. NR: 23.6%, P <0.01). In angiographic findings, the distribution of the culprit vessels and the initial TIMI flow were similar among groups (p=0.48, and p=0.95 respectively). There were no significant differences in reference diameter, % stenosis, and minimum lumen diameter in QCA. The lesion length in SCAD was significantly longer than those in others (SCAD: 33.8±28.8 mm vs. PR: 15.6±8.0 mm vs. NR: 14.8±7.5 mm, P <0.01).

Conclusions: We should remind the presence of SCAD when angiography shows long lesion especially in female with less risk factors. In such cases, OCT should be recommended for accurate diagnosis for SCAD.
P1730 | BEDSIDE
Features of coronary artery disease in 2776 type 1 diabetes patients undergoing coronary angiography
V. Rittinger1, C. Hero2, K. Eeg-Olofsson3, A.M. Svensson3, N. Saleh1, B. Lagerqvist4, A. Norhammar1,1, Karolinska Institute, Cardiology Unit, Department of Medicine, Karolinska University Hospital Solna, Stockholm, Sweden;2Department of Gothenburg, Department of Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden;3National Diabetes Registry Centre, Centre of Registers, Region of Västra Götaland, Gothenburg, Sweden;4Uppsala University Hospital, Department of Medical Sciences, Cardiology, Uppsala, Sweden.

Background: Individuals with diabetes mellitus (DM) have more widespread coronary artery disease (CAD) than those without which partly can explain their increased risk for cardiovascular death. However few studies have addressed type 1 diabetes in this context.

Purpose: To assess features of coronary artery disease in type 1 diabetes undergoing coronary angiography.

Methods: All patients undergoing a coronary angiography during the years 2001–2009 included in the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) as well as in the Swedish National Diabetes Registry (NDR) with type 1 diabetes and onset age before 50 years were included. CAD was visually judged and divided into normal (atheromatosis/stenosis <50%), one-, two-, three- and left main-vessel disease.

Results: Of 2776 type1 DM (58% male) with complete data on coronary angiogram, mean age was 57 years (SD 11), mean DM duration 35 years (SD 14, range 0–78) and mean HbA1c 67 mmol/mol (SD 14). The most common indications for coronary angiography were stable CAD (31%), non-ST-elevation myocardial infarction (STEMI;38%) and ST-elevation myocardial infarction (STEMI;10%), heart failure (3.6%), chest pain (5%), silent ischemia (3%) and other rare reasons. Coronary angiography revealed 21% without significant stenosis, 23% had one-vessel, 18% had two-vessel, 29% had three-vessel and 9% had left main stem disease. Among those with stable CAD 23% had a normal angiography and 28% had one-vessel disease. The corresponding figures for NSTEMI were 24% and 37%.

Conclusion: In patients with type 1 diabetes the coronary angiography was “normal” more often than expected or with only one-vessel affected despite a long diabetes duration.

P1731 | BEDSIDE
Comparison of 1 year clinical outcomes of IVUS plus OCT guided PCI and IVUS guided PCI
T. Kajiy, J. Takaoka, K. Fukunaga, R. Arima, A. Miyamura, N. Atsuchi, Y. Atsuchi. Teryoukai Central Hospital, Department of Cardiology, Kogashima, Japan.

Background: In the modern percutaneous coronary intervention (PCI) era, imaging guided PCI is routinely performed. Optical Coherent Tomography (OCT) is an emerging device to evaluate coronary artery at a higher resolution, however whether OCT provides additional clinical benefits over intravascular ultrasound (IVUS) guided PCI remains unclear.

Methods: From January 2011 to December 2013, a total of 994 consecutive patients who underwent elective PCI in our hospital were enrolled for analysis. The primary endpoint of this study was all-cause death and major adverse cardiac events (MACE) at 1 year after elective PCI. Secondary endpoints were total radiation dose and amount of contrast use during procedure.

Results: Single IVUS guided PCI were performed in 772 patients (77.7%), and IVUS and OCT guided PCI were performed in 24% of patients (22.3%). Sixteen patients (1.6%) had OCT only and 2 (0.2%) did not have any imaging. Total radiation dose was significantly lower in IVUS plus OCT group compared with IVUS only group (879.1±585.5 vs 1173.6±766.9mGy, p < 0.01). There was no statistical significant differences in contrast amount used in both groups (162.5±63.5 vs 162.9±70.0mL, p=0.4). All-cause death at one year occurred 4.0% (N=38) in the single IVUS guided PCI group and 3.9% (N=8) in the IVUS plus OCT group (p=0.05). There was no significant differences in composite of MACE in both groups (p=0.07).

Conclusion: Compared with single IVUS guided PCI, IVUS plus OCT guided PCI does not improve 1-year mortality or increase the amount of contrast use, however, it reduces total procedure radiation dose.

P1732 | BEDSIDE
Safety of elective transfemoral coronary angiography during uninterrupted warfarin therapy
W. Wongcharoen, K. Pinyosamosorn. Chiang Mai University, Faculty of Medicine, Chiang Mai, Thailand.

Background: The common practice of patients receiving warfarin therapy prior to elective coronary angiography (CAG) is to discontinue warfarin with heparin bridging before beginning the procedure. This practice may delay the planning procedure, prolong hospitalization and increase a risk of thromboembolism due to sub-therapeutic anticoagulation. The uninterrupted warfarin strategy has been suggested to be an alternative way for patients with high risk of thromboembolic complications.

Purpose: The aim of this study was to assess the safety of elective CAG during uninterrupted warfarin therapy compared to the conventional heparin bridging therapy.

Methods: This study was a prospective, randomized open-label design with blinded event evaluation. Sixty-nine consecutive patients (age ≥18 years) receiving warfarin before the planned transfemoral CAG were randomly assigned to either heparin bridging therapy or uninterrupted warfarin with targeted INR (2.0–3.5). The primary outcome was the incidence of vascular access site complications defined as presence of hematoma ≥5 cm in diameter, pseudoaneurysm or arteriovenous fistula.

Results: The baseline characteristics were comparable between 2 groups (mean age was 61.1±8.3 years, 32 males). The mean INR on the day of CAG of heparin bridging group and uninterrupted warfarin group was 1.350.2 and 2.1±0.5 (p<0.001), respectively. The vascular access site complications occurred in 4 of 37 (10.8%) heparin-bridging patients and in none of 32 uninterrupted warfarin patients (p=0.117). No patient developed bleeding at other sites apart from the vascular access site.

Conclusions: We demonstrated that an uninterrupted warfarin strategy did not increase vascular access site complications in patients undergoing transfemoral CAG when compared to heparin bridging therapy. Due to the safety and the ease of uninterrupted warfarin strategy, this approach should be encouraged in patients receiving warfarin prior to elective transfemoral CAG.

Acknowledgement/Funding: The Faculty of Medicine Endowment Fund for Medical Research, Chiang Mai university, Chiang Mai, Thailand.

P1733 | BEDSIDE
Rate and predictors of contrast-induced nephrotoxicity after coronary intervention depend on renal function at baseline

Background: Contrast induced nephrotoxicity (CIN) after coronary angiography or angioplasty (CA) has been shown to be related to mortality. The rate and predictors of CIN when preventive measures are applied are poorly documented.

Methods: All consecutive patients submitted to non-urgent CA in 2014 with low-osmolar contrast medium were stratified for CIN risk: patients with renal dysfunction (defined as eGFR < 60 ml/min) had interruption of diuretics and received a 250–500 ml intravenous saline infusion before and after CA. Serum Creatinine (SCr) levels were measured before CA and daily thereafter up to 5 days after CA. CIN was defined as an absolute increase of 44 μmol/L SCr or of 25% over baseline SCr level. Predictors of CIN and of recovery were determined by logistic regression. Patients had clinical follow-up for death or end-stage renal dysfunction.

Results: SCr results were available in 958 patients, 72% male, 25% diabetics, median amount of contrast was 129 ml (IQ= 90; 186). At 2–4 days, CIN was observed in 188 (20%), driven by a 25% increase in SCr (n=185, 19%) whereas 81 (8.5%) had an increase of <44μmol/L SCr. CIN rate was related to quartiles of eGFR before CA: 20% when eGFR<53, 14% for eGFR between 53 and 88 and 30% for eGFR>87ml/min. The amount of contrast medium was not a predictor of CIN. In patients without renal dysfunction, a lower SCr was a predictor of CIN. Conversely, in patients with renal dysfunction, older age and diabetes were associated with CIN (figure).

Invasive and non-invasive functional coronary imaging 301
Conclusions: In contemporary routine practice, CIN occurs in 20%, driven by a relative 25% increase in SCR, and irrespective of the amount of contrast medium. In patients with renal dysfunction, older age and diabetes were associated with CIN.

P1734 | BEDSIDE
Incidence and plaque characteristics of calcified nodules, plaque erosion and plaque rupture in diabetic patients with acute coronary syndrome – an optical coherence tomography study
S. Reith, S. Bernet, N. Marx, M. Burmgarner. Med. Clinic I, University Hospital Aachen, Aachen, Germany

Background: Calcified nodules (CN), plaque erosion (PE) and plaque rupture (PR) are the most common mechanisms contributing to an acute coronary syndrome (ACS) with subsequent coronary thrombosis. However, these features have not systematically been investigated in vivo in an exclusively diabetic cohort.

Purpose: This study aimed to investigate the incidence and corresponding morphological plaque characteristics of CN, PE and PR in vivo using optical coherence tomography (OCT) in culprit lesions of ACS-patients with diabetes.

Methods: We performed OCT prior to coronary intervention in 47 patients with diabetes and ACS. Coronary culprit lesions at the minimal lumen area-site were classified as CN, PE and PR and morphologic plaque characteristics were ascribed to these categories.

Results: The incidence of CN, PE and PR was 11 (23.4%), 9 (19.1%) and 25 (53.2%), respectively. As depicted in table 1 PR was associated with a significantly larger lipid arc and a higher lipid volume index (LVI), whereas frequency of lipid-rich plaques as well as fibrous cap thickness (FCT) remained below statistical significance compared to lesions with CN and PE. In contrast, lesions with CN or PE presented with a higher frequency of calcium and fibrous plaque compared to PR.

Table 1. OCT findings of underlying plaque features

<table>
<thead>
<tr>
<th>Feature</th>
<th>CN (n=11)</th>
<th>PE (n=9)</th>
<th>PR (n=25)</th>
<th>CN vs. PR</th>
<th>CN vs. PE</th>
<th>CN vs. PE vs. PR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrous plaque</td>
<td>7 (63.6%)</td>
<td>6 (66.7%)</td>
<td>1 (4%)</td>
<td>p=0.001</td>
<td>ns</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Calcium plaque</td>
<td>11 (100%)</td>
<td>8 (88.9%)</td>
<td>11 (44%)</td>
<td>p=0.001</td>
<td>ns</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Lipid plaque</td>
<td>5 (45.5%)</td>
<td>6 (66.7%)</td>
<td>20 (80%)</td>
<td>p=0.114</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Lipid arc</td>
<td>142±34.7</td>
<td>151±32.1</td>
<td>188±43.2</td>
<td>p=0.007</td>
<td>ns</td>
<td>p=0.043</td>
</tr>
<tr>
<td>LVI</td>
<td>7489±2817</td>
<td>6766±4180</td>
<td>12127±3275</td>
<td>p=0.009</td>
<td>ns</td>
<td>p=0.014</td>
</tr>
<tr>
<td>FCT</td>
<td>53.4±10.4</td>
<td>52.5±10.4</td>
<td>51.4±8.8</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Macrophages</td>
<td>8 (72.7%)</td>
<td>6 (66.7%)</td>
<td>19 (76%)</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Thrombus</td>
<td>5 (45.5%)</td>
<td>4 (44.4%)</td>
<td>18 (72%)</td>
<td>ns</td>
<td>ns</td>
<td>ns</td>
</tr>
</tbody>
</table>

ns, not significant.

Conclusion: OCT is a valuable intracoronary imaging device to identify CN, PE and PR in vivo. In patients with diabetes and ACS PR is associated with a higher plaque lipid content but not with the presence of lipid plaques, whereas CN and PR are associated with dense fibrous tissue and fibrous cap thickness. These distinct pathological features may implicate tailored treatment strategies for ACS-patients with diabetes according to the underlying plaque morphology.

P1735 | BEDSIDE
Impact of optical coherence tomography findings during percutaneous coronary intervention on 9-month follow-up outcomes
T. Sugiyama1, S. Kimura1, Y. Yamakami1, K. Kojima1, Y. Sagawa2, H. Ohtani3, K. Hishikari1, H. Hikita1, A. Takahashi1, M. Isobe1, Y. Yokosuka Kyojai Hospital, Cardiovascular Center, Yokosuka, Japan; 2Tokyo Medical and Dental University, Cardiovascular Medicine, Tokyo, Japan

Purpose: In patients undergoing percutaneous coronary intervention (PCI) for coronary artery disease, the impact of periprocedural lesion morphologies and stent findings by optical coherence tomography (OCT) on long-term outcomes remain unclear. We sought to investigate the relationship between peri-PCI OCT findings and the outcomes during follow-up by serial OCT examination.

Methods: We evaluated 104 native coronary lesions with stable angina pectoris that underwent elective PCI and follow-up coronary angiography with OCT examination. All lesions were treated with stent implantation (94 lesions with drug-eluting stents [DES]; 10 lesions with bare metal stents [BMS]). Plaque morphologies at the narrowest culprit sites before PCI and the presence of stent findings such as stent edge dissection, tissue prolapse and malapposition just after PCI were investigated. At 9-month follow-up coronary angiography (mean interval: 9.2±1.9 months), the prevalence of in-stent restenosis (ISR) and OCT findings were evaluated.

Results: Stent edge dissection, tissue prolapse and malapposition just after PCI was detected in 28.8%, 9.3% and 31.7% of the lesions. At 9-month follow-up OCT, edge dissection and tissue prolapse was not detected in all lesions. There was no event of sent thrombosis. The frequency of persistent malapposition, resolved malapposition and late-acquired malapposition was 15.4%, 16.3% and 14.4% of the lesions. The lesions with ISR (n=8) had greater pre-PCI lipid arc (250.9±106.8 degrees vs. 155.0±105.5 degrees, p=0.003) than lesions without ISR. The frequency of edge dissection, tissue prolapse and malapposition just after PCI was not significantly different between the lesions with and without ISR. The presence of persistent malapposition and late-acquired malapposition was not related with the occurrence of ISR.

Conclusion: In our serial OCT examination, the occurrence of 9-month in-stent restenosis was associated with the underlying plaque morphologies at the initial PCI, but might not be affected by post-PCI stent findings.

P1736 | BEDSIDE
Incidence and treatment of calcified nodules in patients with acute coronary syndrome
T. Nishiguchi, A. Tanaka, A. Taruya, Y. Matsuo, Y. Ito, K. Hirata, T. Kubo, T. Hozumi, T. Akasaka, Wakayama Medical University, Department of Cardiovascular Medicine, Wakayama, Japan

Aims: Pathological studies have shown that coronary calcified nodules (CN) are a third cause of acute coronary syndrome (ACS). Recent studies reported that optical coherence tomography (OCT) could distinguish coronary CN from other etiologies in vivo. However, little is known about the characteristics and prognosis of patients with CN.

Methods: This study consisted of 245 patients with ACS who underwent pre-intervention OCT to explore the entire culprit artery. Patients were divided into a calcified nodule group (CN) and a non-CN group depending on the culprit lesion morphologies. The OCT criterion of CN was defined when fibrous cap disruption was detected over a calcified plaque characterized by protruding calcification, superficial calcium, and the presence of substantive calcium proximal and/or distal to the lesion. The composite end-point was defined as occurrence of major adverse cardiac events including cardiac death, non-fatal myocardial infarction, and unstable angina pectoris.

Results: The prevalence of OCT verified CN was 5.3% (n=13). There were no differences in the baseline clinical characteristics between groups, including age, gender, culprit vessel, and risk factors for coronary artery disease. Moreover, clinical presentation (ST elevation ACS or non-STEMACS) and peak CK or CK-MB level were similar in both group. The mean follow up periods was 29.8 (range 1–36) month. During the period, cardiac death occurred in 7 (CN: 1, non-CN: 6), MI in 4 non-CNs, and UAP in 8 non-CNs. Kaplan-Meier curve showed similar prognosis in both groups (Figure, p=0.97).

Conclusion: The prevalence of OCT verified CN was 5.3%. No differences were observed between CN and non-CN groups including patient characteristics and prognosis.

P1737 | BEDSIDE
Impact of optical coherence tomography findings on long-term outcomes in diabetic patients with acute coronary syndrome

Background: Impaired glucose tolerance (IGT) patients are known to have a higher risk of cardiovascular events and their prognosis is reported to be poor. We, therefore, aimed to compare the coronary plaque characteristics among non-diabetics (non-DM), IGT and diabetes (DM) by optical coherence tomography (OCT).

Methods: One-hundred-one stable coronary artery disease patients (67.9±10.4 years and 82.4% male) were enrolled in the present study. OCT was performed not only for target but for non-target vessels during elective percutaneous coronary intervention. All of the patients except those already given the diagnosis of DM underwent 75g oral glucose tolerance test (OGTT). The study cohorts were divided into 3 groups; non-DM (n=27), IGT (n=29), and DM (n=45). IGT was defined as 2 hour post-load plasma glucose ≥140mg/dl during the OGTT.

Results: Glycated hemoglobin (HbA1c) level was significantly higher in DM group (7.1±0.8%) than IGT (5.9±0.3%, P<0.01) or non-DM group (5.6±0.5%, P<0.01). There were no significant differences in low-density lipoprotein cholesterol (LDL-C) level, high-density lipoprotein cholesterol (HDL-C) level, or percentage of statin use among the 3 groups. Of the 137 non-target residual plaques, 72 plaques were identified to contain lipid core by OCT (16, 29, and 27 in non-DM, IGT and DM groups, respectively). The size of lipid core expressed as mean angles of lipid arc was significantly greater in IGT group than DM group (162.0±58.7°, 171.4±59.3°, P<0.05). Fibrous cap covering the lipid core was significantly thinner in IGT group than non-DM group (0.08±0.03 mm and 0.11±0.05 mm, P<0.05).

Conclusions: Coronary plaques of IGT patients were as vulnerable as those of
DM patients. This finding may explain a higher risk of cardiovascular events in IGT patients.

**P1738 | BEDSIDE**

Repeat coronary angiography in patients with previously normal coronary arteries

V. Androschuk, M. Prott, P. Freeman, N. Ossei-Gerning. University Hospital of Wales, Cardiology, Cardiff, United Kingdom

**Background:** Coronary artery disease (CAD) is a major public and economic health problem. Coronary angiography is a gold standard for diagnosing CAD and is indicated in patients with ~60–90% pre-test probability of the disease when the diagnosis cannot be made on clinical grounds alone and when revascularisation is being considered. The natural history of normal coronary angiogram is poorly understood.

**Objectives:** To evaluate the progression of disease in patients with normal coronary angiography and to assess the overall survival and event-free survival from acute myocardial infarction in these patients.

**Methods:** We interrogated the Central Cardiac Audit Database (CCAD) between November 2005 and December 2013 to identify patients with normal or “near-normal” coronary angiography. Demographic, clinical and angiographic data was recorded. This database was linked with the Patient Episode Database for Wales (PEDW) and the datasets from the Office for National Statistics (for mortality) using the Secure Anonymised Information Linkage (SAIL) databank. This allowed for the extraction of information from all the sources above on the basis of the International Statistical Classification of Diseases (ICD-10) using the Structured Query Language (SQL).

**Results:** Out of over 20,000 patients undergoing coronary angiography between November 2005 and December 2013, 5032 patients had normal coronaries and minor CAD. Of 5032 patients, 136 underwent repeat angiography, with 131 (96.3%) and 5 (3.7%) patients having two and three repeat investigations respectively. Mean time between procedures was 3.3 (±1.82) years. Of those 136 patients, at the median follow-up of 6.8 years, no change in disease progression was demonstrated in 108 (79.4%) patients on the follow up studies. In the remaining 28 (20.6%) patients, normal coronaries progressed to minor CAD. No patients progressed beyond minor CAD. Patients with normal coronaries had significant better survival than patients with minor CAD (p<0.05), but survival free from MI was ~99.5% in both groups at the median of 5 years follow up (p=0.09).

**Conclusions:** Normal coronary angiography and minor CAD is unlikely to progress to significant disease at 7 years and the incidence of MI in these patients is rare at 5 years. Therefore, repeating coronary angiography within at least 5 years is not indicated.

**P1740 | BEDSIDE**

Image-based FFR during coronary catheterization

R. Kornowski1, I. Lavi1, M. Pellicano2, B. De Bruyne2. 1 Rabin Medical Center, Interventional Cardiology, Petach Tikva, Israel; 2 OLV Hospital Aalst, Cardiovascular Center, Aalst, Belgium

**Background:** Fractional flow reserve (FFR) is a less-invasive, physiological index determining the hemodynamic severity of coronary lesions.

**Methods:** We have developed an image-based FFR technology based solely on already-available angiographic images. The algorithms estimate the functional significance of a coronary lesion by classifying the dynamic characteristics of the vessel as well as the patient’s hemodynamic information. An FFR measurement is provided for each segment of the coronary tree (Figure).

A validation study was performed in order to assess the diagnostic performance of the image-based FFR in comparison to invasive FFR. Each lesion, indicated for invasive FFR measurement, was analyzed with the image-based technique, taking several views into consideration. The three-dimensional shape of the vessel was used to initiate the flow analysis, and the FFR index at the exact location of the wire tip was compared to the pressure-based measurement.

**Results:** Invasive FFR index was measured during diagnostic cardiac catheterization and image-based FFR was calculated at the exact location of the invasive measurement. 82 lesions were analyzed and the image-based FFR demonstrated good correlation (r=0.89) to the conventional invasive method. The Bland-Altman analysis indicates that the 95% limits of agreement between the two methods ranged from ~8% to 7%.

**P1741 | BEDSIDE**

The role of optical coherence tomography in prediction of coronary ischemia assessed by fractional flow reserve: meta-analysis of diagnostic test accuracy

I.H. Tanboga1, S. Topcu1, E. Aksakal1, U. Aksoy1, M. Kurt2, A. Kaya3, T. Isik4, S. Sevimli1. 1 Ataturk University, Faculty of Medicine, Erzurum, Turkey; 2 Mustafa Kemal University, Hatay, Turkey; 3 Ordu University, cardiology, Ordu, Turkey; 4 Balikesir University, cardiology, Balikesir, Turkey

**Aim:** Optical coherence tomography (OCT) has been recently emerged diagnostic imaging tool to assess coronary lesions. However, there is a few data related to OCT in coronary intermediate lesion. Therefore, in this meta-analysis, we aimed to investigate the role of OCT compared to fractional flow reserve (FFR) in intermediate coronary lesion.

**Methods:** We searched the MEDLINE, EMBASE and Cochrane Library for studies published from January 2000 to January 2014. We included nine trials in which had at least one OCT-derived anatomic measurements such as minimal luminal diameter (MLD), minimal luminal area (MLA) and/or area stenosis (AS) compared to significant FFR cut-off value (0.75 or 0.80) into this meta-analysis.

**Results:** We included nine trials with lesion-level data for 457 coronary lesions in...
P1740 | BEDSIDE
Age-related coronary artery disease: clinical imaging versus coronary angiography
T. Yokoi1, S. Yamaguchi1, T. Amano 2, T. Murohara 3.
1 Saiseikai Minami Hospital, Saitama-shi, Japan;2 Teikyo University Hospital, Tokyo, Japan;3 Kyocera University Graduate School of Medicine, Kyoto, Japan
Background: The NOBORI™ Biolimus-Eluting versus XIENCE™/PROMUS™ Everolimus-eluting stent Trial (NEXT) was designed to evaluate non-inferiority of biolimus-eluting stent (BES) relative to everolimus-eluting stent (EES).
Objective: The aim of this study was to compare the vessel response between BES and EES using serially repeated intravascular ultrasound observation for 2 years after stent implantation.
Methods: Data were obtained from NEXT. Patients with serial (baseline and 12-months follow-up) intravascular ultrasound analysis were available in 110 patients (BES = 56 EES = 54). Twenty-four months follow up IVUS observation was available in 43 patients (BES = 25 EES = 18). Qualitative analysis including incomplete stent apposition (ISA) was examined. Volumetric analysis was performed for ISA, vessel, lumen, plaque, stent and neointima.
Results: At 12 months, BES had 10.7% of late incomplete stent apposition (LISA) and EES had 9.2%, demonstrating a significant vessel response of BES relative to EES (P=0.52, 12 month: BES 0.4±0.7mm³ vs. EES 0.8±2.6mm³, P=0.27). At 24 month (24m) after stent implantation, ISA was observed in 12.0% of BES, in 11.1% of EES, resulting comparable vessel response between BES and EES through 24 months. Serial change of ISA volume through 24 months was insignificant between both groups (BES −0.1±1.0mm³ vs. EES −0.1±1.2mm³, P=0.49).
Conclusion: The volume of necrotic plaque measured by iMAP is associated with Hs-TnT in patients with stable angina or silent coronary ischemia.

P1745 | BEDSIDE
Comparison of vascular response to biolimus-eluting stent versus everolimus-eluting stent; two-year serial intravascular ultrasound observation from NEXT
A. Miyazawa1, K. Kozuma4, K. Hibi2, M. Endo3, N. Nakayama4, T. Muramatsu5, T. Akasaka5, Y. Morino6, T. Kimura7 on behalf of NEXT Investigators.
1 Aichi Medical University, Aichi, Japan;2 Aizu Medical Center, Niigata, Japan;3 Saiseikai Minami Hospital, Saitama-shi, Japan;4 Teikyo University Hospital, Tokyo, Japan;5 Yokohama City University Medical Center, Yokohama, Japan;6 Saiseikai Yokohama City Eastern Hospital, Yokohama, Japan;7 Yokohama Medical University, Yokawaya, Japan
Background: The NOBORI™ Biolimus-Eluting versus XIENCE™/PROMUS™ Everolimus-eluting stent Trial (NEXT) was designed to evaluate non-inferiority of biolimus-eluting stent (BES) relative to everolimus-eluting stent (EES).
Objective: The aim of this study was to compare the vessel response between BES and EES using serially repeated intravascular ultrasound observation for 2 years after stent implantation.
Methods: Data were obtained from NEXT. Patients with serial (baseline and 12-months follow-up) intravascular ultrasound analysis were available in 110 patients (BES = 56 EES = 54). Twenty-four months follow up IVUS observation was available in 43 patients (BES = 25 EES = 18). Qualitative analysis including incomplete stent apposition (ISA) was examined. Volumetric analysis was performed for ISA, vessel, lumen, plaque, stent and neointima.
Results: At 12 months, BES had 10.7% of late incomplete stent apposition (LISA) and EES had 9.2%, demonstrating a significant vessel response of BES relative to EES (P=0.52, 12 month: BES 0.4±0.7mm³ vs. EES 0.8±2.6mm³, P=0.27). At 24 month (24m) after stent implantation, ISA was observed in 12.0% of BES, in 11.1% of EES, resulting comparable vessel response between BES and EES through 24 months. Serial change of ISA volume through 24 months was insignificant between both groups (BES −0.1±1.0mm³ vs. EES −0.1±1.2mm³, P=0.49).
Atherosclerosis develops in saphenous coronary grafts and lower LCBI.

In ATHEROREMO-IVUS, imaging of a non-culprit coronary artery was performed in 142 women and 439 men, who underwent percutaneous coronary intervention (PCI) or invasive diagnostic coronary exploration for various indications between 2008 and 2011. In 53 women and 139 men also NIRS was performed in the same segment. Imaging data were analyzed off-line in a dedicated core-lab. We applied linear regression analyses to relate gender with VH-IVUS findings and NIRS derived lipid core burden index (LCBI).

Results: Women had a significantly lower median plaque burden than men (36.9 vs. 39.5%, p=0.014). The median LCBI was also significantly lower (p=0.011) in women (30.0, inter-quartile range 9.4 to 64) than in men (48, 21 to 95). There were no gender differences in the presence of thin-cap fibroatheroma lesions. Women were older than men (64.3 vs. 60.7 years), and were more likely to have a history of hypertension (66 vs. 47%). Men were more often classified as smokers (30 vs. 24%) and had longer lesions (median 45.0 mm (inter-quartile range 35.4 to 56.0) vs. 42.1 mm (30.5 to 54.2), p=0.021. After adjustment for these factors, women still had on average 3.4% lower plaque burden (p=0.002) and 0.58 points lower LCBI (p=0.005) than men.

Conclusion: In ATHEROREMO-IVUS, female patients had lower plaque burden and lower LCBI.

P1747 | BEDSIDE

Optical coherence tomography imaging of coronary saphenous vein graft lesions morphology, OCTOPUS registry

T.M. Roldér1, E. Pociask2, W. Wanha1, P. Gasior1, G. Smolka1, M. Skowerski1, D. Dudek1, A. Ochala1, Z. Gasior1, W. Wojakowski1, 1Medical University of Silesia, Katowice, Poland; 2Jagiellonian University Medical College, Krakow, Poland

Purpose: The accelerated atherosclerosis that occurs in saphenous coronary grafts is often not only in de novo SVG lesions (42% vs. 0%, p=0.028) in older graft, as compared to younger grafts. The purpose of the study was to analyze the difference in the morphology of de novo lesions of SVG occurred later as compared to ISR in SVG (131±63 vs. 32±23 months, p<0.001). There were 24 lesions in 18 patients and 8 ISR analyzed (8 patients) by OCT. De novo lesions of SVG occurred later as compared to ISR in SVG (131±63 vs. 32±23 months, p<0.001) and MLA was smaller in ISR as compared to SVG lesions [1.49 (IQR 0.71–2.0) vs. 2.05 (IQR 1.45–4.20), p=0.022]. Calculations were detected only in de novo SVG lesions (42% vs. 0%, p=0.028) in older graft, as compared to non-calciﬁed de novo SVG lesions (16±8±3 vs. 109±55 months post CABG, p=0.037). Heterogeneous tissue was found only in neointima of ISR (38% vs. 0%, p=0.02) at 19 (IQR 17–27) months post stent implantation. The lipid-rich tissue occurred in de novo SVG lesions and in ISR (50% vs. 67%, p=0.39) with no difference in lipid arc [245 (IQR 164–340) vs. 224 (IQR 175–285), p=0.63] and in the thickness of fibrous cap covering lipid core [85 (IQR 60–110) vs. 75 (IQR 55–98), p=0.53]. Plaque rupture was present in 1 (12.5%) of ISR and in 3 (12.5%) of de novo SVG lesions (p=1.0) and thrombus was found in 1 (12.5%) of ISR and 5 (21%) of de novo SVG lesions (p=0.60). Intimal tear (1.4%) and tissue friability (1%) was seen only in de novo SVG lesions. On the other hand, stent malapposition was found in 3 (38%) and uncovered struts were detected 2 (25%) of ISR of SVG.

Conclusion: ISR of SVG occurred earlier as compared to de novo SVG lesions. Both ISR and de novo SVG lesion were lipid rich. Calcification occurred only in de novo SVG lesions and in elder grafts. Heterogeneous tissue occurred only in ISR of SVG.
Superficial EA was observed in 22/35 (63%), and deep EA in 13/35 (31%). CAS color grade of grade ≥2 (intensive yellow and yellow plaque) was observed in 19/22 (86%), and grade <2 (light yellow and white plaque) was observed in 3/22 (14%) in superficial EA group. In deep EA group, the color grade ≥2 was observed in 4/13 (31%), and plaque with color grade <2 was observed in 9/13 (69%) (P<0.0001). Thrombus was detected in 6/22 (27%) in superficial EA group, and 2/13 (15.4%) in deep EA group (P=0.69). Post-PCI troponin elevation (<5 XUL) was detected in 10 patients (45%) in superficial EA group, and in 1 (8%) with deep EA group (P=0.051).

Conclusions: Majority of EA plaques, especially superficial EA plaques, showed unstable angiographic features, although no unique angiographic feature was observed and the mechanism of EA seems to be multifactorial. Angiographic examination may provide incremental information of EA plaques.

P1750 | BEDSIDE
Older age is associated with overestimation of coronary artery stenoses
N.M. Berren, J.P. Ottervanger, E.M. Engbers, A.W.J. Van ‘T Hof. Isala Hospital, Zwolle, Netherlands

Background: Invasive coronary angiography may either over- or underestimate functional importance of a coronary stenosis. Fractional flow reserve (FFR) proves the functional significance. Overestimation (mismatch) of lesions may result in unnecessary revascularization, and is possibly more prevalent with increasing age.

Aim: The purpose of this study is to identify clinical predictors of overestimation.

Methods: FFR was performed in 260 consecutive patients with storable coronary artery disease (335 coronary stenoses: 187 LAD lesions and 148 non-LAD lesions (RCA=58, LM=15, CX=75)). A visually assessed diameter stenosis of >50% was considered significant. A cut-off value of ≤0.80 was defined as abnormal FFR. To adjust for differences in baseline variables, multivariable analyses were performed.

Results: Mean age of the total population was 65±10 years. Angiographically, LAD lesions were considered significant in 29%, compared to 53% of the non-LAD lesions (p<0.02). FFR demonstrated significant stenosis of the LAD in 52%, compared with 24% in non-LAD lesions (p<0.001). Mismatch was observed in 14 (6%) of LAD lesions, compared with 23 (16%) in non-LAD lesions (p=0.02). Mean age of patients with mismatch was 68.5±11 years and mean age of patients without mismatch was 64.6±10 years (p=0.01). The adjusted odds ratio for mismatch in LAD lesions in comparison with non-LAD lesions was 0.46 (95% confidence interval 0.22–0.97). The adjusted odds ratio for mismatch associated with age was 1.06/year (95% confidence interval 1.02–1.11).

Conclusion: Non-LAD lesions and increasing age are predictors of overestimation of the functional severity of coronary stenoses. Particularly in older patients and those with non-LAD lesions, FFR should be more often considered to demonstrate functional significance of a coronary stenosis.

P1751 | BEDSIDE
Transradial coronary angiography: registry data on the one-cath-concept
C. Langer1, J. Riehle1, S. Dwuernold2, N. Frey1, M. Wiemer2 on behalf of NA.

1 University Medical Center of Schleswig-Holstein, Department of Cardiology, Angiology and Critical Care Medicine, Kiel, Germany; 2 Johannes-Wessling-Klinikum Minden; Universitätssklinik der Ruhr-Universität Bochum, Department of Cardiology, Pulmonology and Critical Care Medicine, Minden, Germany

Background: Transradial coronary angiography (TRC) has been growing worldwide. However, upper limb vessels are thinner, may present with arterial tortuosity, adverse bifurcations and arterial spasmals while the brachiocephalic trunk shows a wide anatomic variability. Such possible vascular obstacles led to the adoption of the one-catheter (cath) -concept for TRC. Allowing for one less catheter change, upper limb vessels may be prevented from unnecessary mechanical irritation or damage. This analyses – drawn from a dual center TRC-registry – reflects the performance of a widely used diagnostic cath designed to fit into both coronary ostia.

Methods: We identified 2954 patients (pts) scheduled for TRC (Figure) in center A and B in 2012 and 2013. All recorded cath films, reports and protocols as well as medical reports were analysed with regard to: 1) Cath stability in the coronary ostia (cath dislocation more than once), 2) the impact of cath instability on the volume of contrast medium (dye) needed, 3) the incidence of complications using the one-cath concept and 4) the inter-center variability. This analysis focuses on the cohort examined by qualified TRC-interventionists only (n=11; doing >80 procedures per year) strictly applying the one-cath-concept by using the tested cath.

Results: The relevant cohort consisted of n=852. The tested cath presented significantly more often or (p<0.05) with an unstable position in the LMT (290/842 pts; 34.4%) than in the RCA (90/837 pts; 10.8%) or both (40/837 pts; 4.8%). Cath instability resulted in a significantly larger volume of dye injected than needed with a cath dislocation >80%: 31.7±6.31 mL vs. 63.4±28.83 mL (p<0.004). Fluoroscopy time appeared to be prolonged in case of unstable ostial landing when compared to stable caths: 113.0±129.85sec vs. 94.38±98.62sec (p<0.024). Strictly applying the one-cath-concept by exclusively using the tested cath was associated with complications in 14/852 procedures (1.6%). Center A vs. B showed significances neither regarding instability of the tested cath in LMT (36.1% vs. 32.7%; p=0.31) and RCA (12.2% vs. 9.1%; p=0.15) nor with regard to complications (p=0.425).

Rates of cath instability and complications did not differ significantly between the involved interventionists (n=11; p=0.99).

Conclusion: The tested TRC cath frequently shows unstable ostial landing not having a significant impact on safety. However, cath instability was proven to be associated with a significantly larger volume of dye and longer fluoroscopy time needed. The present data suggests further development of TRC-caths designed for the one-catheter-concept.

Acknowledgement/Funding: NA
pared to ACS with non-EA. SAP lesions with EA had similar minimum lumen area than in ACS-non-EA than in SAP-EA lesions (88.7%; 75.9%; 23.6%; 12.3%, p<0.001).

Conclusion: SAP lesions with EA may have unstable plaque components and lesion morphology, which is similar to ACS lesions with non-EA. The presence of thrombus may be a significant related factor with occurrence of ACS.

P1754 | BEDSIDE
Global myocardial perfusion quantified in mild to severe systemic sclerosis; novel insights from MR stress imaging of coronary sinus flow
T. Gylenhammer1, M. Kanski1, H. Engblom1, D. Wuttge2, M. Carlsson1, R. Hesselstrand3, H. Ahrendt1 on behalf of Lund Cardiac MR Group. 1 Lund University Hospital, Lund University, Dept. of Clinical Physiology, Lund, Sweden; 2 Lund University, Lund University, Dept. of Reumatology, Lund, Sweden

Background and purpose: Patients with systemic sclerosis (SSc) have high cardiovascular mortality even though there is no or little increase in prevalence of epicardial coronary stenosis. This may be related to perfusion defects indicative of microvascular disease, but the quantitative extent of hypoperfusion in SSc is not known. Therefore, we aimed to determine if patients with SSc have decreased global myocardial perfusion at rest and during adenosine stress.

Methods: Sixteen SSc patients (14 females, 45–74 years) and eleven controls (6 females, 44–66 years) underwent cardiovascular magnetic resonance imaging (CMR). Twelve patients had limited SSc and 4 patients had diffuse cutaneous SSc. One patient had pulmonary arterial hypertension (PAH). Myocardial perfusion (MP) was quantified using coronary sinus flow (CSF) measurements at rest and adenosine stress divided by left ventricular mass (LVM). Myocardial fibrosis was assessed using late gadolinium enhancement (LGE).

Results: There was no difference in MP at rest between patients and controls (1.2±0.2 vs. 1.1±0.1 ml/min/g, p=0.94, Fig.1) whereas SSc patients showed significantly decreased MP during adenosine infusion (2.7±0.2 vs 4.1±0.4 ml/min/g, P<0.017, Fig. 1). Five out of the thirteen SSc patients investigated with LGE showed fibrosis in the right ventricle instead of PAH despite absence of PAH. None had signs of myocardial infarction.

Conclusion: Patients with mild form of SSc have decreased global MP during adenosine stress compared to healthy controls. Thus hypoperfusion at stress may be an early marker of cardiac disease in SSc patients possibly signifying microvascular disease.

P1755 | BEDSIDE
Non-invasive cardiac imaging in patients with myocardial injury after non cardiac surgery
R.B. Grobben1, J.A.R. Van Waes2, T. Leiner1, L.M. Peelen4, G.J. De Borst5, H.C. Vogel6, D.E. Grobbée4, P.A.F.M. Doevendans1, W.A. Van Klei2, H.M. Nathoe1 on behalf of CHASE Investigators. 1 University Medical Center Utrecht, Cardiology, Utrecht, Netherlands; 2 University Medical Center Utrecht, Anaesthesiology, Utrecht, Netherlands; 3 University Medical Center Utrecht, Radiology, Utrecht, Netherlands; 4 Julius Health Center - Julius Gezondheidscentra, Epidemiology, Utrecht, Netherlands; 5 University Medical Center Utrecht, Vascular surgery, Utrecht, Netherlands; 6 University Medical Center Utrecht, Orthopedic surgery, Utrecht, Netherlands

Introduction: Myocardial injury after noncardiac surgery, as defined by troponin elevation, is a strong predictor of short- and intermediate-term mortality. Such postoperative myocardial injury (PMI) is believed to be primarily attributable to pre-existing coronary artery disease (CAD), yet other perioperative factors may be influential as well. We aimed to assess the prevalence of CAD in patients with and without PMI using minimally invasive cardiac imaging.

Methods: Prospective cohort study in patients older than 60 years who underwent intermediate- and high-risk noncardiac surgery. Troponin-I values were measured as part of a routine postoperative care protocol on the first three postoperative days; PMI was defined as a serum troponin level of >50 ng/L. Patients with known CAD or renal insufficiency were excluded. All included patients underwent echocardiography and Coronary CT Angiography (CCTA) during hospitalization. A stress perfusion MRI was performed within two weeks after surgery. The primary outcome was CAD defined by a >50% stenosis on CCTA in one or more major epicardial vessels. Secondary outcomes were acute coronary syndrome, pulmonary embolism, and hypertrophic cardiomyopathy.

Results: After exclusion of patients due to insufficient imaging quality, 45 patients were included in the PMI group and 19 in the control group. Median troponin levels (median ±IQR) in the PMI and control group were 150±190 vs 18±21 ng/L, respectively. Acute Coronary Syndrome was diagnosed in 6 (13%) patients with PMI vs none in the control group. CAD was found in 23 (51%) vs 3 (16%) patients (RR 3.2, 95% CI 1.1–9.5). Pulmonary embolism was diagnosed in 15 (33%) patients with PMI vs 4 (21%) control patients (RR 1.6, 95% CI 0.6–4.2) and hypertrophic cardiomyopathy in 3 (7%) vs none, respectively. None of the MRIs showed cardiac enlargement. A perfusion defect was observed in 2 patients with PMI vs none without. Medication was optimized in 32 (71%) patients with PMI and 5 (29%) patients in the control group. No major cardiovascular events occurred within 30 days of surgery.

Conclusion: Myocardial injury after noncardiac surgery is associated with CAD. In addition, one third of patients with PMI was diagnosed with pulmonary embolism. Non-invasive cardiac imaging may facilitate an adequate diagnosis and subsequent treatment of patients with postoperative myocardial injury.

Acknowledgement/Funding: none

SAFETY AND EFFICACY OF SECONDARY PREVENTION MEDICATIONS
P1756 | BEDSIDE
Clinical equivalence of evolocumab among patient subgroups in a pivotal phase 3 study
E. Stroes1, J. Robinson2, F. Raaij4, D. Sullivan5, M. Blagden6, H. Kassahun7, J. Yang5, S. Wasserman5, M. Koren5. 1 Academic Medical Center of Amsterdam, Department of Vascular Medicine, Amsterdam, Netherlands; 2 University of Iowa, Departments of Epidemiology and Medicine, Iowa City, United States of America; 3 University of the Witwatersrand, Department of Medicine, Johannesburg, South Africa; 4 Institut de recherches cliniques de Montréal, Hypertension Clinic, Montreal, Canada; 5 Prince Alfred Hospital, Department of Clinical Biochemistry, Camperdown, Australia; 6 Avondale Surgery, Chesterfield, United Kingdom; 7 University of Minnesota Medical School, Minneapolis, United States of America; 8 AstraZeneca Inc., Thousand Oaks, United States of America; 9 Jacksonville Center for Clinical Research, Jacksonville, United States of America

Purpose: Evolocumab (EvoMab), a human monoclonal antibody against PCSK9, demonstrates a significant LDL-C reduction when dosed SC either 140 mg every 2 weeks (Q2W) or 420 mg monthly (QM). LDL-C changes were compared to assess efficacy among different patient population subgroups.

Methods: 3146 patients completed one of four 12-week phase 3 studies. Percent change in LDL-C in EvoMab vs control (placebo-pbo or ezetimibe-eze) with EvoMab 140 mg Q2W or 420 mg QM were reported as the average of week 10 and 12 values.

Results: Differences in percent change from baseline in LDL-C for 140 mg Q2W; 420 mg QM dosing ranged from −74.9% to −56.5% compared to pbo; from −44.9% to −36.9% compared to eze in the individual studies, respectively. Treatment differences for pbo or eze were similar for both 140 mg Q2W and 420 mg QM doses across age ≤65 years (−65.4%; −65.3% vs pbo, −39.5%; −44.0% vs eze); >65 years (−65.9%; −64.4% vs pbo, −40.1%; −35.6% vs eze); males (−68.5%; −67.2% vs pbo, −43.0%; −43.8% vs eze); females (−62.6%; −62.9% vs pbo, −36.8%; −38.8% vs eze); glucose tolerance status as type 2 diabetes mellitus (−66.4%; −62.0% vs pbo, −36.5%; −42.5% vs eze), metabolic syndrome (−70.0%; −63.8% vs pbo, −40.9%; −44.8% vs eze); or neither type 2 diabetes nor metabolic syndrome (−63.5%; −66.7% vs pbo, −39.7%; −39.1% vs eze), ESC/EAS risk: very high (−68.5%; −67.2% vs pbo, −41.1%; −40.4% vs eze); high (−65.7%; −68.9% vs pbo, −44.2%; −45.5% vs eze), moderate (−66.0%; −65.0% vs pbo, −37.9%; −38.8% vs eze), or low risk (−60.9%; −67.8% vs pbo, −41.5%; −48.5% vs eze).

Conclusion: Patients on evolocumab demonstrated significantly greater reduc-
On subgroup analysis, the rate of MACE was significantly lower in the OMT group versus the PCI group (10.9%) of the OMT group versus 41 patients (14.2%) of the PCI group (p=0.38).

Methods and results: Between March 2003 and February 2012, we enrolled 2,024 CTO patients in a prospective, observational registry and retrospectively analyzed 435 patients with CTO of a single coronary artery. We divided patients into the OMT group (n=147) and the PCI group (n=288) according to initial treatment strategy. One-to-many (1:N) propensity score matching with non-duplicate pairs was performed using the nearest neighbor method with Mahalanobis distance. The median follow-up duration was 47.6 (interquartile range: 22.9 to 68.9) months. MACE occurred in 16 patients (11.5%) of the OMT group and 47 (16.3%) of the PCI group. The rate of MACE was lower in the OMT group (p=0.02). On subgroup analysis, the rate of MACE was significantly lower in the OMT group than in the PCI group among patients with APPROACH score ≥18 and SYNTAX score ≥12.

Conclusions: As a treatment strategy in patients with single-vessel CTO, PCI did not reduce the risk of MACE or cardiac death. These results suggest that OMT may be a better initial strategy for patients with low ischemic burden, as assessed by low APPROACH and SYNTAX scores.

P1758 | BENCH
Dabigatran vs. warfarin in venous thromboembolism: a meta-analysis
I. Sipahi, C. Cuhadaroglu, Acibadem University, Cardiology, Istanbul, Turkey; Acibadem University, Pulmonary Medicine, Istanbul, Turkey

Introduction: Dabigatran has recently been approved for treatment of venous thromboembolism, including pulmonary embolism. The randomized trials testing this drug against warfarin for this indication were non-inferiority trials. However, the non-inferiority margins of these trials were wide (a relative risk of 2.75 or 2.85), which meant accepting more than a 2.5 fold relative risk increase as non-inferior.

Purpose: Because several randomized trials of dabigatran with very similar study designs have now been reported, a meta-analysis of such studies would provide tighter confidence intervals and increase the certainty about the effectiveness of dabigatran vs. warfarin in venous thromboembolism. Our purpose was to perform this analysis.

Methods: The three randomized trials submitted to the US Food and Drug Administration for approval of dabigatran for venous thromboembolism were included. Number of events for the common primary outcome (venous thromboembolism or related death) and number of patients in each group were extracted. Fixed-effect models were used to obtain meta-analytic risk ratios.

Results: Data of a total of 7963 patients were obtained for the primary outcome. In all 3 trials dabigatran was given at a dose of 150 mg twice daily and target INR was 2 to 3 with warfarin. On meta-analysis dabigatran had a risk ratio of 1.20 (95% CI 0.88–1.61) (P=0.4) for venous thromboembolism or related death (Figure).

Conclusions: The confidence intervals of dabigatran for treatment of venous thromboembolism as compared to warfarin are tighter on meta-analysis, ruling out a 65% increase in risk (as compared to the boundary of 175% to 185% set in the individual trials). Smaller degrees of risk increase compared to warfarin are not ruled out.
P1761 | BEDSIDE

A phase 1, randomized, placebo-controlled, single ascending and multiple dose study of subcutaneously administered ALN-PCSSC in subjects with elevated low density lipoprotein cholesterol

K. Fitzgerald, D. Kallend, S. White, A. Borodovsky, J. Sutherland, J. Kallend, B. Bettencourt, V. Clausen, P. Wijngaard, J. Horton, A. Simon. 1Alnylam Pharmaceuticals, Cambridge, United States of America; 2The Medicines Company, Parsippany, United States of America; 3University of Texas Southwestern Medical School, Dallas, United States of America

Background and introduction: Hypercholesterolemia, specifically elevated low density lipoprotein cholesterol (LDL-C), is one of the major risk factors for the development of coronary heart disease, despite statin treatment, there remains a clear unmet medical need for novel drugs that lower LDL-C with increased patient compliance. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a genetically validated novel target for the lowering of LDL-C, whose reduction has been linked to lower cardiovascular risk. RNA interference is a naturally occurring cellular mechanism mediated by small interfering RNA (siRNA) that allows for the specific inhibition of protein synthesis through the cleavage and degradation of a selective mRNA. ALN-PCSSC is an investigational RNAi therapeutic that inhibits the synthesis of PCSK9 protein. ALN-PCSSC has been shown to be highly active in NHP models, lowering plasma PCSK9 up to 95% and LDL-C up to 67% in NHP. In addition, knockdown of PCSK9 and lowering of LDL-C were rapid and durable, with maximal effects lasting greater than 90 days and returning to baseline at approximately 160 days. These data support the evaluation of a once-monthly, and possibly a once-quarterly, subcutaneous dosing regimen in the clinic. Given the rapidity of the effect, and the translation of preclinical data across multiple investigational RNAi therapeutics, we anticipate an attractive profile relative to anti-PCSK9 antibodies.

Purpose: We are currently conducting a phase 1, randomized, placebo-controlled, single ascending and multiple dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of subcutaneously administered ALN-PCSSC in subjects with elevated LDL-C on and off of statin therapy.

Methods: Subjects ages 18 to 60 years with LDL-C -100 mg/dl on and off of statins are being enrolled in the United Kingdom, ClinicalTrials.gov identifier NCT0231442.

Results and conclusions: We will report, for the first time, interim data from this trial, including safety, PCSK9 protein, LDL-C and other relevant lipid endpoint measurements.

Acknowledgement/Funding: Alnylam Pharmaceuticals

P1762 | BEDSIDE

Erythropoietin improves long-term neurological outcome in acute ischemic stroke patients: a randomized, prospective, placebo-controlled clinical trial

T.H. Tsai, S. Chua, P.H. Sung, Y.L. Chen, S. Lee, J.J. Sheu, H.K. Yip. 1Kaohsiung Chang Gung Memorial Hospital, Chang Gung University, College of Medicine, Kaohsiung, Taiwan, ROC; 2Kaohsiung Chang Gung Memorial Hospital, Chang Gung University, College of Medicine, Kaohsiung, Taiwan, ROC

Background: Mortality and disability following ischemic stroke (IS) remains unacceptably high in with respect to the conventional therapies. This study tested the effect of erythropoietin (EPO) on long-term neurological outcome in patients after acute ischemic stroke (IS).

Aims of the study: The primary objective was to evaluate the safety and efficacy of two consecutive doses of EPO (5,000 IU/dose, subcutaneously administered at 48 h and 72 h after acute IS) on improving the 90-day combined endpoint of recurrent stroke or death that has been previously reported. A secondary objective was to evaluate the long-term (i.e. five years) outcome of patients who received EPO.

Methods: This was a prospective, randomized, placebo-controlled trial that was conducted between October 2008 and March 2010 in a tertiary referral center. IS stroke patients who were eligible for EPO therapy were enrolled into the study. The results showed that long-term recurrent stroke and mortality did not differ between group 1 (placebo-control, n=71) and group 2 (EPO-treated, n=71). Long-term Barthel index -35 (defining a severe neurological deficit) was lower in group 2 than group 1 (p=0.007). Multiple-stepwise logistic-regression analysis showed that EPO therapy was significantly and independently predictive of freedom from a Barthel index of -35 (p=0.029). Long-term major adverse neurological event (MANE; defined as: death, recurrent stroke, or long-term Barthel index -35) was lower in group 2 than group 1 (p=0.034). Multiple-stepwise Cox-regression analysis showed that EPO therapy and higher Barthel Index at day 90 were independently predictive of freedom from long-term MANE (all p<0.04).

Conclusion: EPO therapy significantly improved long-term neurological outcomes in patients after IS.

P1763 | BEDSIDE

Assessment of intra- and inter-atrial asynchrony in patients with systolic and diastolic heart failure

F.Q. Huang, L. Zhong, T.T. Le, J.I. Wong, R.S. Tan. National Heart Centre Singapore (NHCS), Singapore, Singapore

Objectives: Heart failure (HF) can lead to electrical and structural remodeling of the heart. It is associated with reduced inter- and intra-atrial synchrony and atrial arrhythmia. We aim to evaluate the intra- and inter-atrial asynchrony using tissue Doppler imaging in patients with systolic (left ventricular ejection fraction <50%) and diastolic heart failure (left ventricular ejection fraction >50%).

Methods: A total of 100 patients with HF were included, 30 patients with systolic HF and 25 with diastolic HF and 50 age matched controls were involved and underwent echocardiography in our study. The time intervals (adjusted by heart rate) between the onset of the P-wave to the onset of the A-wave at the left atrial free wall (P-LA), inter-atrial septum (P-IAS) and right atrial free wall (P-RA) were measured in 4-chamber view. Intra-atrial synchrony was defined as the differences between P-IAS and P-RA (P-RA synchronicity), and between P-LA and P-IAS (LA synchronicity). Inter-atrial synchrony was defined as the difference between P-LA and P-RA.

Results: The time intervals of P-IAS and P-RA were significantly prolonged in patients with HF, but the time intervals of P-RA was significant prolonged only in patients with systolic HF compared with normal controls. LA, RA and Inter-atrial synchronicity were significantly different between patients with systolic HF and controls, whereas only RA synchronicity was significantly different between patients with diastolic HF and normal controls (Table1).

Table 1. Parameters in 3 groups

<table>
<thead>
<tr>
<th>Normal controls (n=50)</th>
<th>Diastolic HF (n=25)</th>
<th>Systolic HF (n=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF (%)</td>
<td>71.5±6.84</td>
<td>60.15±7.75</td>
</tr>
<tr>
<td>P-IAS (ms)</td>
<td>44.3±13.54</td>
<td>58.93±21.25</td>
</tr>
<tr>
<td>P-LA (ms)</td>
<td>64.8±17.21</td>
<td>75.06±19.33</td>
</tr>
<tr>
<td>P-RA (ms)</td>
<td>51.60±3.58</td>
<td>47.46±15.58</td>
</tr>
<tr>
<td>LA synchronicity</td>
<td>20.99±9.23</td>
<td>16.12±1.99</td>
</tr>
<tr>
<td>RA synchronicity</td>
<td>1.72±32.17</td>
<td>13.37±19.95</td>
</tr>
<tr>
<td>Interatrial synchrony</td>
<td>22.73±7.06</td>
<td>28.03±18.19</td>
</tr>
</tbody>
</table>

Conclusion: In patients with diastolic HF, there was a time delay on left atrial sepal and lateral wall, but no changes on right atrial free wall, and only RA synchrony was observed. In patients with systolic HF, both intra- and inter-atrial synchrony were documented.

P1764 | BEDSIDE

Resting heart rate shows an inverse correlation with left ventricular ejection fraction in patients with chronic heart failure: results from reality HF

Y. Cavusoglu, O. Kozan, S. Kucukoglu, A. Temizhan 1 on behalf of REALITY HF Investigators. 1Eskisehir Osmangazi University, Cardiology, Eskisehir, Turkey; 2Dokuz Eylul University, Cardiology, Izmir, Turkey; 3Istanbul University Cardiology Institute, Cardiology, Istanbul, Turkey; 4Türkiye Yüksek İhtisas Hospital, Cardiology, Ankara, Turkey

Objectives: Although both resting heart rate (HR) and left ventricular ejection fraction (LVEF) are known to be strong predictors for worse clinical outcomes in HF patient population, less is known about the resting HR levels in relation to LVEF. REALITY HF (Resting Heart Rate and Real Life Treatment Modality in Outpatients with Left Ventricular Systolic Dysfunction) data were analyzed for the assessment of any relationship between resting HR and LVEF.

Methods: REALITY HF was a multicenter, prospective, observational, national registry designed to evaluate HF patients’ clinical characteristics and the effects of current treatment modalities on resting heart rate (HR) and enrolled 1251 patients (mean age 61±12 years, 76% male) from 16 centers who were admitted to the outpatient clinic with the diagnosis of chronic HF, LVEF <40% and > 18 years of age. 791 patients in sinus rhythm were included in this analysis. Patients with recent acute coronary syndromes, severe hepatic or renal dysfunction, severe chronic obstructive pulmonary disease, severe anemia, hyper-hypothyroidism and pregnant women were excluded from the study. Resting HR was obtained from 12-lead ECG. Patients were classified into 3 groups according to the tertiles of LVEF: lowest tertile: LVEF -27.6% (n=254), second tertile: LVEF 27.7% to 34.7% (n=305) and highest tertile: LVEF >34.7% (n=306).

Results: At the time of enrollment, 93% of patients were receiving evidence-based HF medication and 82% were on ≥2 drug therapy including ACEI or ARB, beta blocker, aldosterone blocker, diuretic or digoxin. Mean resting HR was 76.8±13.6 bpm and 69.1% of the patients had a resting HR > 70 bpm. Resting HR was found to be 78.9±13.6 bpm in those in the lowest tertile, 76.8±13.5 bpm in those in the second tertile and 74.9±14.3 bpm in those in the highest tertile (Kruskal-Wallis, p<0.001). Mean HR was significantly higher in the lowest LVEF tertile compared to the highest LVEF tertile (Mann-Whitney, p<0.001) and significantly higher in the second LVEF tertile as compared to the highest LVEF tertile (Mann-Whitney, p<0.043). Moreover, there was a significant negative correlation between resting HR and LVEF (p<0.001).

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475 by guest on 07 February 2019
Conclusions: The results of this study suggest that resting HR shows a significant inverse correlation with LVEF in patients with chronic HF.

Acknowledgement/Funding: This study is supported by Servier

P1767 | BEDSIDE

Endothelium-enriched microRNAs predict the presence of cardiac allograft vasculopathy

B. De Geest1, N. Singh1, W. Heggermont1, S. Fieuws2, J. Vanhaecke3, J. Van Cleemput3, B. De Geest1, 1 Center for Molecular and Vascular Biology, Catholic University of Leuven, Leuven, Belgium; 2Interuniversity Institute for Biostatistics and Statistical Bioinformatics (I-BioStat), University of Leuven and University of Hasselt, Leuven, Belgium; 3Cardiology, Catholic University of Leuven, Leuven, Belgium

Aims: Cardiac allograft vasculopathy (CAV) is a limiting factor for the long-term survival of heart transplant recipients. Clinical decisions and care may be improved by the development of prediction models based on circulating biomarkers. The endothelium may play a central pathogenetic role in the development of CAV. We evaluated the hypothesis that endothelium-enriched microRNAs (miRNAs) discriminate between patients with CAV and patients without CAV.

Methods: Fifty-two patients undergoing coronary angiography between 5 and 15 years after heart transplantation were recruited in this cross-sectional study. Circulating levels of endothelium-enriched miRNAs (miR-21–5p, miR-92a-3p, miR-92a-1–5p, miR-126–3p, miR-126–5p) were quantified by real-time RT-qPCR. The discriminative ability of logistic regression models was quantified using the concordance statistic (c-statistic).

Results: Median plasma levels of miR-21–5p, miR-92a-3p, miR-126–3p, and miR-126–5p were 1.82-fold (p<0.05), 1.87-fold (p<0.05), 1.94-fold (p<0.05), and 1.59-fold (p=0.06) higher, in patients with CAV than in patients without CAV. Receptor c-statistic (c-statistic 0.699 (95% CI 0.537–0.842), serum creatinine (c-statistic 0.703 (95% CI 0.552–0.854)), levels of miR-92a-3p (c-statistic 0.682 (95% CI 0.533–0.831)), and levels of miR-126–5p (c-statistic 0.655 (95% CI 0.502–0.807)) predicted CAV-status in univariable models. In multivariable logistic regression analysis, miR-126–5p was an independent predictor of CAV (c-statistic 0.800 (95% CI 0.674–0.926)).

Conclusion: Endothelium-enriched miRNAs have predictive ability for CAV beyond clinical predictors.

Acknowledgement/Funding: This work was supported by grant G.0529.10N of the Fonds voor Wetenschappelijk Onderzoek-Vlaanderen.

P1768 | BEDSIDE

Improved survival after heart transplantation in patients with cardiac amyloidosis

M.A. Castel Lavilla, E. Santiago, M. Farrero, M. Cardona, A. Garcia-Alvarez, F. Perez-Villa. Hospital Clinic de Barcelona, Cardiology Department, Barcelona, Spain

Introduction and aims: Previous studies reported poor outcomes after heart transplantation (HT) in patients with cardiac amyloidosis. After 2008 we performed changes in the treatment of these patients in our center consisting in: 1) A more strict selection of patients and 2) Autologous stem cell transplantation (ASCt) after HT for AL amyloidosis or simultaneous HT and liver for familial transthyretin (TTR) amyloid patients. The aim of this study is to assess outcomes after these changes.

Methods: Retrospective analyses of the outcome of amyloid patients who received a HT in our center. Data regarding type of amyloidosis, other organ dysfunction and outcomes after HT were assessed. Survival of amyloid patients transplanted before and after 2008 was compared to other heart failure patients who underwent HT.

Results: There were 12 amyloid patients undergoing HT (4% of total). The type of amyloid was 5 AL and 7 TTR (6 familial, 1 senil). Four patients (80%) of the AL patients and 1 patient (14%) of the TTR group were women, mean age 54±8 yrs. 80% of AL amyloid patients received chemotherapy previous to HT and in 60% of them ASCt was performed after HT. Four patients in the TTR group had a liver-heart transplant (3 simultaneous). Survival of amyloid patients was 91% and 68% after 1 and 5 years HT; there were no significant differences with survival of other HT patients (93% and 74%, respectively). Survival of amyloid patients after 2008 improved significantly compared to patients before this period (100% vs. 75% at 1 year and 100% vs. 25% at 5 years, p<0.016).

Conclusions: Outcomes after HT of patients with cardiac amyloidosis has significantly improved and is similar to survival of other HT recipients. Changes in patient selection and the association of ASCt for AL amyloid patients and liver transplant for TTR amyloid patients are probably related to this survival benefit.
Conclusion: In this series of HT recipients with uneventful postoperative course, LV and RV GLS values were significantly reduced early after HT and improved progressively until their complete normalization two and one year after HT, respectively. This is the first study to show a full recovery of LV and RV deformation parameters and offers “normal” ranges of strain values that could be useful for monitoring the evolution of HT recipients.

P1769 | BEDSIDE Favorable medium-term outcome of transplanted hearts selected from marginal donors by pharmacological stress echocardiography

T. Bombardini1, M. Carmeli2, R. Del Bene3, M. Maccherini2, L. Potena4, E. Pilato5, E. Picano5. 1University of Siena, Heart Transplantation Division, Department of Cardiac Surgery, Siena, Italy; 2Careggi Hospital, Firenze, Italy; 3University Hospital Polyclinic S. Orsola-Malpigh, Cardiac Surgery, Heart and Lung Transplantation Program, Bologna, Italy; 4NU School of Medicine, Astana, Kazakhstan

Background: Due to the shortage of donor hearts, the criteria for acceptance have been considerably expanded. Regardless of the changes made in the acceptance of marginal donors, any such mechanism cannot be considered successful unless recipient graft survival rates remain acceptable.

Aim: The aims of this study are: 1 - to establish the feasibility of an approach based on pharmacological stress echocardiography (SE) as a gatekeeper for extended heart donor criteria; 2 - to assess the outcome of recipients of marginal donor hearts selected with new echocardiographic techniques over standard criteria.

Methods: From April 2005 to November 2014, 119 marginal (< 50 years old, n=100) or < 50 years old with > 3 concomitant risk factors, n=19) candidate donors (age 55±8 years, 71 male) were enrolled. After legal declaration of brain death, donors underwent resting and, if normal, dobutamine (0.84 mg/kg in 6; n=58) or dobutamine (up to 40 mcg/kg, n=4) SE.

Results: We found 54 eligible hearts with normal findings. Of these, 14 were not transplanted due to lack of a matching recipient. The remaining 40 eligible hearts were transplanted in emergency recipients. All showed normal (n=36) or near-normal (minor single-vessel disease, in 4) angiographic and hemodynamic findings at 1 month. After follow-up (median 40, interquartile range 17–65 months), 32 recipients survived and 8 died; 2 at 2 months from general sepsis, 2 at 3 months for graft failure, 1 at 15 months from neoplasia, 1 at 32 months from myeloma, 1 at 45 months from sepsis and 1 at 84 months from heart rejection (Figure 1).

Conclusion: Pharmacological SE can be safely performed in candidate heart donors with brain death, and shows potential to substantially increase the number of donor hearts without adverse effects on recipient outcome.

Acknowledgement/Funding: CCM 2010. Centro Nazionale per la Prevenzione e il Controllo delle Malattie

P1770 | BEDSIDE Insulin resistance is a predictor of long term prognosis in chronic systolic heart failure

L. Voronkov1, M. Ilyntyska1, T. Gavrilenko1, S. Potashev1, P. Babich2. 1NSC Institute of Cardiology M.D. Strazhesko, Heart Failure, Kiev, Ukraine; 2State Expert Centre of the Ministry of Healthcare of Ukraine, Kiev, Ukraine

Background: Despite the fact that chronic heart failure (CHF) is a potentially insulin resistance state, there is lack of data regarding the influence of insulin resistance (IR) on a clinical prognosis of CHF.

Objective: To define prognostic value of IR in systolic CHF.

Methods: The study involved 107 patients (pts) with CHF (NYHA class II–IV with left ventricular ejection fraction <40%) without diabetes. IR was defined as HOMA index ≥2.77. Cox regression analysis was used to searching the predictors of composite outcome (time to death from cardiovascular causes or cardiovascular hospitalization) during 12-month follow-up.

Results: IR was observed in 45 (42%) pts. According to univariate Cox regression model the predictors of composite outcome during 12 months was HOMA index ≥2.77. Cox regression analysis was used to searching the predictors of composite outcome (time to death from cardiovascular causes or cardiovascular hospitalization) during 12-month follow-up.

Conclusion: Insulin resistance is a strong predictor of poor 12-month clinical prognosis in systolic CHF.

P1771 | BEDSIDE Change in relaxation pattern of the left and right ventricle after freedive training

R. Pudil1, M. Zajac2. 1Charles University Prague, Faculty of Medicine in Hradec Kralove, 1st Department of Medicine, Hradec Kralove, Czech Republic; 2Charles University of Prague, Faculty of Physical Education and Sport, Prague, Czech Republic

Background: Freediving becomes a popular sport activity which requires good mental and physical training. During the dive, the cardiovascular system has to face up to water environment (temperature, significant pressure changes), breathing (hypoxia, hypercapnia), and physical activity. Little is known about the reaction of cardiovascular system to these factors.

The aim of the study was to assess the effect of freeing dive training on the functional parameters of the left and right ventricle.

Methods: The group consisted of the 19 well-trained competitive freedivers (37.2±6.6 years, 2 women, 17 men). Echocardiography was performed just before and immediately after freeing dive training. All freedivers completed at least 20 dives into the depth of 20 m (constant weight discipline, 5mm neoprene wet suits, water temperature 12°C).

Results: We observed significant changes in pulse-wave Doppler parameters of left ventricle diastolic function (E/A: 1.5±0.3 vs. 1.2±0.2, p<0.001; E: 92.1±16.2 vs. 70.3±10.5 cm/s, p<0.001; A: 62±14.3 vs. 58.5±10.1 cm/s, p ns; E-wave deceleration time: 129.8±34.2 vs. 157.8±38.6 ms, p<0.001). Similarly, tissue Doppler imaging-derived early diastolic myocardial velocities measured at the mitral annulus were decreased after the training (e'septal: 14.5±3.2 vs. 11.2±2.8 cm/s, p<0.01; e' lateral: 16.8±3.0 vs. 14.5±3.1 cm/s, p<0.05). Systolic parameters of the left ventricle (EF and FS) were not affected. Right ventricle parameters: TAPSE showed significant decrease (26.8±2.8 vs. 21.1±2.7 cm, p<0.001), tissue Doppler imaging-derived early diastolic velocities measured at the tricuspid annulus were decreased after the dive (e': 15.8±3.1 cm/s vs. 12.7±2.2, p<0.05). Also right ventricle myocardial performance index decreased (0.51±0.07 vs. 0.46±0.07, p<0.01). Peak gradient of the tricuspid regurgitation significantly increased (6.52±4.8 vs. 15.3±1.2 mmHg, p<0.01).

Conclusion: For the first time, the echocardiography was used to detect changes in diastolic function induced by freeing dive training in fresh water. The study showed decrease in diastolic characteristics of the left ventricle, which can be attributed to the change in relaxation pattern of the left ventricle. Similar changes were observed in right ventricle, where additional factor can play important role (increase in pulmonary artery pressure). We consider these changes as reactive to changes in ambient pressure and temperature. This study underlines the necessity of good physical condition of competitive freedivers.

Acknowledgement/Funding: PRVOUK P37/03

P1772 | BENCH Altered torsion mechanics in patients with hypertrophic cardiomyopathy: blame it on the LVOT-obstruction?

L. Halmal1, A. Kardos1, T. Forster2, A. Nemes2, N. Banner3, S. Neubauer4. 1Milton Keynes Hospitals NHS Trust, Department of Cardiology, Milton Keynes, United Kingdom; 2University of Szeged, Faculty of Medicine, 2nd Dept of Internal Medicine & Cardiology Center, Szeged, Hungary; 3Harefield Hospital, Heart Transplant Unit, London, United Kingdom; 4Centre for Clinical Magnetic Resonance Research, Department of Cardiovascular Medicine, Oxford, United Kingdom

The 3-dimensional Myocardial Deformation Imaging (3D-MDI) is able to characterize complex events of myocardial function, however, changes of deformation mechanics have not been well defined in different forms of hypertrophic cardiomyopathy (HCM). We aimed to examine parameters of LV deformation in patients with HCM using 3D-MDI and to detect if there were any effects of outflow tract obstruction on deformation patterns.

Figure 1. Kaplan - Meier curves for the composite outcome in patients with chronic heart failure and left ventricular systolic dysfunction depending on presence of IR.
**Methods:** 45 consecutive patients with HCM (age 43.8±9.3yrs, 14 females, 20 with LVO-obstruction>30mmHg, HOCCM), including 18 from the MAGYAR-PATH HCM-Registry were compared with 25 gender and age-matched control subjects. Inclusion done by standard echocardiographic criteria, confirmed by T1-weighed cMri findings. Systolic MDI indices: peak systolic strain (S), strain-rate (SR) in longitudinal, circumferential and radial directions. Twist was given as difference in apico-basal rotation angles, Torsion (Tor) as LV-twist normalized to ventricular length (lcm), its rate as Tor-Rate measured (° /s). Corrected recoil rate (REC) calculated as [[TwistES–TwistLV]/TwistES] x 100|VR as a relative load-independent diastolic index.

**Results:** Controls, HCM patients had increased peak LV twist (12.3±4.0° vs 9.1±3.2°, p<0.01) with increased apical rotation of HOCCM cases (obstructive, 15.7±3.4° vs non-obstructive, 10.7±1.8°, p<0.001). The Tor-R was quicker with obstruction (66.8±10.1 vs 53.6±3.3 °/s, p<0.05) or that in controls (50.5±4.4°). HOCM cases had slower UTR (98.8±29.1 vs 110±28.2 °/s, p<0.01), longer UTR (195.8±20.3 vs 129.1±23.0ms, p<0.01), the onset of untwist occurred closer to aortic valve closure (90.9±3.1 vs 75.9±6.6%, p<0.001; as time normalized by length of systole). The REC diminished more in HOMC (31±5.9 vs 52.3±8.8 °/s, p<0.01), and both were less than in controls (49.1±6.6°, p<0.001).

**Conclusions:** LV Torsion links systolic contraction with diastolic relaxation and plays a major role in cardiac physiology. HOCM patients had more increased systolic Torsion implying hyperdynamic contraction. Untwist and recoil started earlier, but remained slower to see just limited completion during early diastole leading to isolated impairment of early diastolic function, contributing to increased LV filling pressures. The 3D-MDI hence appears to be able to reflect the changes of Torsion behaviour, which might have a role in screening subclinical cases.

**P1774 | BEDSIDE**

**Diastolic dysfunction precedes overt systolic dysfunction in chemotherapy-induced cardiotoxicity**

G. Portugal, A. Galrinho, L. Branco, M. Mota Carmon, J. Feliciano, A.V. Monteiro, P. Pinto Teixeira, T. Pereira Da Silva, M. Nogueira, R. Ferreira. Hospital Santa Marta, Department of Cardiology, Lisbon, Portugal

**Background:** Diastolic dysfunction (DD) is considered an early marker of myocardial injury in a variety of clinical settings. The aim of this study was to evaluate the potential relationship between diastolic dysfunction in patients submitted to chemotherapy (CT) with anthracyclines.

**Methods:** Consecutive breast cancer patients undergoing QT referred for a transthoracic echocardiogram (TTE) between August 2010 and October 2014 were included. Data was collected on baseline characteristics, TTE measurements including tissue doppler, QT regimen and adjacently therapy. Systolic dysfunction (SD) was defined as ejection fraction (LVEF) ≤55% and diastolic dysfunction as mean E/e’ ratio ≥13. Patients with baseline SD or DD were excluded. A cut-point defined as dysfunction in >10% of patients was used to calculate time-related incidence.

**Results:** 110 patients were submitted to a total of 234 TTE during a mean follow-up of 381 days. Mean age was 56±14.5 yrs, basal heart rate 79.7±18.8 bpm. Baseline TTE: LVEDD 46.6±7.0 mm, LVESD 28.1±4.6 mm, LVEF 68.3±6.8%, E velocity 76.7±19.8 cm/s, septal e’ 8.2±3.1, lateral 10.7±3.8 cm/s. At 1 year, the incidence of DD was 18.0% vs 8.0% for SD (odds ratio 2.25, p=0.0028, chi sq). The threshold for >10% of patients with DD was reached after 203 days, while for SD only after 378 days. DD preceded significant LVEF decline by 175 days for this quantile. The Kaplan-Meier survival function for DD and SD after 1 year is plotted on graph 1.

**Conclusion:** Standard ETT follow-up with serial LVEF evaluation may underestimate the true incidence of QT cardio toxicity. A high proportion of patients submitted to QT will develop diastolic dysfunction, as assessed by TD analysis. Diastolic dysfunction was common and preceded LVEF decline in this population.

**HEART FAILURE: FROM BENCH TO BEDSIDE III**

**P1775 | BENCH**

**Left ventricular calcium-handling proteins in the type 2 diabetic human heart with preserved ejection fraction**


**Background:** Diabetes mellitus type 2 is the most common form of diabetes with the global prevalence set to increase at least fivefold over the next two decades. The prevalence of heart disease is significantly increased in patients with type 2 diabetes mellitus (DM) compared with non-diabetic controls. Despite advances in the understanding of the molecular basis of diabetes-associated cardiomyopathy, the precise nature of the underlying molecular and cellular alterations is still not well defined. This study aimed to determine the expression of the calcium-handling proteins SERCA2a, phospholamban (PLB) and correlated to plasma glycated haemoglobin (HbA1c) and the potential role of beta-blocker use in HFPEF should be studied.

**Methods:** Inclusion done by standard echocardiographic criteria, confirmed by T1-weighed cMri findings. Systolic MDI indices: peak systolic strain (S), strain-rate (SR) in longitudinal, circumferential and radial directions. Twist was given as difference in apico-basal rotation angles, Torsion (Tor) as LV-twist normalized to ventricular length (lcm), its rate as Tor-Rate measured (° /s). Corrected recoil rate (REC) calculated as [[TwistES–TwistLV]/TwistES] x 100|VR as a relative load-independent diastolic index.
blood glucose levels. The study conformed to the principles of the Declaration of Helsinki of the World Medical Association.

Expression of SERCA2a and PLB were not different between non-diabetic and diabetic LV biopsies (SERCA2a: 2.3±0.4 vs. 2.3±0.5; PLB: 1.1±0.1 vs. 1.3±0.3, arbitrary units, both non-DM vs. DM, p<0.05). However, consistent with our previous findings diabetic RA tissue showed increased SERCA2a expression (1.9±0.2 vs. 2.7±0.2, non-DM vs. DM, p<0.05), and its endogenous inhibitor PLB was reduced (2.3±0.1 vs. 1.3±0.1, non-DM vs. DM, p<0.05). The SERCA/PLB ratio in the RA correlated with HbA1c (R2=0.34, p<0.05) and blood glucose (R2=0.19, p<0.05). Nonetheless, this discrepancy was not in the LV. Moreover, the postoperative incidence of atrial fibrillation was increased in diabetic compared to non-diabetic patients (25%, 6/24 vs. 50%, 10/20, non-DM vs. DM, Chi-square, p<0.05).

In conclusion, our study shows that the impact of type 2 diabetes on calcium-handling in the human atrial heart with diastolic dysfunction is chamber specific, and suggests that changes in RA may occur prior to those in the LV. The observed changes in the RA might contribute to the higher incidence of postoperative atrial fibrillation in diabetic patients with coronary artery disease. Our study addresses important aspects of the underlying mechanisms of diabetes-associated diastolic dysfunction, which will be crucial in developing new treatments.

Acknowledgement/Funding: National Heart Foundation Taylor Charitable Trust #1491; Otago Medical Research Foundation’s Laurenson Award #LA306, Healthcare Otago Charitable Trust.

P1776 | BEDSIDE

The Relationship of Intima-Media Thickness in the Brachial Artery and Endothelial Function with Left Ventricular Diastolic Dysfunction

Y. Ohno, T. Miyoshi, T. Ono, H. Oe, K. Nakamura, H. Ito. Okayama University, Cardiovascular Medicine, Okayama, Japan

Purpose: LV diastolic dysfunction (LVDD) is shown to be linked with endothelial dysfunction. Recently, the measurement of flow-mediated vasodilation (FMD) as an index of endothelium-dependent vasodilation has widely been used as a method for assessing vascular endothelial function. At measuring FMD in the brachial artery, intima-media thickness (IMT) can be simultaneously assessed in the same brachial artery using semi-automatic vessel wall tracking system. Although increased carotid IMT is reported to be associated with LVDD, there is limited data regarding brachial IMT. The aim of this study was to investigate the relationship between brachial IMT and LVDD.

Methods: A total of 211 patients (mean age 63±15 years, 50% men) with suspected coronary artery disease (CAD) underwent FMD by ultrasound using 10-MHz pulsed linear array transducer. Brachial IMT was automatically measured on A-mode images of the far wall of the same right brachial artery. Left ventricular structure (left ventricular mass index [LVM], left atrial volume index[LAVI]) and function (Early diastolic annular velocity[ e‘]) were assessed using echocardiography. LVDD was defined using E/e’, LAVI, and LAVI according to ASE guideline.

Results: Semi-automatic measurement of brachial IMT was feasible in all subsets. Of all, brachial IMT and FMD were 0.33±0.07mm and 5.6±2.7%. Brachial IMT was thicker in patients with hypertension (0.34±0.07mm vs. 0.31±0.07mm, p<0.001) and male (0.34±0.07mm vs. 0.31±0.07mm, p<0.002) compared to no-hypertension and female, respectively. Brachial IMT was related to FMD (r=−0.152; P=0.027, age (r=−0.184; P=0.007), LVM (r=−0.19; P=0.019) and septal e’ (r=−0.171; P=0.014). FMD was related to age (r=−0.269; P<0.001), septal e’ (r=−0.261; P<0.001), s’ (r=0.170; P=0.021) and lateral e’ (r=−0.234; P=0.002). Next, patients were classified into four groups according to the median value of brachial IMT and FMD. The prevalence of LVDD in the larger IMT and the lower FMD group (47%) was significantly higher than others (31%) (p<0.024). Multiple logistic analysis revealed that LVDD was associated with the larger IMT and the lower FMD (OR: 2.077, 95% CI: 1.068 to 4.038, p=0.031) along with hypertension (OR: 1.962, 95% CI: 1.022 to 3.769, p=0.043) and diabetes mellitus (OR: 0.043, 95% CI: 0.203 to 0.797, p=0.009).

Conclusion: The simultaneous measurements of the brachial IMT and FMD may be informative for assessment of LVDD.

P1777 | BEDSIDE

Association of cystatin C with heart failure with preserved ejection fraction. Potential role of altered collagen metabolism


University Hospital, Dept. of Cardiology, San Sebastian;1 Donostia University Hospital, Dept. of Cardiology, San Sebastian;2 Donostia University Hospital, Dept. of Internal Medicine, San Sebastian;3 Donostia University Hospital, Dept. of Cardiovascular Surgery, Pamplona, Spain

Background: Heart failure with preserved ejection fraction (HFPEF) is a complex entity that includes factors contributing to myocardial fibrosis, contributing to diastolic dysfunction in HFPEF patients. Methods: The population consisted of 141 elderly patients with HFPEF of hypertensive origin. Cardiac morphology and function was assessed by echocardiography. Circulating levels of cystatin C, the pro-fibrotic matricellular protein osteopontin, and biomarkers of collagen type I synthesis (carboxy-terminal proppeptide of procollagen type I, PICP) and degradation (matrix metalloproteinase-1, MMP-1) and its inhibitor TIMP-1 were analyzed by ELISA. 20 elderly subjects with no cardiac disease and normal age-adjusted renal function were used as a control group. In vitro studies were performed in cardiac human fibroblasts. Results: Compared to controls, cystatin C was increased (P<0.001) in HFPEF patients, even in those with normal age-adjusted estimated glomerular filtration rate (eGFR). Cystatin C levels were higher (P<0.05) in those HFPEF patients with an abnormally high estimated pulmonary capillary wedge pressure (ePCWP > 15 mmHg) compared to the patients with normal filling pressures. Cystatin C was directly correlated with the ePCWP (P<0.01), TIMP-1 (P<0.001) and osteopontin (P<0.001) and inversely correlated with MMP-1:TIMP-1 (P<0.01). However, the association was independent of the eGFR and a number of potential confounding factors. Interestingly, in human cardiac fibroblasts an excess of cystatin C induced osteopontin (P<0.01) and TIMP-1 (P<0.001) accumulation in the cell culture media without changes in mRNA or intracellular protein content, pointing to an inhibition of their extracellular degradation, which in turn could favor myocardial fibrosis.

Conclusion: In HFPEF patients of hypertensive origin, cystatin C is increased and associated with diastolic dysfunction and alterations in collagen metabolism independently of eGFR. An excess of cystatin C may contribute to elevated filling pressures by facilitating myocardial fibrosis via accumulation of osteopontin and TIMP-1.

Acknowledgement/Funding: Ministry of Economy and Competitiveness (Spain) and FP7 of the European Commission
characterized as impaired left ventricular (LV) relaxation and left atrial (LA) function. LA function may be associated with long-term outcome in HFpEF.

**Objectives:** The aim of this study was to assess prognostic impact of the LA function in HfPEF.

**Methods:** Seventy-one HfPEF (mean age 73 years, 38 male) were studied. Late mitral annular velocity (a') was measured as an index of the LA function. Cardiac event (a composite of all-cause death and heart failure)-free survival was compared between high a' (a' ≥ 7.85 cm/s, n=36) and low a' (a' < 7.85 cm/s, n=35) groups.

**Results:** Age and gender were similar between the 2 groups. Low a' group had significantly lower left ventricular ejection fraction (60.0±7.3 vs. 64.1±7.9%, P<0.03) and higher E/e' (19.9±7.1 vs. 13.9±4.3, P=0.0001). HfPEF with low a' had significantly lower cardiac event-free survival than HfPEF with high a' (Log rank, P=0.02).

**Conclusions:** Impaired LA function may be associated with worse prognosis in HfPEF.

---

**P1780 | BEDSIDE**

**Predictors of heart failure with preserved systolic function after ST-segment elevation myocardial infarction**

J.-H. Ahn, J.R. Park, S.-J. Hwang, J.-S. Koh, Y.H. Jung, C.H. Kwak, J.-Y. Hwang. Gyeongsang National University Hospital, Division of Cardiology, Department of Internal Medicine, Jinju, Korea, Republic of

**Background:** A considerable number of patients led to heart failure with preserved systolic function (HfPEF) after ST-segment elevation myocardial infarction (STEMI). Nevertheless, there are limited data on the characteristics and risk factors of patients with HfPEF after STEMI.

**Methods:** We conducted a single-center, retrospective cohort study on patients between 2010 and 2013. We included only patients who were undergoing primary PCI with achieved angiographic success and ejection fraction ≥50% at 1 month after discharge (n=283). Patients with HfPEF (having diastolic dysfunction after 1 month) were categorized as new-onset (normal diastole on admission) and pre-existing (having diastolic dysfunction on admission), or normal, with comparisons made between groups.

**Results:** Total HfPEF was identified in 128 (30.4%) patients (new-onset n=62 [48.4%]; preexisting n=66 [52.6%]). Compared with those without diastolic dysfunction, older age, female, higher Killip class, longer symptom to balloon time, and larger myocardial area at risk and infarction size were predictors of HfPEF. Multivariable analysis showed older age, female, longer symptom to balloon time, and larger infarction size were independent significant predictors of total HfPEF. Similarly, older age, longer symptom to balloon time, and larger myocardial area at risk and infarction size were independent significant predictors of new-onset HfPEF.

**Conclusions:** We classified patients with HfPEF after STEMI into two subcategories: new-onset and preexisting HfPEF. Values for infarct size and area at risk determine risk for new-onset HfPEF versus normal diastole and preexisting HfPEF. This result may enable the design of therapeutic target for prevention of HfPEF after STEMI.

---

**P1782 | BENCH**

**S100/calgranulin mediated inflammation promotes FGF23 expression in cardiac fibroblasts and LVH**

M. Hofmann-Bowman1, A. Daugherty2, D. Rateri2, L.Y. Yan2, The University of Chicago Medical Center, Chicago, United States of America; 2 University of Kentucky, Lexington, United States of America.

**Background:** Serum S100A12 and fibroblast growth factor (FGF) 23 are biomarkers for cardiovascular mortality in patients with chronic kidney disease (CKD) and are associated with left ventricular hypertrophy (LVH). FGF23 is induced in cultured cardiac fibroblasts in response to cytokines including IL-6, TNF-a, LPS and S100/calgranulins. Moreover, S100A12 transgenic mice with CKD had increased FGF23 in valvular interstitial cells and exhibited LVH. The present study was designed to examine cardiac FGF23 expression in other murine models of LVH in the absence of CKD.

**Results:** Hearts from five groups of male mice were studied: (i) C57Bl6/J with transgenic expression of a bacterial artificial chromosome containing the human S100/calgranulins (S100A8/9 and S100A12, HBAC-S100), (ii) wild type littermates, (iii) LDLR−/− infused with saline (29 days, 0.9%), (iv) LDLR−/− infused with angiotension (Ang) II (29 days, 1000 ng/kg/min), and (v) fibroblast specific depletion of angiotension II type 1a receptor (AT1aR) (S100A4-Cre x AT1aR−/− x LDLR−/−) infused with AngII.

**Results:** HBAC-S100, but not wild type littermate mice, developed significant LVH at 10 months by heart weight/body weight (5.9±1.1 mg/g vs. 4.2±0.8, p<0.04), decreased E/A ratio, and increased LVWall thickness, and associated with increased expression of FGF23 mRNA and protein in cardiac tissue lysates (2–4 fold increase). Similarly, Ang II induced significant LVH compared to saline infused LDLR−/− mice (6.1±1.3 vs. 3.6±0.9 mg/g, p<0.01), and (vi) fibroblast specific depletion of angiotension II type 1a receptor (AT1aR) (S100A4-Cre x AT1aR−/− x LDLR−/−) infused with AngII.

**Conclusions:** Monitoring the levels of S100A12 could be useful for identifying patients with LVH development. Conversely, S100A12 levels do not seem to be useful in early detection of CAV. Further studies with larger number of patients may provide more information on the utility of these biomarkers in the early detection of CAV.

---

**P1783 | BEDSIDE**

**Effect of alcohol intake on diastolic function: the Ethnic-Echocardiographic Heart of England Screening Study (E-ECHOES)**

E. Shantsila1, A. Shantsila1, P.S. Gall2, G.Y.H. Lip1, University of Birmingham, Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom; 2 University of Birmingham, Primary Care Clinical Sciences, School of Health and Population Sciences, Birmingham, United Kingdom.

**Background:** Moderate alcohol intake is known to have some beneficial effects on cardiovascular health, but limited data are available on specific cardiac function per se (such as diastolic function) that may mediate these effects.

**Objective:** To evaluate whether alcohol intake was associated with diastolic function in a large British population.

**Methods:** We analyzed 3145 adults participating in the E-ECHOES cohort study between 2010 and 2013. We included only participants who were undergoing primary PCI with achieved angiographic success and ejection fraction ≥50% at 1 month after discharge (n=283). Patients with HfPEF (having diastolic dysfunction after 1 month) were categorized as new-onset (normal diastole on admission) and pre-existing (having diastolic dysfunction on admission), or normal, with comparisons made between groups.

**Results:** Total HfPEF was identified in 128 (30.4%) patients (new-onset n=62 [48.4%]; preexisting n=66 [52.6%]). Compared with those without diastolic dysfunction, older age, female, higher Killip class, longer symptom to balloon time, and larger myocardial area at risk and infarction size were predictors of HfPEF. Multivariable analysis showed older age, female, longer symptom to balloon time, and larger infarction size were independent significant predictors of total HfPEF. Similarly, older age, longer symptom to balloon time, and larger myocardial area at risk and infarction size were independent significant predictors of new-onset HfPEF.

**Conclusions:** We classified patients with HfPEF after STEMI into two subcategories: new-onset and preexisting HfPEF. Values for infarct size and area at risk determine risk for new-onset HfPEF versus normal diastole and preexisting HfPEF. This result may enable the design of therapeutic target for prevention of HfPEF after STEMI.
Purpose: To establish the relationship of alcohol intake with diastolic dysfunction, in the ethnic minority general population, in the United Kingdom.

Methods: Echoangiography was used to establish presence of diastolic dysfunction (based on ESC criteria) in 5074 participants of the E-ECHOES study (age ≥45 years, mean age 61±11 years, 48% male; 36% South Asian and 36% African-Caribbean). Of these 49% had history of hypertension, 30% diabetes and 6% myocardial infarction; 58% had never drank alcohol (Group I), 7% drank on the past but stopped completely by the time of the study (Group II), 30% drank occasionally (Group III), and 5% drank regularly (Group IV). In the last group 84 subjects (17% of the total population) admitted drinking more than recommended amount (~14 units for women and ~21 units for men per week).

Results: Diastolic dysfunction was present in 63% of Group I, 65% of Group II, 59% of Group III and 48% of Group IV (p<0.001). Occasional or regular alcohol intake was associated with lower risk of diastolic dysfunction on univariate logistic regression, as well as after multivariable adjustment (see Table). Discontinued alcohol intake was not related to any reduced risk of diastolic dysfunction vs. those with those who never used alcohol.

Effect of alcohol intake history

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (95% CI) p value*</th>
<th>Group II (95% CI) p value*</th>
<th>Group III (95% CI) p value*</th>
<th>Group IV (95% CI) p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>1.05 (0.87–1.36)</td>
<td>0.45</td>
<td>0.81 (0.62–1.04)</td>
<td>0.10</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>0.85 (1.74–0.96)</td>
<td>0.008</td>
<td>0.83 (0.72–0.96)</td>
<td>0.01</td>
</tr>
<tr>
<td>CI</td>
<td>0.83 (0.69–0.99)</td>
<td>0.04</td>
<td>0.83 (0.69–0.99)</td>
<td>0.04</td>
</tr>
<tr>
<td>CI</td>
<td>0.54 (0.41–0.71)</td>
<td>0.006</td>
<td>0.62 (0.45–0.84)</td>
<td>0.002</td>
</tr>
<tr>
<td>CI</td>
<td>0.45–0.05</td>
<td>0.002</td>
<td>0.62 (0.45–0.85)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

*Univariate, †adjusted for age, gender, BMI, history of hypertension, diabetes and myocardial infarction; ‡additional adjusted for ethnicity. OR, odds ratio; CI, confidence interval.

Conclusions: Occasional or regular alcohol intake is associated with better diastolic function in general population amongst ethnic minority groups.

P1785 | BEDSIDE Heart rate as a diagnostic and prognostic marker in patients with heart failure with preserved ejection fraction

C.M. Stanescu, C. Gutu, G.A. Dan, Colentina University Hospital, Bucharest, Romania

Background: Morbidity and mortality in patients (pts) with heart failure with preserved ejection fraction (HFpEF) are similar to those with HF with reduced EF. Resting heart rate (RHR) is recognized as a predictor of cardiovascular (CV) mortality.

Purpose: To investigate if RHR has diagnostic and/or predictive value in HFpEF.

Methods: 217 patients (pts) with clinical HF, with EF greater than 50% and diastolic dysfunction were included. Pts with atrial fibrillation or flutter were excluded. The parameters evaluated: NYHA class, RQS, quality of life (QoL) score, indexed left atrial volume (ILAV), E/E’ ratio and NT-proBNP value.

Results: Initially, pts with E/E’ ratio between 8–15 were divided into pts with severe HFpEF and with less than 220 pg/dL (82), RHR cut-off value of 72 bpm had a 72% sensitivity and 73% specificity for detecting pts with HFpEF (AUC 0.713, CI 0.637–0.789). Subsequently, 114 pts (age 56.9±24 years, 56 males) with confirmed HFpEF (74% in NYHA class II, 18% in class I and 20% in class III) were followed up for 1 year. The end-point - adverse outcome (AO)- comprised: death, myocardial infarction, stroke, hospitalization for HF; increased NYHA class, doubling NT-proBNP value. Fifty pts (group 1) had an AO, 64 had not (group 2). The following parameters were significantly different between groups 1 and 2 (NT-proBNP, 1339±420 vs. 522±180 pg/ml, p<0.002; CI 313–1320; QoL, 62±21 vs. 48±11, p=0.001; CI 1.1–4; ILAV, 6.2±3.3 vs. 3.3±2.1 mm²/m², p<0.03; CI 0.2–4.8; RHR, 83.6±13.6 vs. 74.2±12.2 b/min, p<0.001, CI 4.3–14.2). Predictive parameter values for AO are tabulated below. Pts with RHR greater than 75 bpm had a 70% increase in relative risk of AO.

Predictive parameter values for AO

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Area under ROC curve</th>
<th>Confidence interval</th>
<th>Cut-off value</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-proBNP</td>
<td>0.699</td>
<td>0.604–0.794</td>
<td>314 pg/ml</td>
<td>73%</td>
<td>56%</td>
</tr>
<tr>
<td>QoL</td>
<td>0.682</td>
<td>0.585–0.780</td>
<td>50</td>
<td>69%</td>
<td>67%</td>
</tr>
<tr>
<td>E/E’ ratio</td>
<td>0.797</td>
<td>0.716–0.878</td>
<td>9</td>
<td>69%</td>
<td>63%</td>
</tr>
<tr>
<td>ILAV</td>
<td>0.616</td>
<td>0.510–0.719</td>
<td>33.5 mm²/m²</td>
<td>65%</td>
<td>56%</td>
</tr>
<tr>
<td>RHR</td>
<td>0.698</td>
<td>0.591–0.786</td>
<td>75 beats/min</td>
<td>73%</td>
<td>56%</td>
</tr>
</tbody>
</table>

Conclusions: Resting heart rate could be useful in the diagnosis of pts with HFpEF and predictive for adverse prognosis, similar to consecrated parameters.

P1785 | BEDSIDE Diastolic dysynchrony has no impact on quality of life in patients with dilated cardiomyopathy

A.A.M. Farrag, E. Fares, S. Bakhoun, W.A. El-Arousy, Cairo University, Kasr Al-Ainy Hospital-Faculty of Medicine, Department of Cardiology, Cairo, Egypt

Introduction: Dilated Cardiomyopathy (DCM) leads to progressive decline in left ventricular (LV) systolic and diastolic function. Among the factors contributing to LV systolic diastolic dysfunction, the diastolic dyssynchrony has been extensively studied, little is known about diastolic dyssynchrony.

The aim of this study was to estimate the prevalence of systolic and diastolic dyssynchrony in patients with DCM and its association with quality of life (QoL).

Methods: Sixty patients with DCM were subjected 6-minutes walk test and full echocardiographic examination. All patients filled 2 quality of life (QoL) questionnaires: the Minnesota Living with Heart Failure Questionnaire (MLWHF) and the Kansas City Cardiomyopathy Questionnaire (KCC). Tissue Doppler echocardiography was performed using a 6-basal, segmental model to assess time to peak systolic (systolic electromechanical delay) and time to peak early diastolic velocity (diastolic electromechanical delay). Opposing wall delay (OWD) was calculated as the difference of electromechanical delay of any of opposing walls, SD in time to peak systolic velocity (SD-S) and early diastolic velocity (SD-E). Systolic and diastolic dyssynchrony was defined as the presence of any systolic OWD >65 msec or SD-S >31.4 msec. Diastolic dyssynchrony was defined as the presence of any diastolic OWD or SD-E that is above the mean ± 2SD of the control group.

Results: There were 25 (41.7%) patients with combined systolic and diastolic dyssynchrony, 10 (16.7%) patients with isolated systolic dyssynchrony, 9 (15%) patients with isolated diastolic dyssynchrony and 16 (26.6%) patients with no dyssynchrony. Patients with systolic dyssynchrony had a higher NYHA functional class (p=0.004). The distance covered during the 6-minute walk test was significantly shorter in systolic dyssynchrony group (228.5±79.8 m vs. 317.2±92.2 m, p=0.001). The KCCQ overall and clinical summary scores were significantly lower in the group with systolic dyssynchrony (36.4±12.2 vs 46.3±11.8, p<0.002, CI 21 units for men per week).

Conclusion: Systolic and diastolic dyssynchrony are prevalent in patients with DCM. Systolic but not diastolic dyssynchrony was associated with impaired QoL.
P1768 | BENCH
NGAL/MMP9 complex: from kidney injury to worsening of heart remodelling in cardiorenal syndrome type II
A. Angelini1, C. Castellana2, M.G. Virzi1, M. Fedrigo1, G. Thiene1, M. Valente1, M. Olesinska 2, A. Siennicka3, P. Niewinski3, E.A. Jankowska3, M. Niewinski3

Purpose:
We studied the role of congestion in the development of kidney injury

Methods:
Ten animals were treated with MCT for 4 weeks until they developed HF. Eleven animals were taken as control. The occurrence of HF was demonstrated by signs of congestion, hypotension and dilatation of the right ventricle.

Results:
Rat born HF showed higher BNP (CHF 4.8±0.5, C 1.5±0.2 ng/mL p<0.0001), marked RV hypertrophy and dilatation (RVMass/RVVolume CHF 1.46±0.31, controls 2.41±0.81 p<0.01), pleural and peritoneal effusions. Pro-inflammatory cytokines were significantly increased. sCreatinine was also increased (CHF 3.06±1.3 vs controls 0.5±0.23 pg/mL p=0.04), Plasma, (CHF 562.7±93.34 vs controls 245.3±58.19 ng/mL p=0.02) renal and heart NGAL (CHF 7068±4337 C 32120±4961 AU, p=0.001) rose significantly and was found to be complexed with MMP9 in CHF rats. A higher number of kidney sELISA cells was also detected (CHF 114.01±45.93 C 16.36±11.60 cells/mm², p=0.0004).

Conclusion:
In this model of CHF with prevalent congestion, kidney injury is characterized by tubular damage and systemic inflammation. The enhanced enzymatic activity of the upregulated NGAL complexed with MMPs produces extra-cellular matrix degradation. This may worsen heart remodelling and perpetuate the vicious circle of kidney/heart damage

P1770 | BEDSIDE
Is hemoconcentration a reliable marker of decongestion in acute heart failure?
D. Aronson, A. Solomonica, S. Chirmici, W. Darawsha, A. Azzam. Rambam Health Care Campus, Haifa, Israel

Introduction:
The principal cause for hospitalization due to acute heart failure (AHF) is related to congestion. Persistent congestion at hospital discharge is associated with increased risk for mortality and rehospitalizations. Recently, hemoconcentration (HC) has been suggested as a surrogate for successful decongestion during fluid removal in AHF.

Methods:
We treated 704 patients with AHF and volume overload. Congestion was assessed at admission and discharge using A 9-point scale (0 to 8) as follows: JVP ≤8 cm water (1 point), hepatomegaly (1 point), peripheral edema (Absent/trace, 0 points; slight 1 point; moderate, 2 points; marked, 3 points; and anasarca, 4 points), pulmonary rales (1 point), and third heart sound (1 point). A composite score calculated by summing the individual scores, with a score >1 denoting congestion. HC was defined as any increase in hematocrit and hemoglobin levels between baseline and discharge. The association between HC and congestion and mortality (mean follow-up 1.5 y) was determined by Cox regression.

Results:
At discharge, of 660 patients without persistent congestion, only 199 were with HC (42%). There was weak correlation between the decline in congestion score and changes in hematocrit levels (Figure, P=0.65). Compared with patients with HC and no congestion (lowest mortality group) the adjusted HR for mortality was 1.5 (95% CI, 1.1–2.1) with no HC and no congestion, 1.7 (95% CI 1.1–2.7) with HC but with persistent congestion and 2.1 (95% CI 1.4–3.0) with no HC and congestion.

Conclusion:
Persistent clinical congestion at hospital discharge is associated with increased risk for mortality even when HC occurs. There is a weak correlation between HC and the improvement in congestion as assessed by clinical examination.
P1791 | BEDSIDE
Diastolic but not systolic dysfunction is prevalent in long term breast cancer survivors
1 Oslo University Hospital, Department of Cardiology, Oslo, Norway; 2 The Norwegian
Radium Hospital, Oslo, Norway; 3 Norwegian University of Science and Technology,
Trondheim, Norway; 4 University of Oslo, Oslo, Norway

Background: Multimodal adjuvant treatment of loco-regionally advanced (stage II
or III) breast cancer (BC) may lead to cardiotoxicity due to irradiation and
chemotherapy. However, the magnitude of cardiac dysfunction and its risk factors
in long term BC survivors are unknown.

Purpose: To evaluate the prevalence and the risk factors for left ventricular (LV)
dysfunction in long term BC survivors by echocardiography compared to healthy controls.

Methods: 216 female patients were evaluated with healthy controls 1:1 matched for age,
weight, and systolic blood pressure. Systolic dysfunction was defined by ejection fraction <55% (Simpson's biplane) or fractional shortening <27%.
Subclinical systolic dysfunction was identified by peak systolic mitral annular
velocity in septal and lateral position (< 0.6 and 6.7 cm/s respectively) using
pulsed wave tissue Doppler (TDI) and by global longitudinal strain <18% using 2
dimensional speckle tracking echocardiography (2D STE). Diastolic dysfunction
was defined by early diastolic velocity (e') of the septal <8 cm/s or the lateral
mitral annulus <10 cm/s by pulse wave TDI. Estimation of LV filling pressures
was performed from parameters of pulsed wave Doppler measures of mitral inflow
(Flow, E, A/E ratio) and pulmonary venous flow (S/D ratio, Ar-A duration), left
atrial volume and E/e' ratio.

Results: Mean age was 62.0±7.8 years with mean follow-up time since diagnosis
of 12.0±1.4 years. 112 (52%) was treated for left sided BC. 129 (60%) received
anthracyclines with the cumulative dose of 360 mg/m2 epirubicin. None were
assigned to receive irinotecan or taxotumab. Irradiation was performed after manual dose plan-
ing in 115 (53%) and CT based dose planning in 101 (47%). There was no
difference in prevalence of systolic dysfunction between patients and controls
even containing chemotherapy. Parameters of systolic function did not discriminate be-
tween patients and controls.

Discussion: Although patients with diastolic dysfunction after AMI and preserved
LVEF are characterized by progressive LA remodelling the change in LA volume
could not be explained by differences in LA pressure overload at rest or during
exercise.

Acknowledgement/Funding: Supported by the Danish Heart Foundation and
The Danish Council for Independent Research

P1792 | BEDSIDE
Endomyocardial biopsy with a J-shaped sheath reduced the risk of tricuspid regurgitation after heart transplantation
Y. Tsukamoto1, T. Ohtani1, Y. Ichibori1, K. Nakamoto1, H. Kioi1, O. Yamaguchi1, K. Toda2, N. Fukushima3, Y. Sawa4, Y. Sakata1.
1 Osaka University Graduate School of Medicine, Department of Cardiovascular Medicine, Osaka, Japan; 2 Osaka University Graduate School of Medicine, Department of Cardiovascular Surgery, Osaka, Japan

Background: Tricuspid regurgitation (TR) is one of the major problems in pa-
patients with heart transplantation (HTx). Endomyocardial biopsy (EMB) plays an
important role in monitoring for acute rejection, but frequent EMB would cause TR.
In 2002, we modified the method of EMB by using a J-shaped sheath. The
purpose of this study was to examine the prevalence of TR in HTx recipients with
modified EMB method.

Methods: From 1999 to 2013, 48 patients underwent HTx in our hospital. 4 pa-
tients who died within 6 months after HTx were excluded. Before 2002, serial EMB
were performed with classical method with short sheath. The short sheath was
placed into superior vena cava. Then specimens were acquired from right ventric-
ular (RV) septum with bended biotome through right atrium and tricuspid valve.
In 2002, EMB method was modified with a J-shaped sheath of 7 French X 35 cm
in length. The head of the J-sheath was advanced into RV. After confirming the
position of the sheath at RV septum, specimens were acquired with a biotome.

Study patients were stratified with EMB methods into J-sheath group (n=40) and
old-method group (n=4). Routine surveillance EMB were performed weekly dur-
ing the 1st month, biweekly during the 2nd and 3rd months, at the 4th, 5th, 6th
and 12th months after HTx and annually following the first year. The severity of
TR was assessed by evaluating the TR jet using color Doppler. Remarkable TR
was defined as moderate or severe TR.

Results: Only 1 patient in J-sheath group developed remarkable TR during
follow-up. The prevalence of remarkable TR in J-sheath group was quite low
(2.5% at 1 and 5 years after HTx) compared to that in old-method group (log-
rank p<0.0001, Figure).

Conclusion: Comparison of conventional measures to estimate right ventricular
function in patients after heart transplantation using 3D and speckle-tracking echocardiography
B. Sax, B. Merkely, A. Kovacs. Semmelweis University, Heart Center, Budapest, Hungary

Right ventricular (RV) dysfunction is a common finding in patients underwent heart
transplantation (HTX). However, certain limitations may apply regarding the
comparability of conventional echocardiographic measures of RV performance. We aimed to
investigate RV function of HTX patients using three-dimensional (3D) and speckle
tracking echocardiography and correlate them with standard parameters.

Thirty patients were enrolled (mean age 54±14 years, 15 patients within one
year, 15 over one year after HTX) and compared to 30 age- and gender matched
healthy volunteers. Beyond the measurement of tricuspid annular plane systolic
excursion (TAPSE) and fractional area change (FAC), we acquired 3D datasets
from apical view using multi-beat reconstruction from 4 or 6 cardiac cycles. Using
a dedicated software for RV quantification (4D RV-Function 2), RV end-diastolic
(EDV), end-systolic (EDV) volumes, ejection fraction (EF) were measured and
furthermore, free wall longitudinal strain were quantified using speckle-tracking
analysis.

Conclusion: Although patients with diastolic dysfunction after AMI and preserved
LVEF were characterized by progressive LA remodelling the change in LA volume
could not be explained by differences in LA pressure overload at rest or during
exercise.

Acknowledgement/Funding: Supported by the Danish Heart Foundation and
The Danish Council for Independent Research

P1794 | BEDSIDE
Comparison of conventional measures to estimate right ventricular function in patients after heart transplantation using 3D and speckle-tracking echocardiography

B. Sax, B. Merkely, A. Kovacs. Semmelweis University, Heart Center, Budapest, Hungary

Right ventricular (RV) dysfunction is a common finding in patients undergoing heart
transplantation (HTX). However, certain limitations may apply regarding the
comparability of conventional echocardiographic measures of RV performance. We aimed to
investigate RV function of HTX patients using three-dimensional (3D) and speckle
tracking echocardiography and correlate them with standard parameters.

Thirty patients were enrolled (mean age 54±14 years, 15 patients within one
year, 15 over one year after HTX) and compared to 30 age- and gender matched
healthy volunteers. Beyond the measurement of tricuspid annular plane systolic
excursion (TAPSE) and fractional area change (FAC), we acquired 3D datasets
from apical view using multi-beat reconstruction from 4 or 6 cardiac cycles. Using
a dedicated software for RV quantification (4D RV-Function 2), RV end-diastolic
(EDV), end-systolic (EDV) volumes, ejection fraction (EF) were measured and
furthermore, free wall longitudinal strain were quantified using speckle-tracking
analysis.

Conclusion: Although patients with diastolic dysfunction after AMI and preserved
LVEF were characterized by progressive LA remodelling the change in LA volume
could not be explained by differences in LA pressure overload at rest or during
exercise.

Acknowledgement/Funding: Supported by the Danish Heart Foundation and
The Danish Council for Independent Research
EDV did not differ between the two groups (HTX vs. control; 87±2 vs 80±2 mL). In HTX patients EF and FAC were lower, however, TAPSE was decreased to a greater extent (EF: 45±7 vs 51±4% [−12%], FAC: 43±7 vs 48±6% [−10%]). TAPSE: 15±4 vs 22±3 mm (<32%), all p < 0.05. There was no correlation between TAPSE and EF in HTX patients, whereas free wall longitudinal strain correlated with it (r = 0.13, p = 0.02). No satisfactory FAC relating to TAPSE was found. Patients over one year after HTX had better TAPSE (17±4 vs 14±5 mm in patients within one year, p < 0.05), whilst EF did not differ between the two groups (43±6 vs 46±7; p = NS). TAPSE correlated with the time elapsed after HTX (r = 0.60, p < 0.01). TAPSE is not a reliable measure of RV systolic function in patients undergoing heart transplantation. Free wall strain describing longitudinal shortening provides a better estimate. If 3D echocardiography is not available, FAC is the method of choice to assess RV performance. Our data also suggest a diastolic right ventricular component in RV function. In time, longitudinal function can recover.

P1797 | BEDSIDE
Evaluation of left ventricular myocardial mechanics and synchrony in heart transplant patients using three-dimensional echocardiography

Speckle-tracking echocardiography gained particular interest as it allows to quantitatively sensitive and precise parameters of myocardial function in numerous cardiac diseases. Significant data on left ventricular (LV) deformation are scarce in patients after heart transplantation (HTX). Early identification of the pathological conditions associated with HTX would be of high importance. We aimed to evaluate LV deformation of multiple directions in patients after HTX and assess some echocardiographic volunteers.

Twenty-four HTX patients (mean age 54±14 years, with a median of 366 days after HTX) were enrolled and compared to 17- age and gender matched healthy volunteers. Patients with history of allograft rejection were excluded. Beyond standard echocardiographic protocol, we acquired 3D datasets from apical view using multi-beat reconstruction from 4 or 6 cardiac cycles. Using a dedicated software for LV quantification (4D LV-Function 3), LV end-diastolic (EDV), end-systolic (EDV) volumes, ejection fraction (EF) were measured. Furthermore, global longitudinal and segmental deformation were quantified. Systolic dyssynchrony index (SDI) was derived from 16 subvolumes of the LV and compared to healthy volunteers. SDI referring to intraventricular dyssynchrony was higher in HTX patients (9±3 vs 4±1; p < 0.001). SDI was significantly higher compared to controls (p < 0.05). SDI referred to EF robustly (r = 0.74, p < 0.001).

Despite the lack of known pathology and maintained ejection fraction, 3D longitudinal strain may indicate subclinical LV dysfunction in HTX patients. Mild degree of intraventricular dyssynchrony is also suggested to be present. Further enrolment and follow-up may verify the importance of our results.

P1798 | BEDSIDE
Prognostic differences among equations for estimated glomerular filtration ratio in acute heart failure syndrome
N. Kagiyama1, Y. Matsue2, T. Kume3, H. Okura3, M. Suzuki4, A. Matsumura4, K. Yamamoto1, Y. Hashimoto2, K. Yoshida1. 1 The Sakakibara Heart Institute of Okayama, Department of Cardiology, Okayama; 2 Kameda Medical Center, Kamogawa; 3 Kawasumaki Medical School, Division of Cardiology, Kurashiki, Japan

Methods: From the RELAX-AHF study, we acquired 3D datasets from apical view using multi-beat reconstruction from 4 or 6 cardiac cycles. Using a dedicated software for LV quantification (4D LV-Function 3), LV end-diastolic (EDV), end-systolic (EDV) volumes, ejection fraction (EF) were measured. Furthermore, global longitudinal and segmental deformation were quantified. Systolic dyssynchrony index (SDI) was derived from 16 subvolumes of the LV and compared to healthy volunteers. SDI referring to intraventricular dyssynchrony was higher in HTX patients (9±3 vs 4±1; p < 0.001). SDI was significantly higher compared to controls (p < 0.05). SDI referred to EF robustly (r = 0.74, p < 0.001).

Conclusion: Potential eligible RELAX-AHF patients are a minority of acute heart failure patients if an advanced heart failure unit population is to be considered. Therefore, the external validity of the RELAX-AHF finding should be made with caution in regard to these type of populations.

P1799 | BEDSIDE
Matosinhos, Portugal

Introduction: Despite the lack of known pathology and maintained ejection fraction, 3D longitudinal strain may indicate subclinical LV dysfunction in HTX patients. Mild degree of intraventricular dyssynchrony is also suggested to be present. Further enrolment and follow-up may verify the importance of our results.

P1800 | BEDSIDE
Patients with advanced heart failure are at increased mortality risk regardless of whether they are treated with angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB) alone or in combination. However, it is not known whether this higher mortality risk is independent of other cardiovascular risk factors. Therefore, the aim of the study was to assess differences in the levels of urinary neutrophil gelatinase-associated lipocalin (NGAL) and cystatin C in patients with acute heart failure (AHF) depending on administered diuretics in relation to the development of acute kidney injury (AKI).

Methods: We measured urinary NGAL levels in 80 patients admitted to coronary care unit with AHF. Urine samples were collected immediately at admission and after 24 hours. The samples were stored at −72°C and examined by ELISA. AKI was defined according to KDIGO and patients were divided into groups without AKI (AKI−, n=49) and with AKI (AKI+, n=31).

Results: Patients in the AKI+ group had significantly higher median admission u-NGAL levels compared with the AKI− group (87.3±8 mg/L vs. 40 mg/L, p<0.0005). Initial parenteral dose of furosamide was higher in the AKI+ compared with AKI− (102.5±20 mg vs. 40 mg, p<0.0005) and correlated with u-NGAL at admission (r=0.43, p=0.001) and after 24 hours (r=0.36, p<0.01).

Conclusions: The presence of elevated admission u-NGAL levels and levels after 24 hours predicts renal impairment before the rise in serum creatinine and correlates with increasing dose of initially administered parenteral diuretics.

Acknowledgement/Funding: This study is supported by Slovak Society Research Grant 2012-2015
± CKD, yet hyperkalaemia (HK) can limit RAASi use in these pts. We evaluated the effect of patiromer, a novel investigational K+ binder, on serum K+ (s-K+) in HK pts with HF and advanced CKD on RAASi.

Methods: OP: HK (OP) was a 12-wk, 2-part, randomised, single-blind study; AMETHYST-DN (A-DN) was a 52-wk, randomised, open-label study. Eligible pts had and OP A-DN had >1RAASI and, in A-DN, had T2DM; pts with NYHA class 4–5 HF were excluded. Entry s-K+ was 5.1–5.6 mEq/L (OP) and >5.0–6.0 mEq/L (A-DN). In a posthoc subgroup analysis, efficacy data were pooled over the 1st 4 wk in pts with HF and stage 3b-5 CKD and analysed for s-K+. The change from baseline (1st endpoint) by s-K+ strata: >5.0–5.5 (mild) and >5.5–6.0 mEq/L (mod/severe) in A-DN; 5.1–5.5 (mild) and 5.5–6.5 mEq/L (mod/severe) in OP.

Results: Of HF pts with advanced CKD, 66 had mild and 66 had mod/severe (mod/severe) in OP. s-K+ was reduced to <5.0 mEq/L by the first post-baseline visit (Day 3) in mild HK and by wk 1 in mod/severe HK pts and continued to improve (Fig). By wk 4, mean (95% CI) s-K+ change from baseline was −0.62 mEq/L (−0.74, −0.50) in mild HK and −1.13 mEq/L (−1.28, −0.97) in mod/severe HK pts; both P < 0.001. One pt developed s-K+ <3.5 mEq/L, through wk 4. AES were predominately mild-to-moderate GI complaints; AES led to patiromer discontinuation in 6 pts in each study over the entire study period.

Conclusions: Patiromer significantly reduced s-K+ in HK patients with HF and asystolic CKD and A-DN. If approved, patiromer may be an option for HK treatment in pts with HF and advanced CKD.

Acknowledgement/Funding: Financial support for this study provided by Re-lypressa, Inc.

P1800 | BEDSIDE The predictors of dysynchrony deterioration in patients with left bundle branch block and normal EF

D. Dublyakov1, Z. Vozhdava2, V. Gluhova2, E. Sysuenkova2,1, Samara Regional Cardiovascular Dispensary, Samara, Russian Federation; 2 VAZ Medical Center, Togliatti, Russian Federation

Aim: To reveal the predictors of electrical and mechanical dysynchrony worsening in patients with LBBB and normal EF during a prospective study.

Methods: 68 consecutive patients (mean age 55.8 ± 9.0 years; M47%) with LBBB revealed during annual check-up were enrolled into the study. History of CAD had 31/51.5%) patients, hypertension - 64 (94.1%), 4 patients had no overt heart diseases after thorough examination. There were no patients with EF below 45%, and NYHA class > II. Fifty two (76.5%) of 68 patients had taken the recommended medication, mainly ACE-inhibitors and beta-blockers; however, 16 patients refused the recommendations. Follow-up period duration was 32±13 months (6–58 mths). Logistic regression (SSPS 11.5) was used to identify characteristics that might have the greatest impact on the dynamics of dysynchrony.

Results: QRS duration during the FU period has increased in 33.9% of patients, mostly in women: 41.9% vs. 25.8% among men; but overall QRS duration has not changed during FU (149±13 ms vs. 152±14 ms, p=0.66). An independent predictor of its progression was end-diastolic volume index (EDVI; OR; 24; 95% CI: 1.00–1.52).

In the beginning of the study only 19 (21.1%) patients had signs of atrioventricular (AV) dysynchrony. During the FU period 10 (14.7%) new cases of AV-dysynchrony have occurred. Multivariate analysis showed the influence of chronic heart failure (CHF; OR= 6.9; 95% CI: 1.95–24.50; p=0.003), and heart rate (HR; OR=1.84; 95% CI: 1.19–2.67; p=0.02).

According to the univariate analysis (univariate) (IV) dysynchrony deteriora-

Conclusion: The predictors of dysynchrony deterioration were associated with CHF and HR was associated with AV dysynchrony worsening. Predictors of IV- dysynchrony were the signs of previous myocardials on cardiac MRI with gadolinium and poor adherence to medical treatment.
for all). Nonlinear logistic regression analysis revealed higher risk of adverse outcomes in patients with higher level of visit-to-visit systolic BPV (OR 1.13, 95% CI 1.0–1.27, p<0.03). Area under curve (AUC) for visit-to-visit systolic BPV−10.9 mmHg was 0.74, 95% CI 0.53–0.94 (sensitivity 72.7%, specificity 80%, p=0.02).

Conclusion: Visit-to-visit systolic BPV is strong significant predictor of adverse outcomes in patients with stable HF at EF. The threshold of visit-to-visit systolic BPV−10.9 mmHg may be used as prognostic criteria in this patient population.

P1805 | BEDSIDE
Optimism and quality of life in patients with heart failure
1 University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands; 2 University Medical Center Groningen, Department of Epidemiology, Groningen, Netherlands; 3 Linkoping University, Faculty of Health Sciences, Department of Social and Welfare Studies, Linkoping, Sweden

Background: Health-related quality of life (HR-QoL) of patients with heart failure (HF) is low despite the aim of HF-treatment to improve HR-QoL. To date, most studies have focused on medical and physical factors in relation to HR-QoL, little data is available on the role of emotional factors like dispositional optimism.

Purpose: This study examines the prevalence of optimism and pessimism in HF-patients and investigates how optimism and pessimism are associated with different patient characteristics and HR-QoL.

Methods: Dispositional optimism was assessed with the Revised Life Orientation Test (LOT-R) and HR-QoL with the disease-specific Minnesota Living with Heart Failure Questionnaire and the generic EQ-5D questionnaire.

Results: 100 HF-patients (mean age 70±9 years, 28% female, mean LVEF 33%) were included. The (mean ± SD) total score on the LOT-R was 14.6±2.9 (theoretical range 0–24), the scores on the subscales optimism and pessimism were 8.1±1.9 and 5.5±2.5 respectively. Higher age was related to more optimism (r=−0.22, p<0.05) and optimism was associated with higher generic HR-QoL (B=0.04, p<0.05). Optimism was not significantly associated with disease-specific HR-QoL.

Conclusions: The association found between optimism and generic HR-QoL of HF patients can lead to promising strategies to improve HF patients’ HR-QoL, particularly since the literature has indicated that optimism is a modifiable condition.


P1806 | BEDSIDE
Ethnic disparity in the clinical characteristics of patients with heart failure
1 Hadassah University Hospital, Jerusalem, Israel; 2 Clalit Health Services, Jerusalem, Israel

Background: The characteristics of heart failure (HF) patients of different ethnic backgrounds in Israel are unknown. The purpose of the present study was to evaluate the clinical characteristics of Arab versus Jewish patients with chronic heart failure.

Methods: Patients with a diagnosis of HF at a health maintenance organization in Jerusalem, Israel were evaluated. All patients were followed for cardiac related hospitalizations and death.

Results: The study cohort included 6,773 HF patients: 4,991 (74%) were Jewish and 1,735 (26%) were Arab. The overall prevalence of HF in the Jewish versus Arab population was similar (Women: 4.3% versus 4.7% respectively, P=0.06; Men: 5.3% versus 5.2%, P=0.61). The prevalence of HF was significantly higher in women (theoretical range 0–24), younger age groups of Arab patients versus Jewish women (P=0.001) and obesity (64% vs 46%, P=0.001). Standard of care based on prescribed medications was similar between the ethnic groups. Glucose and cholesterol levels were higher in the Arab cohort. Mortality was similar between the groups at median follow-up (576 days) with the exception of cardiovascular hospitalizations and death that were higher in Arab men.

Conclusions: Arab subjects develop heart failure at a much younger age compared to their Jewish counterparts and have a higher prevalence of diabetes and obesity. Standard of care and clinical outcome are comparable. Implementation of prevention programs to reduce risk factors, particularly diabetes and obesity may help reduce the disparity between Arabs and Jews.

Ethnic disparity in the clinical characteristics of patients with heart failure

Heart Failure Prevalence Ratio: Arab / Jew

Prevalence Rate of Heart Failure

Heart Failure Prevalence Rate: Arab / Jew

Figure: Prevalence rate of heart failure in younger age groups.

Arabs had a significantly higher prevalence of heart failure in the younger age groups.

Ethnic disparity in the clinical characteristics of patients with heart failure

Heart Failure Prevalence Rate: Arab / Jew

Prevalence Rate of Heart Failure

Heart Failure Prevalence Rate: Arab / Jew

Figure: Prevalence rate of heart failure in younger age groups.

Arabs had a significantly higher prevalence of heart failure in the younger age groups.
P1800 | BEDSIDE
Effect of newly developed left ventricular dysfunction on galectin-3 dynamics in patients with first episode of an acute coronary syndrome
treated with percutaneous coronary intervention
M. Stachura1, P.J. Kwasiński2, R. Ryczek3, A. Krzesiak-Lodyga3, E. Korzeniewski4, A. Karasek5, A. Mikulska5, P. Kowalczynski5, A. Cwetsch6, Clinical Heart Failure, Department of Internal Affairs, Institute of Invasive Cardiology, Warsaw, Poland; 2Medical University of Warsaw, Department of Biochemistry and Human Physiology, Warsaw, Poland; 3Military Institute of Medicine, Department of Interventional Cardiology, Warsaw, Poland

Purpose: Galectin-3 (gal-3) is a well-established marker of fibrosis in heart failure and is associated with poor prognosis. However, gal-3 was not extensively studied in patients with an acute coronary syndrome. As it’s hard to distinguish a homogenous group in such a clinical setting, we found it interesting to assess the possible impact of lesion severity, epicardial coronary flow and left ventricular function on gal-3 levels in patients with previous history of heart failure symptoms, with presented with their first episode of acute coronary syndrome and were treated with percutaneous coronary intervention (PCI).

Methods: 57 patients with ACS (STEMI and NSTEMI) and no previous history of heart failure (HF) symptoms were enrolled. Patients were divided into two groups based on heart failure symptoms occurrence (HF and no-HF) and NT-proBNP levels higher than 1000 pg/mL before PCI. Both groups were assessed in the context of coronary lesion severity (SYNTAX Score), coronary flow (Corrected TIMI Frame Count, CTF/C), biochemical and echocardiographic parameters. Galectin-3 analyses were done with the ready-to-use human ELISA assays (R&D Systems, USA). NT-proBNP levels were measured with a ready-to-use human ELISA assays (R&D Systems, USA).

Results: In total group 23 patients had heart failure symptoms and NT-proBNP levels higher than 1000 pg/mL before PCI (HF group). There were no significant differences in gal-3 at baseline (med. 1016.4 vs no-HF med. 1053.4 pg/mL, NS) and after 1-month follow-up (med. vs 1398 vs med. 1195.5 pg/mL, NS). Patients with HF had higher NT-proBNP levels before PCI (med. 1574.5 vs no-HF med. 140.4 pg/mL, p <0.0003), higher SYNTAX scores (med. 20.5 vs no-HF med. 8, p <0.0002), lower initial left ventricular ejection fraction (LVEF) (med. 45% vs no-HF 53%, p <0.0001) and average global longitudinal strain rate (med. −13.7 vs no-HF −15.9, p <0.03). There were no differences in epicardial coronary flow before (CTFC 74.3 vs no-HF 72.4, NS) and after procedure (19 vs no-HF 18, NS). ATBF 1 month follow-up, despite stable gal-3 levels, patients from HF group had lower LVEF (50% vs 55%, p <0.001), average global strain rate (med. −16.3 vs no-HF −18.7, p <0.05) and NT-proBNP levels (med.1057 vs no-HF 281.5 pg/mL, p <0.0001).

Conclusions: In patients without previous history of heart failure and presented with first acute coronary episode, gal-3 levels are stable in short term observation, irrespectively to lesion severity, left ventricular function and NT-proBNP concentrations.

Acknowledgement/Funding: WIM young investigator grant no 227

Heart failure, other / Heart failure: from bench to bedside II 321

Heart failure, other / Heart failure: from bench to bedside II 321

P1810 | BEDSIDE
Fluid status predicts adverse outcome in patients with heart failure and preserved ejection fraction
B. Koel1, C. Zotter-Tufaro1, J. Mascherbauer1, F. Duca1, S. Aschauer1, A. Kammerlander1, M. Antlanger2, M. Saemann2, D. Bonderman1.
1 Medical University of Vienna, AKH – Vienna, Cardiology Clinic, Vienna, Austria; 2Medical University of Vienna, Department of Internal Medicine III - Clinical Division of Nephrology and Dialysis, Vienna, Austria

Background: Heart failure with preserved ejection fraction (HFpEF) is an increasingly recognized syndrome associated with multiple symptoms, including peripheral oedema. Fluid overload plays an important role in the pathogenesis of HFpEF and is a well-known predictor of hospitalization in patients with acute heart failure. Whether fluid status in HFpEF is associated with outcome is currently unknown.

Materials and methods: Between December 2010 and July 2013, 97 consecutive patients in HFpEF and pulmonary hypertension (PH) as confirmed by right heart catheter, were enrolled in our prospective registry. Patients with clinically overt decompensation were excluded from the protocol (n=6). To assess the fluid status we performed a bioimpedance spectroscopy in every patient. An overhydration relative to baseline was defined as the change in extracellular water [OH-ECW] mean −0.7±5.7%). And 33 (36%) patients presented overhydration relative to baseline. The primary outcome measure was a combined endpoint consisting of cardiovascular death, hospitalization for HF, or cardiovascular arrest. To assess the possible impact of fluid overload, we performed a division in 2 groups: group A with fluid overload and group B without fluid overload.

Results: Between December 2010 and July 2013, 97 consecutive patients in HFpEF were enrolled in our registry. An overhydration relative to baseline was defined as the change in extracellular water [OH-ECW] mean −0.7±5.7%). And 33 (36%) patients presented overhydration relative to baseline. The primary outcome measure was a combined endpoint consisting of cardiovascular death, hospitalization for HF, or cardiovascular arrest. To assess the possible impact of fluid overload, we performed a division in 2 groups: group A with fluid overload and group B without fluid overload.

Conclusions: Fluid overload was identified as a predictor of an adverse prognosis in patients with HFpEF. Biospectroscopy devices could therefore help to guide diuretic therapy in the clinical setting, as they are easy to use and provide an accurate assessment of affected patients.

P1819 | BEDSIDE
Relationship between arterial stiffness and the degree of change in exercise induced left ventricular end-diastolic pressure in patients with preserved left ventricular ejection fraction
S.J. Choe1, J.H. Shin1, S.G. Kim1, Y.H. Im2, J.H. Shin2.
1Hanyang University Guri Hospital, Cardiology, Guri, Korea, Republic of; 2Hanyang University, College of Medicine, Seoul, Korea, Republic of

Background: The prevalence of preserved left ventricular ejection fraction (HFpEF) and arterial stiffness increase with age. Although a causal relation is not certain, recent some studies showed the association between aortic stiffness and left ventricular (LV) diastolic function. However, there have been few studies regarding the relationship between arterial stiffness and left ventricular end-diastolic pressure (LVEDP) in exercise or ambulation. Thus, this study was designed to investigate the relationship between arterial stiffness and the degree of change in exercise induced LVEDP in patients with HFpEF.

Methods: This study population was composed of 156 patients who underwent left cardiac catheterization, coronary angiography, transesophageal echocardiography and brachial-ankle pulse wave velocity (baPWV) during same admission period. In patients with non-significant coronary stenosis and normal left ventricular ejection fraction, the baseline and peak exercise baPWV and leg-raise exercise were performed during LV catheterization under polygraphy monitoring. The LVEDP was measured by automatically mechanical mechanization.

Results: The mean age was 59.83±13.15 years, average RbaPWV 1533.3±292.85 cm/s, 101.4±54.8 cm/s, and LbaPWV 1524.13±419.23 cm/s. As the average LVEDP was 20.66±3.3 mmHg at rest, 21.96±7.57 mmHg at passive leg-raise and 23.47±7.86 mmHg at active leg-raise, the leg raise increased LVEDP by an average of 3.33±5.25 mmHg. The LVEDP measured at rest and at leg-raise were correlated with the degree of change in LVEDP during active leg-raise was corelled with baPWV (R=0.273, p<0.02 for RbaPWV, R=0.272, p<0.02 for LbaPWV). The subjects with increased LVEDP by active leg raise had significantly higher value of baPWV than those with decreased LVEDP (1393.35±287.62 cm/s vs. 1530.20±376.91 cm/s for RbaPWV, p<0.013, 1380.69±281.70 cm/s vs. 1522.63±392.10 cm/s for LbaPWV, p=0.012, respectively).

Conclusions: BaPWV, non-invasive marker of central arterial stiffness, was closely associated with the degree of LVEDP variation during active leg-raise exercise, whereas it was not correlated with absolute LVEDP values at rest and during passive leg raise. It indicates that the coupling of ventricular-arterial stiffness is dynamic rather than static process.

Heart failure, other / Heart failure: from bench to bedside II 321

Heart failure, other / Heart failure: from bench to bedside II 321

Heart failure, other / Heart failure: from bench to bedside II 321
Methods: The study included 140 patients (39±3±9,11) who underwent heart transplantation (HTx) during the period from 2008 to 2014 (mean follow-up 53±2±6±9 months); 25 (17,9%) women and 115 (82,1%) men. Initial diagnosis was 106 (75,7%) patients were dilated cardiomyopathy, ischemic disease in 34 (24,3%). In all cases basic immunosuppressive therapy included tacrolimus, corticosteroids and mycophenolate mofetil. The presence of anti-HLA I and/or II, plasma levels of PAPP-A and scD40L before HTx were identified by ELISA. Nonspecific anti-HLA and donor-specific anti-HLA (DSA) were measured in early transplant period (up to 1 month) by Luminex. After HTx DSA were detected in 16 (11,43%) pts., AMR - in 23 (16,42%) pts.

Results: Preformed anti-HLA were detected in 45 (32,1%) pts. 21 (47%) pts. had anti-HLA up to 1 month after HTx by Luminex. Donor-specific antibodies (DSA) after HTx were detected in 11% of patients with preformed HLA. AMR and/or CAV in early and late periods after HTx were found in all DSA positive recipients; without DSA – in 10 (25%) recipients. CAV and AMR development in DSA positive recipients was 4,0 times higher (RR 4,0: CI 95% 3,34–6,84 p=0,002).

Conclusion: Our data suggest that pretransplant anti-HLA as well as high levels of PAPP-A and scD40L are significant predictors of cardiovascular complications after HTx. The risk of AMR and CAV was higher in posttransplant DSA.
6.5±1.3 vs 15.0±1.5. In the in vivo human hearts, there was an increase of the end-diastolic pressure (EDP) from 12±3 to 18±3 mmHg after the increase of the end-diastolic volume (EDV) from 182±32 to 305±32 mL, and a subsequent drop of the EDP, after 15 minutes of adaptation, to 12±4 mmHg, whereas the EDV did not decrease significantly (187±30 mL).

Conclusion: Our results showcase a new mechanism of diastolic adaptation, which consists of an acute decrease in LV stiffness after stretch. This mechanism was also observed in the in vivo human heart and is preserved at the myocardial level. This original description identifies a new element central to the cardiac response to haemodynamic overload.

P1815 | BEDSIDE
Left atrial to left ventricular size ratio by 2D echocardiography can predict elevated left atrial pressure in heart failure patients with preserved ejection fraction
C. Katsikreddy, B. Khatri, M. Singh, N. Shaﬁ. University of California San Francisco, Cardiology, Fresno, United States of America

Background: Noninvasive imaging parameters to estimate left atrial pressure (LAP) in heart failure with preserved ejection fraction (HFpEF) lack desirable diagnostic sensitivity and speciﬁcity.

Purpose: We hypothesized that in HFpEF, increased LAP leads to an increase in LA to left ventricle (LV) size ratio due to relative dilatation of LA and reduction of hypertrophic LV cavity size. Our aim was to determine if the left atrial to left ventricular diameter ratio (LA/LV) on 2D echocardiography (2D Echo) is a diagnostic marker of elevated LAP.

Methods: We retrospectively identiﬁed 81 consecutive HFpEF subjects with elevated LAP (pulmonary capillary wedge pressure >12 mmHg) and 24 controls with normal LAP as conﬁrmed by right heart catheterization (RHC). Significant valve disease and atrial ﬁbrillation were excluded. We examined the baseline clinical characteristics and 2D Echo variables including chamber morphology, LA/LV (end systolic chamber anteroposterior diameter ratio to parasternal long axis view as illustrated in the ﬁgure) and other established markers of elevated LAP. Multivariate (MVA) and ROC analyses were performed to determine the independent predictors of LAP.

Results: No signiﬁcant difference was noted among the baseline demographics between the two groups. In MVA controlled for 6 clinical variables (including hypertension), LA/LV > 1.2±0.2 was found to be the strong predictor of elevated LAP (p=0.005), followed by lateral E/e’ > 12 (p=0.04). On ROC analysis, in comparison to lateral E/e’ (> 12) and LA size (> 4cm), LA/LV was shown to have a superior diagnostic sensitivity (60%, 64%, 90% respectively) and comparable speciﬁcity (80%, 86%, 80%) in predicting increased LAP.

Conclusion: The LA/LV on 2D Echo is an accurate predictor of elevated LAP in HFpEF.

P1816 | BEDSIDE
Treating advanced heart failure with biventricular assist devices in a low organ donation environment
A. Giouzouli, G. Karavallia, L. Louca, S. Adamopoulos, P. Sifra. Onassis Cardiac Surgery Center, Athens, Greece

Background: Heart transplantation remains the gold standard treatment for patients with end stage heart failure. Low organ donation combined with delayed readmissions are still frequent.

Methods: We retrospectively reviewed the number of the patients treated with this paracorporeal device between June 2004 and August 2014 at our institution. Sixty-nine patients (mean age 41.9±13.3 years, range: 11 to 59 years) were supported as a bridge to transplantation. Sixty out of 69 (87%) patients were in INTERMACS 1 Level while 15 of them had survived after a successful resuscitation (intravenous inotropes, 60; ventilated, 10; mean: CI 1.9 L/min/m2; CVP 19 mmHg; total bilirubin 3.75 mg/dl; NT-proBNP, 35,500 pg/ml). Various short-term devices were used as a bridge to bridge (IABP: 52, Impella: 2, Levitronix: 4 and ECMO: 12) and LA/LV was shown to have a superior diagnostic sensitivity (60%, 64%, 90% respectively) and comparable speciﬁcity (80%, 86%, 80%) in predicting increased LAP.

Conclusion: The LA/LV on 2D Echo is an accurate predictor of elevated LAP in HFpEF.

P1817 | BEDSIDE
Cardiac progenitor cell infusion in patients with univentricular heart disease in heart failure with preserved ejection fraction
T. Goto1, D. Usakai1, S. Ishigami1, S. Otsuki2, S. Kasahara3, S. Sano3, Ookayama University Hospital, Cardiovascular Surgery, Ookayama, Japan; 2Ookayama University Hospital, Pediatrics, Ookayama, Japan; 3Ookayama University, Gerontology Research, Ookayama, Japan

Background: The clinical outcomes of heart failure with reduced and preserved ejection fraction (HFREF and HFpEF) after staged palliation in patients with univentricular heart disease remain unknown as is the question whether cardiosphere-derived cell (CDC) transfer may have impact on either type of cardiovascular disease.

Purpose: We sought to characterize the heart failure patients, include HFREF and HFpEF, with single ventricular physiology and investigate the clinical responsive after CDC therapy. Methods: Forty-three patients, aged 2.2±1.4 years, undergoing staged shunt procedures were divided into two groups by cardiac function based on cMRI (HFREF: EF<40%, n=30; HFpEF: EF>40%, n=13). Baseline characteristics and cardiac function measurement by cMRI and echocardiogram during the staged palliation with or without additional intracoronary CDC infusion were assessed.

Results: Compared with HFpEF patients, HFREF patients showed increased cardiac volume (P<0.02) and mass index (P<0.04), those were associated with reduced global circumferential strain in HFREF compared with HFpEF (P=0.0004). Although there was no difference in the incidence of late gadolinium enhancement detected by cMRI in both groups (20% in HFREF and 15% in HFpEF), ventricular diastolic dysfunction identiﬁed by early diastolic strain rate (e’sr) was higher in HFpEF patients compared with HFREF group (46% vs. 27%). When patients underwent staged shunt procedures, HFpEF group had signiﬁcant reduction in EF and atrial strain (P<0.02), resulting in increase in Tdi index 1 month after palliation (P<0.02).

To investigate whether CDC infusion may affect the cardiac function in these two types of HF, patients were subjected to receive CDC injection 1 month post palliation. In contrast to HFpEF group, HFREF patients demonstrated a 5% improvement in EF (P<0.001), right ventricular e’sr (P=0.0001) 3 months after CDC infusion. Similarly, diastolic function improvements were found in CDC-treated HFREF group but not HFpEF patients as shown by increased atrial fractional area change (P=0.01) and reduced E-wave/e’sr (P=0.049).

Conclusions: HFpEF in univentricular heart disease could be partially coupled with diastolic dysfunction that may lead to early peroperative right ventricular failure with poor clinical response to CDC therapy.

Acknowledgement/Funding: The Ministry of Health, Labour and Welfare
values of all 16 LV-segments from three apical planes. Radial and circumferential strain and strain rate were assessed by averaging values of the 6 segments from the basal and apical LV short axis.

**Results:** Treatment with perindopril/amlopidine was effective and well tolerated. Target blood pressure level was achieved in 70% of the patients. The LV mass index decreased from 137 (104–163) g/m² to 123 (105–149) g/m² (p=0.008). The LV ejection fraction raised from 68.7±7.3% to 70.9±7.1% (p=0.012). The basal LV circular strain and strain rate improved significantly after 6 months of treatment (Table). There were no significant changes in longitudinal and radial deformation throughout the study period.

**Dynamics of myocardial deformation**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>6 month</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global longitudinal LV strain, %</td>
<td>16.1±2.48</td>
<td>16.2±2.22</td>
</tr>
<tr>
<td>Global longitudinal LV strain rate, 1/s</td>
<td>0.96±0.15</td>
<td>0.96±0.2</td>
</tr>
<tr>
<td>Basal circular LV strain, %</td>
<td>18.6±4.5</td>
<td>19.7±4.65</td>
</tr>
<tr>
<td>Basal circular LV strain rate, 1/s</td>
<td>1.3±0.3</td>
<td>1.4±0.37</td>
</tr>
<tr>
<td>Basal radial LV strain, %</td>
<td>25.6±1.02</td>
<td>25.8±1.12</td>
</tr>
<tr>
<td>Basal radial LV strain rate, 1/s</td>
<td>2.03±0.54</td>
<td>2.03±0.46</td>
</tr>
<tr>
<td>Apical circular LV strain, %</td>
<td>29.2±7.1</td>
<td>29.8±7.1</td>
</tr>
<tr>
<td>Apical circular LV strain rate, 1/s</td>
<td>1.84±0.55</td>
<td>1.86±0.57</td>
</tr>
<tr>
<td>Apical radial LV strain, %</td>
<td>26.2±1.19</td>
<td>271±0.4</td>
</tr>
<tr>
<td>Apical radial LV strain rate, 1/s</td>
<td>1.56±0.15</td>
<td>1.63±0.46</td>
</tr>
</tbody>
</table>

Values are given as mean ± standard deviation.

**Conclusions:** The study with fixed-dose combination of perindopril/amlopidine is associated with improved basal LV strain and strain rate without significant dynamics of longitudinal and radial deformation.

---

**P1819 | BEDSIDE**

Combination with low-dose dextromethorphan improves the effect of amlopidine monotherapy in clinical hypertension


**Background:** Amlodipine (AM) is one of the most widely used antihypertensive drugs. Dextromethorphan (DXM), a non-opioid cough suppressant, was reported with potential neuro-protection by inhibiting NADPH oxidase. We previously demonstrated that combination of low rather than high dose of DXM with antihypertensive drugs is associated with improved basal LV strain and strain rate. The treatment with fixed-dose combination of perindopril/amlopidine was effective and well tolerated. Target blood pressure level was achieved in 70% of the patients. The LV mass index decreased from 137 (104–163) g/m² to 123 (105–149) g/m² (p=0.008). The LV ejection fraction raised from 68.7±7.3% to 70.9±7.1% (p=0.012). The basal LV circular strain and strain rate improved significantly after 6 months of treatment (Table). There were no significant changes in longitudinal and radial deformation throughout the study period.

**Methods:** This was a first-in-human, concept-proven, prospective, dose-escalation, multicenter study. After 2-week run-in treatment of AM 5mg/day, hypertensive patients who met the treatment goal of 140/90 mmHg were kept with AM monotherapy. The others were then given AM 5mg/day combined with DXM 2.5mg/day, who met the BP goal in the next 4 weeks were kept on the same combination. The others were then given AM 5mg/day combined with DXM 7.5mg/day for another 4 weeks. The patients who did not meet the BP goal were given the highest combination dose of DXM 30mg/day with AM 5mg/day for the final 4 weeks. In each treatment group, both the achieve rate of BP goal and BP changes from week 2 to the end of 14-week treatment were recorded.

**Results:** Among a total of 78 patients on treatment by protocol, 31 patients (40%) reached the BP goal with AM 5mg/day (DXM0 group). Of the non-responders, 16 patients (34%) achieved the BP goal with the combination of AM 5mg/day with DXM 2.5mg/day (DXM2.5 group). The up-titration of DXM to 7.5mg/day enabled 6 more patients (13%) meet BP goal (DXM7.5 group). Only 4 patients (8%) with DXM 2.5mg/day (DXM2.5 group) improved BP goal achievement in 47% of the non-responders to AM. There were no differences in adverse events between the patients with and those without the combinations of DXM.

**Conclusions:** The combination with low-dose DXM is feasible to improve the BP control rate in patients who failed to achieve the BP goal by standard AM treatment.
The study results clearly demonstrate the strong adherence under and without diabetes.

**Materials and methods:** The first part of the study included single intravenous infusion of the drug (5 mg/kg or 2.0 I mol/kg of DNIC, respectively) in 14 healthy male volunteers. The next part of the study included 30 male patients aged 35 to 73 years (mean age 55.5±10.8). All patients had essential or symptomatic arterial hypertension. 13 patients (43.3%) had hypertensive crisis at the point of inclusion, 17 patients (56.7%) had persistent elevation of blood pressure. DNIC was injected at a dose of 1.5 or 3 mg per 1 kg of body weight. The administration of DNIC stopped at the point of 20% blood pressure reduction from initial. Patients’ blood pressure was monitored during intravenous injection of DNIC and 24 hours after.

**Results:** The response of healthy men on DNIC administration manifested as a 3–4 min drop by 24–27 mm Hg of both diastolic and systolic AP with its subsequent restoration within the next 8–10 h. The heart rate quickly normalized after an initial increase. Cardiac output was unchanged despite reduced cardiac filling. A comprehensive analysis of clinical and biochemical data failed to establish any significant pathological changes in these parameters.

**Discussion:** The results reveal the high efficiency of DNIC in patients with uncomplicated hypertensive crisis and stable hypertension. The medication has a low percentage of side effects that suggests its safety.

**P1824 | BENCH**

**Persistence of initial antihypertensive therapy in patients of outpatient specialized cardiac clinic**

A. Kontsevaya, T. Romanenko. National Research Center for Preventive Medicine, Moscow, Russian Federation

**Aim:** To analyze the persistence of initial antihypertensive therapy (AHT) of outpatient specialized cardiac clinic of Moscow for 6 months.

**Study design:** Study includes two stages. The first stage included studying of medical records of all patients with arterial hypertension (AH) (1766 persons), who came for the first time to specialized cardiac clinic, and extraction of medical data for every patient coming to the clinic in 2010 year. The second stage included telephone survey of 1419 patients at 6 months after the first visit to the clinic in terms of AHT persistence rate (80%).

**Results:** On the first visit hypertension treatment was recommended to all patients, with 6 months antihypertensive medications received 91.1% of them, p<0.001.

During 6 months 74.9% of patients changed treatment scheme, and 52.4% of the patients made the decision to change the treatment regimen of cardiovascular diseases by themselves, without any physicians’ recommendations. A significantly higher chance of non-persistence with recommended treatment scheme was find in patients who had medications reimbursement (OR 2.4, 95% CI 1.8 to 3.0, p<0.001), patients with >3 drug treatment scheme with 3 or more medications (OR 2.9, 95% CI 1.9 to 3.1, p<0.001).

**Conclusion:** Patients of specialized cardiac clinic had low persistence of initial antihypertensive treatment scheme and they change scheme by themselves. Low persistence to recommended AHT is associated with certain factors that should be considered in patients’ follow-up.

**P1825 | BENCH**

**Clinic and home blood pressure lowering effect of fimasartan in postmenopausal women with hypertension**

S. Joo¹, K. Kim², D. Kim³, S. Lee⁴, K. Hwang⁵, M. Kim⁶, D. Kang⁷, J. Park⁸ on behalf of K-Mets Studies investigators. ¹Jeju National University Hospital, Jeju, Korea, Republic of; ²Seoul National University Bundang Hospital, Seongnam, Korea, Republic of; ³Busan Paik Hospital, Busan, Korea, Republic of; ⁴Wonju Christian Hospital, Wonju, Korea, Republic of; ⁵Chungbuk National University Hospital, Cheongju, Korea, Republic of; ⁶Cheil General Hospital, Seoul, Korea, Republic of; ⁷Ajou University Hospital, Suwon, Korea, Republic of

**Background and purpose:** Although the activation of renin-angiotensin system is suggested as one possible mechanism of postmenopausal hypertension, calcitonin gene-related peptide (CGRP) has been recognized as a potential blood pressure lowering drug in women. This study aimed to investigate clinical and home BP lowering effect of fimasartan in postmenopausal women with hypertension.

**Methods:** K-Mets Studies recruited 10,375 hypertensive patients treated with fimasartan in 6 Korean institutional trials from 2007 to 2009. Among them, 382 premenopausal women (preMPW) and 990 postmenopausal women (postMPW) with 3 months follow-up data and fimasartan as a first antihypertensive drug were selected.

**Results:** Baseline clinic systolic BP (SBP) (preMPW 152.9±15.2 vs. postMPW 152.8±13.5 mmHg) was not different, but diastolic BP (DBP) was lower in postMPW (preMPW 95.7±9.4 vs. postMPW 91.9±9.4 mmHg; p<0.001). After 3 months, clinic SBP and DBP declined effectively in both groups (Table). Home morning and night SBP were not different in both groups, but DBP of postMPW was lower both in the morning and at night. After 3 months, home SBP showed a similar decline in the morning (preMPW –21.3±1.7 mmHg) and at night (preMPW –23.1±1.5 mmHg vs. postMPW –20.4±1.7 mmHg) and at night (preMPW –23.1±1.5 mmHg vs. postMPW –20.2±1.9 mmHg). Home DBP after 3 months was not different in both groups, but it was more decreased in preMPW in the morning (preMPW –13.2±2.0 mmHg vs. postMPW –10.0±1.6 mmHg; p=0.005) and at night (preMPW –13.8±1.0 mmHg vs. postMPW –9.7±1.0 mmHg; p<0.001).

**Conclusions:** Fimasartan lowered both clinic and home BP effectively in postmenopausal women as well as in premenopausal women with hypertension.
P1828 | BEDSIDE
Can brain natriuretic peptide predict Prognosis in resistant hypertension?
A.O. Konradi, I. Emelyanov, V. Dorofeykov, P. Beltukov. Federal North-West Medical Research Center, St.Petersburg, Russian Federation

Purpose: To assess the prognosis of patients with true resistant hypertension (RHTN) without heart failure during 5 year follow-up in association with baseline brain natriuretic peptide (BNP) level.

Patients and methods: In 2008–2009 years we enrolled 336 uncontrolled hypertensive patients (98 males and 238 females) from 39 to 69 (±54±3) years old who were followed up in ambulatory HTN specialized center. The ambulatory BP monitoring (ABPM) was performed in all patients. Plasma levels of creatinine, potassium, fasting glucose, aldosterone and plasma renin activity were measured. For exclusion of secondary causes of HTN Doppler evaluation of renal arteries was performed. Obstructive sleep apnea (OSA) was diagnosed according to Berliner’s questionnaire confirmed by polysomnography. Echocardiography by Vivid 7 (GE) was performed and NT-proBNP level was estimated by ELISA (EIA Kit, Peninsula Laboratories International). During first 3 months of follow-up correction of treatment regimen was performed. Repeat visits to specialist were conducted every 6–12 months during 5 years follow-up. Outcome was assessed in 2014.

Results: The secondary HTN was diagnosed in 29 patients (8.6%); 16 – renovascular HTN (5.5%); 9 - primary aldosteronism (2.7%); 2 – pheochromocytoma (0.6%) and 2 – intracranial tumor (0.6%). In 45 (13.4%) patients OSA was revealed, 34 (10.1%) patients had “white-coat” HTN. 182 cases (55.3%) received suboptimal treatment regimen and 73 (21.9%) patients had poor compliance. True RHTN was found in 46 patients (15.6%). Baseline NT-proBNP values in patients with RHTN (n=46) were higher than in general group (250±60 pg/ml vs 86±30 pg/ml, P<0.05). 1 patient with RHTN had fatal hemorrhagic stroke, 1 patient ischemic stroke, 2 – transient ischemic attacks, 2 developed permanent atrial fibrillation, 1 patients had successful coronary revascularization, 1 acute coronary syndrome. Baseline NT-proBNP level in patients with RHTN and poor prognosis was higher compare patients with uncomplicated RHTN (372±30 pg/ml and 170±100 pg/ml, P<0.05). Discrepancies were confirmed after adjustment for BP level, size of heart chamber, left ventricle ejection fraction. In RHTN NT-proBNP was associated with systolic (r=0.44, P<0.05) and diastolic (r=0.35, P<0.05) after 12 months of treatment.

Conclusions: True resistance to treatment is rather infrequent cause of poor BP control. High level of BNP can be a predictor of poor prognosis of RHTN even without heart failure.

P1827 | BEDSIDE
Temperature, reduce the seasonal variability of blood pressure
K. Nomoto1, T. Mitsui1, M. Miyagi1, M. Kokubo1, A. Shimizu 1, T. Murohara2.

Conclusions: This study suggested that additional doses of thiazide diuretic to hypertensive patients improve the seasonal office blood pressure variability.

P1828 | BEDSIDE
Cirulating miR-21 and eNos in subclinical atherosclerosis in patients with hypertension
M. Cengiz1, S. Yavuzer1, M. Yuruyen3, H. Yavuzer1, S. A. Dikici2, B. Kiliçkiran Avci1, O.F. Karatas3, H. Uzun1, M. Ceniz1, Z. Ongen3. 1 Istanbul University, Cerrahpasa Medical School, Internal Medicine, Istanbul, Turkey; 2 Istanbul University, Cerrahpasa Medical School, Radiology, Istanbul, Turkey; 3 Istanbul University, Cerrahpasa Medical School, Cardiology, Istanbul, Turkey; 4 Istanbul University, Cerrahpasa Medical School, Medical Genetics, Istanbul, Turkey; 5 Istanbul University, Cerrahpasa Medical School, Biochemistry, Istanbul, Turkey

Background: Primary hypertension (HT) is a highly prevalent pathological condition that is considered one among the traditional risk factors for cardiovascular disease (CVD) and is an important cause of adult morbidity and mortality worldwide.

Methods: A total of 28 hypertensive and 28 healthy controls were enrolled. CIMT was evaluated by ultrasonoscopy and CIMT≥0.6 was accepted as increased CIMT (CIMT).

Results: CRP, miR-21 expression levels and CIMT measurements were significantly higher in the hypertension group than in the control group (p=0.009, p=0.002 and p<0.001 respectively). NOx and eNos levels were significantly lower in the hypertension group than in the control group (p=0.001 and p=0.001). Microalbuminuria levels in both groups were within normal limits. MI-21 was positively correlated with the clinical systolic blood pressure, clinical diastolic blood pressure, CRP and CIMT. MI-21 was negatively correlated with NOX and eNos. Eighteen patients with hypertension had CIMT. MI-21 expression and CRP levels were significantly higher (p<0.001 and p=0.001), whereas NOX and eNos levels were significantly lower in patients with CIMT (p<0.001 and p=0.001).

Conclusions: The decreased levels of NOX and eNos found in this study indicate the co-existence of endothelial dysfunction and hypertension once more. In the absence of microalbuminuria, the increased miR-21 expression in patients with CIMT might lead us to consider the possibility that miR-21 might be involved in the early stages of atherosclerotic process in hypertensive patients.

Acknowledgement/Funding: This work was supported by grants from the Research Fund of Istanbul University (Project Number: 40447).

P1829 | BEDSIDE
Persistence of fixed and free combination of ramipril and amlodipine in hypertension
G. Simonyi1, T. Ferenci2. 1 St. Imre University Teaching Hospital, Metabolic Center, Budapest, Hungary; 2 John von Neumann Faculty of Informatics, Óbuda University, Physiologic Controls Group, Budapest, Hungary

Introduction: Adequate patient adherence is of outstanding importance during the management of chronic disorders including hypertension. In particular, target blood pressure and the reduction of cardiovascular risk can be reached only by prolonged, effective pharmacotherapy. Patients taking the fixed combination were regarded as the reference group.

Methods: Information from the National Health Insurance of Hungary prescription database, on pharmacy-claims between October 1, 2012 and September 30, 2013 was analyzed. We identified patients who filled prescriptions for free of fixed combinations of ramipril and amlodipine, prescribed for the first time. Using the Kaplan-Meier method we constructed persistence curves. We used semi-parametric Cox’s regression where antihypertensive therapy was the only (categorical) explanatory variable. Patients taking the fixed combination were regarded as the reference group.

Results: Combination antihypertensive therapy with ramipril and amlodipine was started with a free or a fixed combination of these agents in 20,066 and 10,449 patients, respectively. One-year persistence rate in patients taking ramipril and amlodipine as a free combination was 34%, whereas it was 54% in those on the fixed combination. Analyzing persistence on treatment with these combinations showed that the actual rate of discontinuation was approx. twice higher during
Results: The study revealed a 3-fold increased risk of hemorrhagic stroke in patients receiving NOA in addition to antplatelet therapy (OR 3.04, 95% CI 1.77 to 5.25, P<0.0001). There was also significantly increased risk of major bleeding in patients receiving NOA (OR 2.45, 95% CI 1.58 to 3.80, P<0.0001). However, use of NOA was associated with significantly reduced risks of ischemic stroke (OR 0.79, 95% CI 0.64 to 0.99, P=0.04) and composite efficacy outcome (death/myocardial infarction/stroke) (OR 0.87, 95% CI 0.81 to 0.93, P<0.0001). There was also a borderline significant reduction in all-cause mortality (OR 0.91, 95% CI 0.82 to 1.00, P=0.05) in favor of NOA therapy. Notably, subgroup analysis revealed that the use of direct Xa inhibitors significantly reduced the risk of all-cause mortality (OR 0.89, 95% CI 0.80 to 0.99, P=0.04) as well as stent thrombosis (OR 0.69, 95% CI 0.54 to 0.89, P=0.004), whereas no reduction was seen with use of PAR1 antagonists or direct thrombin inhibitors.

Conclusion: In patients with ACS, the addition of a NOA to antplatelet therapy led to a modest but significant reduction in ischemic stroke and overall composite efficacy outcome at the cost of a substantial increase in hemorrhagic stroke and major bleeding events.

1832 | B ED SIDE
Stroke and recurrent haemorrhage associated with antithrombotic treatment following gastrointestinal bleeding in patients with atrial fibrillation: A Danish nationwide cohort study
L. Staerk1, G.Y. Lip1, J.B. Olsen1, E.L. Fosbol2, J.L. Pallisgaard1, A. Gundlund1, T.B. Lindhardt1, M.L. Hansen1, C. Torp-Pedersen1, G. Gislason3, L. Melgaard4, A. Gorst-Rasmussen2, L.H. Rasmussen1, G.Y. Lip1, T.B. Larsen2, L. Melgaard1, A. Gorst-Rasmussen2, L.H. Rasmussen1, G.Y. Lip1, T.B. Larsen2, Aalborg University, Aalborg Thrombosis Research Unit, Department of Clinical Medicine, Faculty of Health, Aalborg, Denmark; 2Aalborg University Hospital, Thrombosis Research Unit, Aalborg, Denmark; 3University of Birmingham, Centre for cardiovascular sciences, city hospital, Birmingham, United Kingdom

Background: The CHA2DS2-VASc score has been useful for risk stratification in atrial fibrillation, but its utility in a population of heart failure patients in sinus rhythm is unclear.

Methods: We performed a register-based cohort study of non-anticoagulated patients diagnosed with incident heart failure in sinus rhythm during 2000–2012 in Denmark. Evaluating a stroke risk score in a high mortality population such as heart failure patients is non-trivial because discriminatory performance depends on the choice of control group. We investigated discriminatory properties of the CHA2DS2-VASc score for predicting stroke within 1, respectively 5 years using two definitions of controls: 1) stroke free and alive; 2) stroke free or dead.

Results: 33,785 incident heart failure patients were followed for an average of 2.4 years. The stroke rate increased with increasing CHA2DS2-VASc score (please see table). Discrimination performance of the CHA2DS2-VASc score at 1- and 5-years follow-up was: C-statistic=0.67 and 0.68 for control group 1, and C-statistics=0.64 and 0.60 for control group 2. With the cutpoint CHA2DS2-VASc=0 for identifying low risk patients, the negative predictive values (NPV) varied according to control group (1- and 5-years follow-up: NPV=91.7% and 77.9% for control group 1, and NPV=98.6% and 96.5% for control group 2). Matrially similar results were found with a cutpoint of 1.0.

Incidence rates for stroke

<table>
<thead>
<tr>
<th>CHA2DS2-VASc score</th>
<th>Patients, % (n)</th>
<th>Events (after 1- and 5-years follow-up)</th>
<th>Stroke rate, %/year (after 1- and 5-years follow-up)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5.1 (2,384)</td>
<td>29 (29)</td>
<td>1.50±0.87</td>
</tr>
<tr>
<td>1</td>
<td>13.4 (4,355)</td>
<td>62 (62)</td>
<td>1.64±1.06</td>
</tr>
<tr>
<td>2</td>
<td>22.3 (7,519)</td>
<td>141 (141)</td>
<td>2.38±1.95</td>
</tr>
<tr>
<td>3</td>
<td>27.3 (9,232)</td>
<td>258 (258)</td>
<td>3.75±2.46</td>
</tr>
<tr>
<td>4</td>
<td>17.7 (5,983)</td>
<td>210 (210)</td>
<td>4.82±3.36</td>
</tr>
<tr>
<td>5</td>
<td>12.2 (4,132)</td>
<td>275 (275)</td>
<td>9.75±5.89</td>
</tr>
</tbody>
</table>

This table presents the distribution of CHA2DS2-VASc scores in the study population, plus number of events and stroke rates after 1- and 5-years follow-up according to CHA2DS2-VASc score (per 100 person-years).

Conclusions: The CHA2DS2-VASc score predicts stroke among heart failure patients with comparable accuracy as in atrial fibrillation. However, in this high mortality population, performance depends crucially on the choice of control group.

1831 | B ED SIDE
Risk of hemorrhagic and ischemic stroke for combined antplatelet therapy and new generation oral anticoagulants in patients with acute coronary syndrome: Meta-analysis of 11 randomized clinical trial
F. Gao, Y.J. Zhou, Z.J. Wang, H. Shen, S.W. Yang, X.L. Liu. Beijing Anzhen Hospital of the Capital University of Medical Sciences, Beijing Heart, Lung & Blood Vessel, Beijing, China, People’s Republic of China

Background: The overall risk–benefit profile of new generation oral anticoagulants (NOA) in addition to antplatelet therapy on hemorrhagic as well as ischemic stroke in patients with acute coronary syndrome (ACS) has not been clearly established.

Methods: Studies evaluating clinical outcomes of NOA (including direct Xa inhibitors, direct thrombin inhibitors and PAR-1 antagonists) in addition to standard antplatelet therapy in patients with recent ACS, published before Nov 2014, were screened. Eleven double blind, placebo-controlled, randomized clinical studies including 46782 patients were identified.

Results: The study revealed a 3-fold increased risk of hemorrhagic stroke in patients receiving NOA in addition to antplatelet therapy (OR 3.04, 95% CI 1.77 to 5.25, P<0.0001). There was also significantly increased risk of major bleeding in patients receiving NOA (OR 2.45, 95% CI 1.58 to 3.80, P<0.0001). However, use of NOA was associated with significantly reduced risks of ischemic stroke (OR 0.79, 95% CI 0.64 to 0.99, P=0.04) and composite efficacy outcome (death/myocardial infarction/stroke) (OR 0.87, 95% CI 0.81 to 0.93, P<0.0001). There was also a borderline significant reduction in all-cause mortality (OR 0.91, 95% CI 0.82 to 1.00, P=0.05) in favor of NOA therapy. Notably, subgroup analysis revealed that the use of direct Xa inhibitors significantly reduced the risk of all-cause mortality (OR 0.89, 95% CI 0.80 to 0.99, P=0.04) as well as stent thrombosis (OR 0.69, 95% CI 0.54 to 0.89, P=0.004), whereas no reduction was seen with use of PAR1 antagonists or direct thrombin inhibitors.

Conclusion: In patients with ACS, the addition of a NOA to antplatelet therapy led to a modest but significant reduction in ischemic stroke and overall composite efficacy outcome at the cost of a substantial increase in hemorrhagic stroke and major bleeding events.
1833 | BENCH
Dex40-GTMAC3, a new tool to reverse unfractiomed heparin effects during intracarosal or cardiac interventions
B. Kalaska1, K. Kaminski2, E. Sokolowska1, D. Czaplicki3, K. Stalinska3, K. Szczubialka2, J. Bereza2, D. Pawlik1, M. Nowakowska2, A. Mogielnicki1, 1Medical University of Bialystok, Department of Pharmacodynamics, Bialystok, Poland; 2Jagiellonian University, Faculty of Chemistry, Krakow, Poland; 3Jagiellonian University, Department of Cell Biochemistry, Faculty of Biochemistry, Biophysics and Biotechnology, Krakow, Poland

Background: Protamine is the only registered antidote preventing bleeding in patients treated with unfractiomed heparin (UFH). However protamine may induce a number of adverse effects, such as anaphylactic shock or serious hypotension. We synthesized a group of polysaccharide polymers able to bind UFH by adding different cationic groups, including glycidyltrimethylammonium chloride (GTMAC). Based on in vitro assays we selected several polysaccharide polymers for further in vivo studies.

Purpose: The aim of the present study was to find the most efficient in vivo UFH antidote.

Methods: We administered UFH (300 U/kg) alone or followed by γ-cycloedrin (GCD-GTMAC, 10.8 mg/kg), low (Dex46-GTMAC, 9.6 mg/kg) or high (Dex40-GTMAC) molecular weight dextrans substituted with GTMAC groups at a ratio of 0.5 (Dex40-GTMAC2, 12.5 mg/kg) or 0.65 (Dex40-GTMAC3, 7.5 mg/kg) per a glucose unit, and protamine (3 mg/kg) to 84 male Wistar rats developing electrically induced arterial thrombosis. The efficacy endpoints were: arterial thrombus weight, tail bleeding time, activated partial thromboplastin time (aPTT) and anti-factor X activity. We measured blood count and blood pressure directly in the carotid artery of rat to exclude the worst tolerated polymers. We also compared the immune response to Dex40-GTMAC3 and protamine administered once a week to female mice for 36 days.

Results: Dex40-GTMAC3 was the most potent and, similarly to protamine, reversed all the measured endpoints when administered in a non-hypotensive dose (Table 1). Unlike Dex40-GTMAC3, Dex6-GTMAC was hypotensive and decreased, whereas GCD-GTMAC increased red blood cell count, hematocrit and hemoglobin values. In contrast to protamine, Dex40-GTMAC3 did not induce immune response.

Table 1. Reversing of UFH effects

<table>
<thead>
<tr>
<th>Vehicle</th>
<th>UFH</th>
<th>UFH+Dex40-GTMAC3</th>
<th>UFH+Protamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombus weight (mg)</td>
<td>0.92±0.17</td>
<td>0.57±0.09***</td>
<td>0.85±0.25**</td>
</tr>
<tr>
<td>Bleeding time (seconds)</td>
<td>104.3±4.6</td>
<td>167.2±14.2***</td>
<td>106.3±15.5***</td>
</tr>
<tr>
<td>aPTT (seconds)</td>
<td>20.3±1.1</td>
<td>28.4±2.8***</td>
<td>28.9±2.9***</td>
</tr>
<tr>
<td>Anti-factor X activity (U/mg)</td>
<td>0.13±0.02</td>
<td>0.93±0.02***</td>
<td>0.34±0.11***</td>
</tr>
</tbody>
</table>

***P<0.001 vs. vehicle; **P<0.01, *P<0.05, **P<0.01 vs. UFH, Mann-Whitney test. Results are shown as mean ± S.D., n=8-10.

Conclusions: Documented efficacy, immunogenic and hemodynamic neutrality of Dex40-GTMAC3 makes this novel UFH antidote advantageous over other polysaccharide polymers and protamine.

1834 | BENCH
Conclusions: We demonstrate for the first time that short TL predicts clinical outcome post revascularization procedures, independently of chronological age. We also show that oxidative stress reduces TL in humans, providing new insights into the role of biological senescence in cardiovascular ageing.

YOUNG INVESTIGATORS AWARDS SESSION: AGEING AND SENESCENCE

1834 | BENCH
Telomere length predicts clinical outcomes post-revascularizations procedures: its role as a novel biomarker of systemic oxidative stress and cardiovascular ageing
M. Margaritis 1, M. Margaritis 1, G. Lazaros 2, S. Patel1, L. Herdman 1, A.S. Antonopoulos 1, I. Akoumianakis1, F. Sanna1, D. Tousoulis2, K.M. Channon1, C. Antoniades1.

1 University of Oxford, RDM, Cardiovascular Medicine Division, Oxford, United Kingdom; 2Zigurta, University of Antwerp, Laboratory of Physiopharmacology, Antwerp, Belgium

Introduction: Telomere length (TL) is described as an important aging-contributor due to accumulation of damaged DNA. Shorter TL is associated with increased oxidative stress and increased risk of age-related disease. We investigated the role of TL in predicting clinical outcomes post revascularization procedures and its association with systemic oxidative stress.

Methods and results: We measured TL in whole-blood DNA by qPCR. Systemic oxidative stress was evaluated by TAC when compared to sham controls (n=5–7; p<0.01). 95% of senescent cells were positive for fibroblast marker vimentin and PDGFR (n=3–9; p<0.01). SA-ß-GAL was increased 4-fold after vehicle. In all diabetic mice a significant induction of cell senescence in the aorta was observed using the methods mentioned above. Consistent with our observations in vitro, NRG-1 treatment significantly attenuated hyperglycaemia-induced senescenece in the aorta.

Conclusions: This study is the first to explore the role of the cardioprotective growth factor NRG-1 in vascular senescence. Our data demonstrate that NRG-1 markedly inhibits senescence induced by oxidative stress in vascular cells in vitro and in the aorta of diabetic mice in vivo.

1835 | BENCH
Neuregulin-1 attenuates stress-induced vascular senescence in vitro and in vivo

Objective: Cardiovascular ageing is a key process determining life expectancy and health of the elderly. Cardiovascular senescence, a state of irreversible cell age-arrest, is described as an important aging-contributor due to accumulation of damaged DNA. Senescence in the aorta is of particular interest as it is a key contributor to age-related cardiovascular diseases. We investigated the effect of neuregulin-1 (NRG-1) on cardiovascular cell senescence in vitro and in vivo.

Methods and results: Cultured aortic rat endothelial cells (AECs) and smooth muscle cells (SMCs) were exposed to 30 μM hydrogen peroxide (H2O2) for 2 hours. Cellular senescence was confirmed 72 hours later using SA-β-galactosidase staining and cell surface area as markers of senescence. In addition, western blot analyses of senescence associated pathways (including acetyl-p53, p21) were performed. In the presence of 20 ng/ml NRG-1, H2O2-induced senescence was significantly attenuated as shown by a decreased number of SA-β-galactosidase positive AECs and SMCs, decreased surface area of NRG-1 treated cells and also decreased expression of acetyl-p53 in cells exposed to NRG-1. To strengthen these observations in vivo, C57BL/6 mice were rendered diabetic with streptozotocin and randomized to receive NRG-1 (20 μg/kg) or vehicle. In all diabetic mice a significant induction of cell senescence in the aorta was observed using the methods mentioned above. Consistent with our observations in vitro, NRG-1 treatment significantly attenuated hyperglycaemia-induced senescence in the aorta.

Conclusions: This work demonstrates a novel role for neuregulin-1 in regulating endothelial and smooth muscle senescence, and identifies NRG-1 as a potential therapeutic target for treating cardiovascular disease.

1836 | BENCH
Matricellular protein CCN1-mediated premature senescence is a negative regulator of cardiac fibrosis
K. Meyer, B. Hodwin, S. Engelhardt, A. Sarikas. Technical University of Munich, Munich, Germany

Introduction: Premature senescence is a tumoursuppressive mechanism leading to p16INK4a and p15INK4b mediated cell cycle arrest upon telomere shortening or oncogenic signaling. Recent studies have demonstrated a novel role for premature senescence in liver and skin fibrosis and identified Cystein-rich 61 protein (CCN1) as a key regulator.

Purpose: To investigate the pathophysiological role of CCN1-mediated prema-
ture senescence in cardiac fibrosis.

Methods: Two established murine models of cardiac fibrosis, transaortic constric-
tion (TAC) and cardiacmyocyte-specific beta1 adrenergic receptor transgenic mice (beta1-TG), were employed to study the role of premature senescence in the heart. Fibrosis was detected by Sirius Red staining and Realtime PCR (Col1a1, Col3a1). Cellular senescence was quantified by immunohistochemistry, histochemistry and Realtime PCR of p16INK4a, p21CIP1/WAF1 and senescence-associated beta-galactosidase (SA-β-GAL). To study the functional role of premature senescence in cardiac fibrosis, CCN1 (or a dominant-negative mutant CCN1-D1) was overexpressed in the heart via AAV9-mediated gene transfer in sham or TAC mice.

Results: Senescence marker p16INK4a and p15INK4b were increased 15- fold in both cohorts (H), suggesting a causal relationship between oxidative stress and TL.

Conclusions: We demonstrate for the first time that short TL predicts clinical outcome post revascularization procedures, independently of chronological age. We also show that oxidative stress reduces TL in humans, providing new insights into the role of biological senescence in cardiovascular ageing.

Downloaded from https://academic.oup.com/euroheartj/article-abstract/36/suppl_1/163/434475 by guest on 07 February 2019
iliar results were observed in the beta-1-TG model. Heart-specific overexpression of CCN1, but not CCN1-DM, resulted in a 4-fold increase of premature senescence in the heart (n=3–9; p<0.05) which was associated with a 50% reduction of perivascular cardiac fibrosis after TAC (20% vs. 10%; n=3–9; p<0.01). Finally, cardiac function after TAC was significantly improved in mice with CCN1-triggered senescence when compared to CCN1-DM or mock controls (ejection fraction: 35% vs. 29% vs. 20%; n=7–10; p<0.05).

Conclusion: Our results demonstrate a critical role of CCN1-mediated premature senescence as a negative regulator of cardiac fibrogenesis. Pharmacological modulation of senescence mechanisms might provide a novel therapeutic target for the treatment of cardiac fibrosis.

1837 | BENCH
Vascular aging, telomere biology, oxidative stress and chronic inflammation in patients with type 2 diabetes mellitus
N. Brailova1, E. Dudinskaya1, I. Strazhesko1, D. Akasheva1, M. Pokrovskaya1, O. Tkacheva1, V. Pykhinya1, S. Boytsov1, M. Shestakova1,2. National Research Center for Preventive Medicine, Moscow, Russian Federation

Background: It is known that glucose disturbances contribute to vascular aging. The telomere-length (TL) and telomerase activity (TA) are considered as biomarkers of cellular aging. It is crucial to determine the role of telomere biology in different vessel changes in diabetic patients.

Purpose: of our study was to determine the role of the TL and TA in vascular aging in patients with T2DM.

Methods: The study group included 50 patients with T2DM with mean age 58±17.8 years. All subjects were measured for TL and TA by quantitative polymerase chain reaction; fasting plasma glucose (FPG), glycated hemoglobin (HbA1c); oxidative stress marked by malondialdehyde; inflammation by interleukin-6 (IL-6), C-reactive protein (CRP), fibrinogen; arterial stiffness (AS) evaluated by carotid-femoral pulse wave velocity (PWV); carotid intima-media thickness (IMT), plaque presence (PP) determined by ultrasonography in carotid arteries; endothelial dysfunction evaluated by flow-mediated endothelium-dependent vasodilation (FMD) and endothelium-independent vasodilation (NDV).

Results: All patients were divided into 2 groups by the median of TL (9.75): “short” telomeres and “long” telomeres. Vessels changes were more pronounced in patients with “short” TL: PWV 14.1±3.22 m/s vs. 11.78±3.26 m/s (p=0.016), IMT 1.00±0.15 mm vs. 0.84±0.16 mm (p<0.001), PP 2.63±0.31 vs. 1.36±0.26 (p<0.003), FMD 7.93±3.40 vs. 10.95±3.10 (p<0.002), NDV 12.63±4.25 vs. 15.68±4.51 (p=0.019). TA was similar in the 2 groups. We found significant increasing of oxidative stress and chronic inflammation in diabetic patients with “short” TL: malondialdehyde 3.4±1.06 mmol/l vs. 2.9±0.87 mmol/l (p=0.058); CRP 9.43±2.01 mg/l vs. 3.30±0.37 mg/l (p<0.006).

Correlation analysis showed significant association between TL and next parameters: FMD (r=−0.50, p=0.0003), IMT (r=−0.39, p=0.006), FMD (r=−0.49, p=0.0003), NDV (r=−0.41, p=0.001), FPG (r=−0.42, p=0.003), CRP (r=−0.40, p=0.004), TA (r=−0.32, p=0.035).

Then patients were divided into 2 groups by the median of TA (0.03): “low” and “high” TA. There were no significant difference in vascular changes, markers of oxidative stress and inflammation between 2 groups. In diabetic patients “high” TA was associated with long telomeres (r=0.40, p=0.0095).

Conclusion: Vascular changes, chronic inflammation and oxidative stress were more pronounced in patients with T2DM and “short” telomeres. Perhaps long telomeres protect vessels of diabetic patients from accelerated vascular aging. The role of telomerase activity in the vascular aging has not been established.

YOUNG INVESTIGATORS AWARDS SESSION: CORONARY PATHOPHYSIOLOGY AND MICROCIRCULATION

1838 | BEDSIDE
Spotty calcification as a marker of vulnerable plaque: novel findings from in vivo study in survivors of cardiac arrest and in vitro study in autopsied patients of sudden cardiac death
J. Pu1,2, P. Zhang1, G. Mintz1, X. Ma1, B. He1,1 Renji Hospital of Shanghai Jiao Tong University School of Medicine, Department of Cardiology, Shanghai, China; People’s Republic of 1University of Maryland, Baltimore, United States of America; 2Columbia University, New York, United States of America; 4Thomas Jefferson University, Philadelphia, United States of America

Aims: We previously reported that spotty calcification detected by IVUS was often associated with histological fibroatheromas (JACC, 2014, 63:2220–33). However, the exact mechanisms underlying spotty calcification and the associated risk for ischemic events remain poorly understood. We performed a study on spotty calcification using IVUS, near-infrared spectroscopy (NIRS) and optical coherent tomography (OCT) in survivors of cardiac arrest and autopsied patients of sudden cardiac death (SCD).

Methods and results: IVUS, NIRS and OCT were performed in vessels from 62 patients who had a documented sudden cardiac arrest but successfully resuscitated and 52 autopsied SCD patients. Spotty calcium was detected in 88.5% survivors of cardiac arrest; 73.3% of them had spotty calcium in superficial location.

About 83.3% superficial spotty calcium co-existed with echo-attenuated plaques on IVUS, 73.9% co-existed with thin-cap fibroatheroma (TCFA) or plaque rupture on OCT, and 88.8% contained lipid core plaque on NIRS (Figure). The arc of spotty calcium was negatively correlated with lipid burden on NIRS (rho=−0.40, P=0.03), and positively correlated with cap thickness on OCT (rho=0.41, P=0.01). In vitro study, IVUS and OCT detected spotty calcification in 80.6% SCD patients. On pathological analyses, the arc of spotty calcium was negatively correlated with 1) inflammation of fibrous cap, 2) level of oxidative stress, and 3) apoptosis and necrotic core (NC) size. Compared with spotty calcium in deep location, that in superficial location was associated with larger NC size (P=0.02) and more TCFA (P=0.001) and plaque rupture (P=0.006).
Method: 40 patients diagnosed with ACS (non-ST segment elevation and ST-segment elevation ACS), 40 patients diagnosed with stable coronary artery disease (CAD) and 40 age and gender-matched subjects with normal coronary arteries were involved. Platelet TLR-2 and 4 expression were evaluated by flow cytometric analysis in peripheral venous blood samples obtained prior to coronary angiography.

Results: 120 patients (50% male, 60±12.3 years) were included. Baseline characteristics of patients did not differ among groups (p>0.05). Platelet TLR-2 expression was found to be significantly higher in patients diagnosed with ACS when compared with the controls [30 (11–90) vs. 3 (1–5), p<0.001] and stable CAD groups [30 (11–90) vs. 11 (5–14), p<0.001]. Platelet TLR-4 expression was also more prominent in ACS patients when compared with the control [41 (20–94) vs. 3 (1–4), p<0.001] and stable CAD groups [41 (20–94) vs. 12 (4–24)], p<0.003](Figure 1).

Conclusions: This is the first study demonstrating the enhanced TLR-2 and 4 expression on platelets in ACS patients. These findings may suggest that platelet TLR expression as a novel potential prophylactic and therapeutic target in ACS.

1840 | BEDSIDE
Impact of aortic valve stenosis on coronary hemodynamics and the instantaneous effect of transcatheter aortic valve implantation

Background: Aortic valve stenosis (AS) induces compensatory alterations in the left ventricle, leading to alterations in coronary hemodynamics. Relief of AS by transcatheter aortic valve implantation (TAVI) decreases ventricular afterload and is expected improve microvascular function immediately.

Purpose: We evaluated the effect of AS on coronary hemodynamics and the immediate effect of TAVI.

Methods: Intracoronary pressure and flow velocity were simultaneously assessed at rest and maximal hyperemia in an unobstructed coronary artery in 27 AS-patients before and immediately after TAVI, and in 28 patients without AS.

Results: Baseline flow velocity was higher and baseline microvascular resistance was lower in AS-patients as compared to controls, which remained unaltered post-TAVI. In AS-patients hyperemic flow velocity was significantly lower as compared to controls (44.5±14.5 vs 54.3±18.6 cm/s; p=0.04). Hyperemic microvascular resistance (HMR, mmHg cm⁻¹ s⁻¹) was 2.10±0.69 in AS-patients, as compared to 1.80±0.60 in controls (p=0.006). Coronary flow reserve (CFR) in AS-patients was lower, 1.9±0.5 vs 2.7±0.7 in controls (p<0.001). Improvement in coronary hemodynamics after TAVI was most pronounced in patients without post-TAVI aortic regurgitation. In these patients (n=20), hyperemic flow velocity increased significantly from 46.24±15.47 to 56.56±17.44 cm/s post-TAVI (p=0.003).

HMR decreased from 2.03±0.71 to 1.6±0.45 (p=0.005). CFR increased significantly from 1.9±0.4 to 2.2±0.6 (p=0.009) (Fig 1).

Conclusion: The vasodilatory reserve capacity of the coronary circulation is reduced in AS. TAVI induces an immediate decrease in hyperemic microvascular resistance and a concomitant increase in hyperemic flow velocity, resulting in immediate improvement in coronary vasodilatory reserve.

1841 | BENCH
Incremental diagnostic value of combined non-invasive assessment of endothelial shear stress and molecular imaging of inflammation for the early identification of high-risk plaque
G. Gitisouidis¹, Y. Chatzizisis³, A. Missiou¹, A. Antoniadis³, D. Mitsouras³, A. Giannopoulos³, M. Stuber⁵, G. Giannoglou⁶, H.A. Katus¹, G. Korosoglou¹.
¹University of Heidelberg, Department of Cardiology, Heidelberg, Germany; ²Brigham and Women’s Hospital, Cardiovascular Division, Boston, United States of America; ³Guy’s Hospital, Cardiovascular Center, London, United Kingdom; ⁴Brigham and Women’s Hospital, Department of Radiology, Boston, United States of America; ⁵Center for Biomedical Imaging (CIBM), Lausanne, Switzerland; ⁶Ahepa University Hospital, First Department of Cardiology, Thessaloniki, Greece.

Introduction: Low endothelial shear stress (ESS) and inflammation are key pathobiologic components for the development of high-risk atherosclerotic plaques.

Purpose: To test the hypothesis that the combination of non-invasively assessed ESS with molecular imaging of inflammation can predict the formation of high-risk plaque.

Methods: 12 hereditary hyperlipidemic rabbits underwent imaging of the thoracic aorta with a 256-slice CT and a 1.5T MRI at 6 months (baseline, BL) and 12 months (follow-up, FU). We calculated the ESS at BL using CT-based 3D reconstruction of thoracic aorta and computational fluid dynamics. We selected 5-mm-long aortic subsegments (n=76), and classified ESS into low, intermediate and high (A). In each subsegment, we quantified plaque composition by CT (B) and wall thickness by MRI at BL and FU. Molecular MRI at BL and FU assessed the severity of inflammation using ultrasmall superparamagnetic nanoparticles (C). Plaque size and inflammation were evaluated by histopathology at FU (D).

Results: Subsegments with low BL ESS exhibited a significantly higher non-calcified plaque volume at FU by CT (E) and significant increase in wall thickness and plaque inflammation by molecular MRI (FG) compared to intermediate/high ESS subsegments. Those subsegments with low BL ESS developed high-risk plaque features by histopathology at FU (D). The composite of low ESS and severe inflammation by molecular MRI at BL was the strongest predictor of plaque progression and high-risk plaque formation (composite ESS/Inflamm.: AUC=0.89, 95% CI 0.8–1.0; ESS only: AUC=0.84, 95% CI 0.7–0.9; inflammation. only: AUC=0.74, 95% CI 0.6–0.8).

Conclusion: This study provides novel evidence that low ESS and severe inflammation have incremental diagnostic value for the early identification of high-risk plaque.
specific death. MI patients had a two-fold increased long-term risk of dying from reinfarction, venous thromboembolism, or chronic pulmonary disease.  

Conclusions: Long-term mortality risk after MI before 50 years of age has decreased remarkably over the last three decades. Still, one-year survivors carry an excess 30-year risk of dying compared with the general population, primarily due to reinfarction, venous thromboembolism and chronic pulmonary disease.

### 1843 | BEDSIDE  
A healthy lifestyle is strongly related to an increased heart rate variability in healthy adults  

S. Aeschbacher1, T. Schoen1, N. Good1, N. Probst-Hensch2, A. Schmidt- Trucksaess3, M. Risch1, L. Risch1, D. Conen5. 1 University Hospital Basel, Basel, Switzerland; 2 University of Basel, Swiss Tropical and Public Health Institute, Basel, Switzerland; 3 Institute of Exercise and Health Sciences, Basel, Switzerland; 4 Neurologisches Zentrum Dr Risch, Schaan, Liechtenstein; 5 University Hospital Basel, Department of Internal Medicine, Basel, Switzerland

Background: The combined influence of a healthy lifestyle on heart rate variabil-
ity (HRV) as a measure of autonomic function in the general population is not well studied.  

Methods: We assembled a population-based cohort of 2170 healthy individuals aged 25–41 years without prevalent cardiovascular disease or diabetes mellitus. Ambulatory 24-hour electrocardiography (ECG) was recorded with a validated de-
vice. All ECG studies were systematically post-processed, and the standard de-
vice used to calculate normal RR Intervals (SDNN) was used as the main marker of HRV. Healthy lifestyle habits were summed to a lifestyle score with a scale from 0–most unhealthy to 7=most healthy. One point was given for never smoking cigarettes in the past, having a BMI <25kg/m2, consuming ≥5 servings of fruits or vegetables per day, being physically active ≥150 minutes per week, having a systolic and diastolic blood pressure <120 and <80mmHg without using antihyperten-
tive treatment, cholesterol levels <200mg/dl without using lipid-lowering therapy and a glycated HbA1c <5.6%. Linear regression analysis adjusted for sex, age, educational status, alcohol consumption and family history of cardiovascu-
lar disease were performed to compare SDNN differences across lifestyle score categories.  

Results: We included 2127 participants (median age: 36.7 years, 47% men) with complete data in this analysis. The mean SDNN was 149ms. The number of in-
dividuals in each lifestyle score category was 153 (score 0–1), 324 (score 2), 482 (score 3), 576 (score 4), 440 (score 5) and 152 (score 6–7). In multivariable linear regression analysis with SDNN as the outcome variable, the β-estimates (95% confidence interval (CI)) across lifestyle score categories were 1.28 (–5.85; 8.42), 6.99 (0.20; 13.79), 14.99 (8.18; 21.79), 20.39 (13.28; 27.50) and 24.60 (15.9; 33.3), respectively (p for trend <0.0001). Using SDNN as a continuous variable, we found a β-estimate (95% CI) of 5.56 (4.31; 6.81), p<0.0001. This re-

lationship was attenuated but remained significant after additional adjustment for con-
ventional HR (β-estimate (95% CI) 3.48 (2.30; 4.65), p<0.001) and was even more even attenuated after adjustment for 24-hour HR (β-estimate (95% CI) 1.77 (0.70; 2.85), p<0.001).  

Conclusion: A healthy lifestyle was strongly associated with greater HRV in this large sample of young and healthy adults, underscoring the importance of a healthy lifestyle for optimal cardiovascular protection. Our study also suggests that a substantial part of this beneficial effect is explained by 24-hour HR, and that the additional information provided by HRV seems to be small.

### 1844 | BEDSIDE  
Thermobold threshold of particulate matter matter level for increasing heart failure incidence may be lower than national standard  

Q. Hyun1, F. Johnston, C.L. Blizzard, T.H. Marwick, K. Negishi. Menzies Research Institute, Hobart, Australia

Background: Daily hospitalizations for heart failure (HF) are reported to be lin-
early associated with acute increase in ambient air pollution. However, it is un-
clear whether there is a threshold level of particulate matter <2.5μm (PM2.5) to the increase in HF incidence. We aimed to answer this research question by per-
forming a time-series analysis of the relationship between daily PM2.5 level and HF admission risk at baseline were matched on propensity score with controls not receiv-
ing treatment at baseline were matched on propensity score with controls not receiv-
ing treatment at baseline were matched on propensity score with controls not receiv-
ing treatment at baseline were matched on propensity score with controls not receiv-

Methods: This Tasmanian statewide data linkage included all patients with a first-
HF admission in Tasmania, which is one of the world's cleanest cities.  

Methods: This Tasmanian statewide data linkage included all patients with a first-
HF admission in Tasmania, which is one of the world's cleanest cities.  

Results: The median PM2.5 level was 2.8μg/m³ [interquartile range: 1.8, 6.0]. There were 1727 new HF admissions (average 1.5±1.4/day) during the study pe-
riod. Greater HF incidences occurred in winter than in other seasons (p<0.001). PM2.5 was detrimentally associated with HF (RR=1.32 [1.21, 1.44]), with a one-
day lagging period. In multivariable analyses, PM2.5 remained independently pre-
dictive of HF incidences (RR=1.14 [1.03, 1.27]). The entire study period was di-
vided into nine periods of approximately 100 days each, based on PM2.5 concen-
tration (Figure). Although the incidences were similar for PM2.5 ranging from 1 to 4μg/m³, there was a significant increase when PM2.5 >4μg/m³.  

Conclusions: The concentration of PM2.5 independently predicted HF inci-
dences, with a one-day lagging period. New HF admissions started to rise with PM2.5 level of 4μg/m³, which is far below the daily Australian national standard of 25μg/m³.

### 1845 | SPOTLIGHT  
Dose and time dependent associations of smoking to incident subarachnoid hemorrhage in men and women  

J.V. Lindbohm1, J. Kaprio1, V. Saloma2, M. Korja3. 1 University of Helsinki, Helsinki, Finland; 2 National Institute for Health and Welfare (THL), Helsinki, Finland; 3 Helsinki University Central Hospital, Helsinki, Finland

Introduction: In addition to age, being female and hypertension, smoking is a known risk factor for subarachnoid hemorrhage (SAH), but the data on dose and time-dependent effect of smoking are limited.  

Purpose: To study the association between the number of cigarettes smoked per day and pack years on the risk of SAH by sex.

Methods: The ongoing National FINRISK study, carried out every five years us-
ing independent, random, and representative population samples from different geographical areas of Finland, provided the risk factor data recorded at enroll-
ment between 1972 and 2007. The follow-up began in the baseline study year and ended at the end of 2011. A total of 492 SAH cases emerged from the nationwide Causes of Death Register and Hospital Discharge Register for the population-based cohort of 31 180 men and 33 504 women with a total of 1.38 million person-years. Cox proportional hazards model, adjusted for age, sex, hy-
pertension, cholesterol, study year and area, provided the hazard ratios (HRs). We used a likelihood ratio test (LRT) to evaluate the significance of the interac-
tion between smoking and sex.

Results: Mean age was 45.3 years in women and 45.4 in men, and at baseline 14% of women and 23% of men were smokers. Among smokers, the mean reported smoking exposure was in women 17.3 (95% CI 17.0–17.7) years and in men 22.3 (95% CI 20.2–22.6). Mean number of cigarettes smoked per day was in women 10.8 (95% CI 10.6–11.1) and in men 15.7 (95% CI 15.4–15.9). Smoking more than a pack of cigarettes per day (21–30) increased the risk of SAH in women more than in men with a HR of 8.2 (95% CI 3.8–17.8) and 3.6 (95% CI 2.0–
6.3). The difference between HRs by sex was significant in all cigarette-per-day cate-
gories (LRT p<0.007). Among smokers mean pack years was in women 11.8 (95% CI 11.4–12.1) and in men 19.8 (95% CI 19.4–20.3). When high number of pack years (~31) was compared to low (0–1), the risk of SAH increased in women with a HR 2.5 (95% CI 1.3–11.2). In men, however, the increase was borderline significant with a HR of 1.9 (95% CI 0.94–4.0) and the difference in HRs by sex was non-significant (LRT p=0.18).  

Conclusion: An increasing number of cigarettes per day raised the risk of SAH more in women, whereas men smoked more cigarettes per day and had a longer history of smoking. Future studies on SAH risk factors should optimally adjust by sex the number of cigarettes smoked per day rather than the categories of current, previous, and non-smokers.

### YOUNG INVESTIGATORS AWARDS SESSION: CLINICAL SCIENCE  
### 1846 | BEDSIDE  
Lower risk of mortality in angiotensin-converting enzyme inhibitor and angiotensin II receptor blocker treated patients with aortic stenosis. A nationwide propensity score matched study  

M.J.D. Buron, K.E. Kristensen, G. Gislason. Gentofte Hospital - Copenhagen University Hospital, Department of Cardiology, Hellerup. Denmark

Purpose: The role of Renin-Angiotensin system (RAS) inhibitors on outcomes in patients with aortic stenosis (AS) is unresolved. We examined the impact of angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II recep-
tor blockers (ARBs) on mortality and risk of aortic valve replacement (AVR) in a nationwide propensity matched cohort of AS patients.  

Methods: By individual-level linkage of the nationwide Danish registers, we iden-
tified all patients with AS from 1997 to 2012. Patients receiving ACEI or ARB treat-
tment at baseline were matched on propensity score with controls not receiv-

*YIA Session: Population Sciences / YIA Session: Clinical Science 331*
ing treatment. Risk of all-cause mortality, cardiovascular mortality or AVR were assessed by Cox regression analyses.

Results: A total of 11 560 patients with AS receiving ACEI or ARB treatment (mean age 76.0 years [SD 10.1], 49.5% male) at baseline were identified and matched with 51 560 patients without treatment (mean age 76.3 years [SD 11.5], 48.7% male). During follow-up, a total of 2902 (11.2%) deaths, 1818 (7.9%) cardiovascular deaths and 2714 (11.7%) AVFs occurred. ACEI and ARB treatment was associated with lower risk of all-cause mortality (hazard ratio [HR] 0.68 [95% CI 0.65–0.72] and HR 0.59 [95% CI 0.49–0.71], respectively), cardiovascular mortality (HR 0.68 [95% CI 0.64–0.72] and HR 0.56 [95% CI 0.52–0.61]), and AVR (HR 0.55 [95% CI 0.52–0.58] and HR 0.60 [95% CI 0.56–0.65]). ARBs were superior to ACEIs in reducing risk of all-cause mortality (p < 0.001) and cardiovascular mortality (p < 0.001).

1848 | BEDSIDE
Sudden death in sport: insights from a national pathology referral center
G. Finocchiaro, M. Papadakis, J.K. Robertus, G. Mellor, E. Behr, S. Sharma, M. Sheppard. St George’s University of London, London, United Kingdom

Background and aims: Sudden deaths (SD) in sport are visible events with significant impact in the communities. The aim of the study was to investigate the burden, the determinants and the most commonly associated aetiologies of SD in a large cohort of physically active subjects.

Methods: From a total of 3684 sudden deaths consecutively referred to a tertiary pathology center from 1994 to 2014 we selected 357 cases (age ≥21 years, males 92%, Caucasian 76%) of individuals who engaged in regular sport activities during life, defined as ≥3h/week of organized physical training (70% competitive athletes). Information about the background were available from the referring coroners and all the patients underwent a complete macroscopic and microscopic evaluation.

Results: The most common aetiology implicated was SD with normal heart (sudden death of unknown origin, SADS) in 24% of the total population (147 cases), followed by cardiomyopathies (9%, 32 cases), while 30% of all cases were secondary to significant underlying cardiac disease. A total of 1849 cases (31%) were investigated further to rule out specific causes of death and 1257 (67.3%) cases were classified as primary SD. The most common aetiology was arrhythmogenic right ventricular cardiomyopathy (ARVC; 225 cases, 12%). The remaining cases were due to other causes: 20% were attributed to atherosclerosis and 28% to other cardiomyopathies, including myocarditis and hypertrophic cardiomyopathy.

Conclusions: SD in athletic population is caused by variable aetiologies according to different age and it occurs more frequently during exertion. ARVC and LV cardiomyopathy (ARVC) were more common in subjects died during exercise (LV fibrosis 39 vs 22%, p < 0.001; ARVC 20% vs 3%, p < 0.001), while SADS was more frequently observed in patients who died at rest (54 vs 34%, p < 0.001). A multivariate analysis showed that ARVC, LV fibrosis and heart weight were independently associated with death during exercise (HR: 6.01, 95% IC 1.97 to 18.32, p = 0.001; HR: 2.11 95% IC 1.15 to 3.88, p = 0.01 and HR 0.96 95% IC 0.95 to 0.97, p = 0.002 respectively).

1847 | BEDSIDE
Low cardiorespiratory fitness predicts arrhythmia recurrence in patients with symptomatic atrial fibrillation

Introduction: Cardiorespiratory fitness (CRF) is an independent predictor of outcomes in patients with cardiovascular disease. There has been little investigation into its relationship with arrhythmia recurrences in AF patients.

Methods: 323 consecutive, symptomatic AF patients (46% non-paroxysmal) and BMI ≥27 kg/m² were followed for a mean duration of 49 ± 18 months. Baseline CRF was assessed by treadmill stress test. Patients were grouped by achieved metabolic equivalents (METs) as a percentage of age and gender predicted values; LOW (< 85%), MOD (85–110%) and HIGH (> 110%). Follow up for AF recurrence consisted of clinic review and 7-day Holter monitoring at 12 monthly intervals. The absence of any arrhythmia ≥30 seconds was determined.

Results: There were no differences in baseline characteristics, number of procedures or follow up duration between groups (p=NS). At final follow-up, ablation free drug unassisted arrhythmia freedom was greater in the HIGH (40.9%) compared to MOD and LOW CRF groups (32% and 12.8% respectively, p < 0.001). Multiple procedure ± drug assisted arrhythmia freedom was markedly better in the HIGH group (83.5%) compared to MOD and LOW CRF groups (73.8% and 39.5% respectively, p < 0.001). On multivariate analysis, baseline CRF status was an independent predictor of outcome. High baseline CRF resulted in a 7.8 fold (95% CI 4.20–14.69, p < 0.001) greater probability of arrhythmia free survival (Fig. 1).

Conclusion: Cardiorespiratory fitness is a predictor of arrhythmia recurrence in a population of symptomatic AF patients. These findings support a possible benefit of improving exercise capacity as a strategy to reduce AF recurrence.

1849 | BEDSIDE
Subclinical left ventricular dysfunction is associated with reduced brain structure and function
C.M. Park1, E.D. Williams1, T. Tiliin2, R. Stewart1, N. Chaturvedi1, A.D. Hughes1, 2. University College London, Institute of Cardiovascular Science, London, United Kingdom; 2King’s College London, London, United Kingdom

Introduction: In our ageing society, the rising prevalence of heart failure (HF) is becoming an increasing concern. Cognitive function has been shown to be significantly affected in HF patients; however the exact mechanisms linking left ventricular (LV) function to cognitive impairment are unknown.

Purpose: To investigate the association between LV function and both functional and structural measures of the brain.

Methods: A community-based sample of 1207 individuals (69±6 yrs) underwent echocardiography and cognitive function assessment using the Community Screening Instrument for Dementia score (CSID). Hippocampal volume was measured by MRI. Fasting bloods including NT-proBNP levels were measured.
Measurements of LV systolic and diastolic function included ejection fraction (EF) and peak shortening velocity in systole (s'), and E- and A- LA diameter (indexed to height2.7 (LADI)) respectively.

Results: After adjusting for age, sex and ethnicity, hippocampal volume was associated with all measures of LV function, except EF (Table 1: Model 1). Cognitive function was significantly associated with NT-proBNP and diastolic but not systolic function. After excluding participants with stroke and further adjusting for diabetes and hypertension (Table 1: Model 2), significant associations remained between hippocampal volume and NT-proBNP and s' but not diastolic function. Associations between CSID and NT-proBNP and LADI also remained significant after adjustment.

Conclusion: In a community-based sample of older people, measures of LV global, diastolic and systolic function were associated with functional and structural changes in the hippocampus.

References were not explained by concomitant risk factors.

YOUNG INVESTIGATORS AWARDS SESSION: BASIC SCIENCE

1850 | BENCH
Platelet-derived growth factor-BB selectively augments non-canonical sonic hedgehog signaling in adventitial fibroblasts
J.-M. Daniel, J. Duttmann, A. Koch, J. Bauersachs, D. Sedding. Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany

Background: Adventitial cells have been shown to contribute to vascular remodeling processes, but the signaling pathways are largely unknown. Sonic hedgehog (Shh) is a regulator of vasculogenesis and promotes angiogenesis in the aorta. The current study contains the adventitia with transcriptional changes mediated by the Gli family of transcription factors and non-canonical pathways excluding Gli-dependent transcription.

Purpose: We analysed the effects of Shh on vascular remodeling processes and described transcriptional mechanisms.

Methods and results: We performed wire-mediated injury of the femoral artery in C57BL/6 mice to induce neointima formation. As determined by immunoblotting and immunohistochemistry, Shh was significantly up-regulated in neointimal cells, whereas the expression of its membrane-bound downstream proteins patched-1 and smoothened (Smoo) were robustly increased in adventitial cells 3 weeks after injury compared to sham-operated controls. In vivo, Shh induced proliferation and migration of human adventitial fibroblasts (AoAF) and human smooth muscle cells (SMC). Importantly, proliferation and migration of AoAF were strongly augmented by stimulation with Shh and additional platelet-derived growth factor (PDGF)-BB compared to Shh or PDGF-BB alone. The specific Smoo inhibitor GDC-0449 (Vismodegib) significantly prevented the proliferative and migratory response of AoAF but not in SMC. Mechanistically, we found that PDGF-BB selectively induced trafficking of Smoo to the plasma membrane of AoAF but not in SMC. This effect was mediated by strongly enhanced activity of the protein kinase A (PKA) and could be nearly completely inhibited by the PKA inhibitor KT5720. Moreover, PDGF-BB-induced activation of PKA resulted in a down-regulation of target genes of the Shh signaling and subsequent oxidative burst in the diabetic heart. These findings are consistent with up-regulated expression of NT-proBNP and diastolic function impairment. These associations were not explained by concomitant risk factors.

1851 | BENCH
CASK is an important regulator of cardiac excitation-contraction coupling
J. Mustrophy 1, S. Gupta 1, A. Dietl 1, F. Baehrel 1, T. Islam 1, A. El-Armouche 2, L.S. Maier 3, S. Wagner 1, 2. Dept. Cardiology, University Medical Center, Goettingen, Germany; 3. Technical University of Dresden, Department of Pharmacology and Toxicology, Dresden, Germany; 4. University Hospital Regensburg, Klinik und Poliklinik für Innere Medizin II, Regensburg, Germany

Rationale: The scaffolding-protein CASK has previously been shown to inhibit CaMKII activity in neurons. CaMKII is critically involved in heart failure (HF) development. The significance of CASK in the heart, however, is completely unknown.

Objective: We investigated the impact of CASK expression on excitation-contraction coupling.

Methods and results: CASK expression was measured (western blotting) in left ventricular biopsies of explanted hearts from heart transplant recipients with dilated cardiomyopathy (DCM); not transplanted healthy donor hearts served as controls (NF). CASK was robustly expressed in the heart. Interestingly, CASK expression (relative to GAPDH) was significantly increased in DCM vs. NF (density-ometric values: 0.89±0.05 vs. 0.7±0.05, n=6 each, P<0.05). Intracellular Ca was measured in Fluor-4-loaded ventricular myocytes isolated from cardiomyocytes-specific CASK knockout (KO) mice (wildtype. WT, littermates as control). Compared to WT, Ca transient amplitude was significantly reduced in KO (F/F0 KO vs WT, 2.75±1.3 vs. 3.84±1.75, n=30 vs n=45, P<0.05). In accordance, caffeine (10mM)-induced Ca transients as a measure of sarcoplasmic reticulum (SR) Ca content were significantly smaller in KO vs WT (F/F0: 4.81±2.7 vs. 16±1.6, n=21 vs n=26, P<0.01). KO myocytes also showed a delayed Ca transient decay, a functional measure of SR Ca ATPase. Ca transient decay RT80 was 0.41±0.15 vs. 0.13±0.10 s, KO vs WT, n=30 vs n=46, P<0.05. Spontaneous SR Ca sparks were measured using confocal microscopy. Compared to WT, KO mice showed a significantly increased SR Ca spark frequency (Total leak: KO, n=15; WT, n=15; SR Ca spark frequency in KO: 3.0±1.2 vs. 3.6±1.8, n=30 vs n=40, P<0.05). Late Na current, known to be enhanced by CaMKII, was also increased in KO vs WT (whole-cell patch clamp). Late Na currents were -0.83±0.35 vs. -5.53±3.7 Ams/F (KO vs WT, n=10 vs n=10, P<0.05). Moreover, in the mannose 6-phosphate receptor (M6PR) knockout (KO) mice, i.p. isoproterenol injection revealed a significantly increased propensity for ventricular arrhythmias in KO mice. Arrhythmias were inducible in 5 of 11 (KO) vs. 0 of 10 mice (WT, P<0.05 Fisher’s exact test).

Conclusion: KO of CASK in mice results in profound dysregulation of excitation-contraction-coupling possibly by lack of inhibition of CaMKII activity. Increased CASK expression in HF may be beneficial by limiting CaMKII activity.

1852 | BENCH
miR-218 and miR-34a induce oxidative stress by orchestrating epigenetic remodelling of DNA/histone complexes in the diabetic heart
S. Costantini 1, F. Paneni 1, L. Berrino 1, M. Volpe 1, T.F. Luscher 2, F. Cosentino 1
1. Karolinska Institute, Cardiology Unit, Stockholm, Sweden; 2. Second University of Naples, Pharmaco-Naples, Naples, Italy; 3. Sapienza University of Rome, Rome, Italy; 4. Cardiovascular Research, Physiology Institute, University of Zurich, Zurich, Switzerland

Background: Intensive glycemic control (IGC) does not reduce the risk of heart failure in patients with diabetes. The molecular cues underpinning persistent myocardial damage despite IGC remain poorly understood. Epigenetic regulatory systems, namely microRNAs and chromatin modification, may contribute to susceptibility and development of cardiovascular diseases.

Purpose: We investigate whether epigenetic networks participate to persistent hyperglycaemia-induced myocardial dysfunction despite IGC.

Methods: 4-month-old C57BL/6J mice (n=30) were used. 28-month-old mice were induced with streptozotocin and animals were followed for 6 weeks. IGC was achieved by slow-release insulin implants placed subcutaneously 3 weeks after the induction of diabetes, and maintained for the remaining 3 weeks. Mouse miRNA profiling was investigated by real-time PCR array in myocardial samples from controls, diabetics and diabetic mice treated with insulin. DNA methylation was detected by bisulfite analysis of transcriptionally active CpG sites whereas chromatin immunoprecipitation (ChIP) was employed to study histone modifications. Mitochondrial levels of superoxide anion (O2-) were detected by ESR spectroscopy. Left ventricular (LV) function was assessed by high resolution Micro-Ultrasound System (Veo 2100, Visualsonics).

Results: Mitochondrial oxidative stress was significantly increased in the diabetic heart and 3-week IGC did not revert this phenomenon. Consistently, normal glycemia restoration did not restore diabetes-related LV dysfunction, assessed by ejection fraction, fractional and fractional shortening, and miRNA analysis revealed that miR-218 and miR-34a were profoundly dysregulated in the heart of diabetic mice, and IGC did not restore their expression. We found that miR-218 and miR-34a respectively caused persistent downregulation of methyltransferase enzymes DNMT1 in both diabetes and diabetic hearts. Disturbed DNMT3b/SIRT1 axis triggered DNA demethylation and histone 3 acetylation, leading to enhanced transcription of the pro-oxidant mitochondrial adaptor p66Shc. Interestingly, in vivo siRNA of p66Shc blunted ROS production while restoring LV function in diabetic mice with IGC.

Conclusions: We show here that a complex epigenetic machinery involving miR-218/34a and DNMT3b/SIRT1 signalling may explain persistent p66Shc overexpression and subsequent oxidative burst in the diabetic heart. These findings provide molecular insights to understand the lack of benefit of glycemic control on diabetic cardiomyopathy phenotype. Targeting epigenetic changes may prevent or delay cardiac dysfunction in patients with diabetes.

1853 | BENCH
Titin phosphorylation by PKG as a mechanism of acute adaptation to myocardial stretch
A.M. Leite Moreira 1, J. Almeida-Coelho 1, J.S. Neves 1, M. Neiva-Sousa 1, A.M. Leite Moreira 1, J. Almeida-Coelho 1, J.S. Neves 1, M. Neiva-Sousa 1, Moreira1 on behalf of Myocardial Function Study Group. 1. Faculty of Medicine University of Porto, Physiology and Cardiothoracic Surgery, Porto, Portugal; 2. Ruhr University Bochum (RUB), Cardiovascular Physiology, Bochum, Germany

Introduction: Acute myocardial stretch leads to an increase in contractility and a progressive decrease in myocardial stiffness. Titin is the main determinant of passive tension at physiological sarcomere lengths and its distensibility is increased by acute shortening of titin by its 218/34a-dependent protein kinase (PKG). PKG can be activated by nitric oxide (NO) and nitrate-rich peptides (NPs), which are mediators released upon acute stretch.

Methods: Myocardial strips dissected from left ventricle (n=10) and right atrium...
Influence of childhood socioeconomic disadvantage in the incidence of cardiovascular disease in adults in Chile

C. Nazzl1, F. Frenz1, F. Cercera2, G. Cavada1, J. Kaufmann2, University of Chile, School of Public Health, Santiago, Chile; Canada

Background: The theory posits that socioeconomic disadvantage in childhood is associated with development of adult cardiovascular disease (CVD) through different mediating pathways, including health behaviors associated with risk factors and adult socioeconomic position (SEP). The aim of the study is to determine the effect of low socioeconomic position (low PSE) in childhood on the incidence of CVD in a Chilean cohort, before and after adjustment for risk factors and other covariates.

Methods: The longitudinal analysis of a representative sample of Chilean adult population uses data from the Social Protection Survey of the Ministry of Labor and Social Welfare, with measurements in the years 2004, 2006 and 2009. The self-reported information includes measures of SEP in childhood (child poverty and SEP index), inter-generational, per capita household income and health insurance system, risk factors (BMI, diabetes) and incidence of CVD (reported as hypertension, “heart problems” and “stroke”). Population averaged relative risks for CVD incidence and 95% confidence intervals were estimated using generalized estimation equations (Poisson family and link-function, adjusted for age, sex, risk factors, adult SEP and use of medical care).

Results: The analysis included 18,140 subjects, mean age 48.0±16.1 years; 50.2% male; average 9.7±4 years of schooling and 44.3% reported low SEP in childhood. 7.2% reported diagnosis of diabetes, 41.4% overweight and 16.8% obese. The incidence of CVD was 22.9%. Multivariable analysis showed age-adjusted RR=1.08; CI 1.04 to 1.13 for low SEP in childhood. After adjusting for risk factors the effect of low SEP remains significant (RR=1.07; CI 1.03 to 1.12). The final adjustment, which includes sex, adulthood SEP and the likelihood of medical care reduces the magnitude of the association (RR=1.05; CI 1.00 to 1.10).

Conclusion: The effect of low SEP in the childhood on CVD risk persists after controlling for adult socioeconomic circumstances and presence of risk factors. These findings reinforce the importance of considering the socioeconomic trajectory of social groups in policies for prevention and control of CVD.

Acknowledgement/Funding: FONS (governmental grant)
Purpose: Our study investigates the comparison between pre-hospital chest pain triage by ambulance nurses with hospital physicians triage at the ER using the modified-HEART score, where “T” is a single high sensitive Troponin T (hs-cTnT) measurement.

Methods: Patients with acute onset chest pain (STEMI excluded) who called the EMS, from June 2013 to December 2014 were assessed at FMC by ambulance nurses. The hs-cTnT blood sample being taken and the HEAR score assessed, as to establish an ambulance modified-HEART score. All patients were transported to the ER and managed by emergency physicians according to standard care without knowledge of the pre-hospital hs-cTnT result. The hospital modified-HEART score was established using medical records. Both the ambulance- and the hospital modified-HEART score agreement were assessed using Cohen’s Kappa statistics.

Results: A total of 548 patients were included. Results are depicted in Table 1. Overall, there was a moderate agreement between the two disciplines (Kappa statistics. 0.05). Leukocyte-derived and platelet-derived microparticles (PMPs) at inclusion and after 1 year (n=99). 32 patients from the REBUS sub-study were included for miRNA analysis at inclusion and after 1 year (n=26).

Conclusion: To investigate if microRNAs (miRNAs) post-transcriptional regulate the TF expression as its 3'UTR contains predicted binding-sites for several miRNAs. Methods: TaqMan Array Human MicroRNA A+B Cards were used to screen for differentially expressed miRNAs in a cell based system where TF can be down- regulated. The Dual-Luciferase Reporter (DLR) Assay system (Promega) was used to investigate if miR-223–3p and the 3'UTR of F3 functionally interact. 105 patients with ACS defined as NSTEMI or STEMI included in the REBUS (Relevance of Biomarkers for future risk of thromboembolic events in Un Selected post-myocardial infarction patients) study were included in a biomarker sub-study. Using flow cytometry TF surface expression was analysed on platelets and CD62P+ platelet-derived microparticles (PMPs) at inclusion and after 1 year (n=99). 32 patients from the REBUS sub-study were included for miRNA analysis at inclusion and after 1 year (n=26).

Results: 211 differentially expressed miRNAs were identified in the screen during TF down-regulation. One of these, miR-223–3p, has a predicted binding site in the 3'UTR of F3. In U937–1 cells undergoing differentiation with vitamin D3 miR-223–3p increased over time while F3 expression decreased. Transfecting a synthetic miR-223–3p mimic into the high level TF expressing human breast cancer cell-line MDA-MB-231 led to a significant reduction in TF expression. The Dual Luciferase assay confirmed binding of miR-223–3p directly to the 3'UTR of F3. In ACS patients we found that miR-223–3p expression was significantly reduced in patients one year after the acute event (p<0.001) and this reduction the levels of circulating TF are elevated for months after the first cardiac event, proving that the molecular regulation of F3, the human TF gene, is complex and needs to be explored further.

Conclusion: The molecular regulation of F3, the human TF gene, is complex and needs to be explored further.

Interobserver variability

<table>
<thead>
<tr>
<th>Hospital modified-HEART score</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>low risk (0–3)</td>
<td>108</td>
</tr>
<tr>
<td>intermediate risk (4–6)</td>
<td>80</td>
</tr>
<tr>
<td>high risk (7–10)</td>
<td>27</td>
</tr>
<tr>
<td>low risk (0–3)</td>
<td>135</td>
</tr>
<tr>
<td>intermediate risk (4–6)</td>
<td>32</td>
</tr>
<tr>
<td>high risk (7–10)</td>
<td>105</td>
</tr>
</tbody>
</table>

Conclusions: Pre-hospital triage of patients with acute onset chest pain by ambulance nurses, using the modified-HEART score model may be feasible and might help in optimizing logistics for patients with chest pain before hospital admission. However, prior to its implementation in clinical practice sufficient training of ambulance nurses is required.

Acknowledgement/Funding: None

MICROPARTICLES, VESICLES, EXOSOMES AND MiRNA: COMMUNICATION IN CARDIOVASCULAR PATHOLOGY

1952 | BENCH

Endothelial microparticles reduce neointimaformation and vascular smooth muscle cell proliferation in a microRNA-126-LRP6-dependent mechanism

F. Jansen, T. Stumpf, G. Nickenig, N. Werner. University Hospital of Bonn, Medical Clinic II, Bonn, Germany

Background: We explored the effect of Endothelial microparticles on neointima formation in a model of acute vascular injury in vivo and on VSMC proliferation and migration in vitro.

Methods and results: Mice treated with EMP showed a significantly reduced neointima formation. Furthermore, VSMCs treated with EMP displayed significantly reduced proliferation and migration capacities in vitro with critical steps in neointima formation. Following experiments revealed a time-dependent uptake of EMP into VSMCs in vitro and into the media of perfused vessels in vivo. To dissect the underlying mechanisms of EMP-promoted inhibition of VSMC proliferation, Taqman microRNA-array was performed and microRNA (miR)-126 was identified as the predominantly expressed miR in EMP. Furthermore, miR-126 was transported into recipient VSMC by EMP. Expression of miR-126 target protein LRP6, regulating VSMC proliferation, was reduced in VSMCs after EMP treatment. Genetic knockdown of miR-126 in EMP abrogated EMP-mediated inhibition of LRP6 expression and subsequently VSMC migration and proliferation in vivo and neointimaformation in vivo, suggesting a crucial role of miR-126 in EMP-mediated neointima formation reduction. Finally, expression analysis of miR-126 in circulating MPs in 176 patients with coronary artery disease revealed that patients with high level of miR-126 within circulating MPs have a significantly reduced MACE- and revascularization rate in a 6-year follow up period, supporting a role for miR-126 in the regulation of MACE in patients with coronary artery disease.

Conclusions: EMP reduce neointima formation and decrease proliferation and migration of vascular smooth muscle cells in a microRNA-126-LRP6-dependent mechanism

1953 | BENCH

MiR-223-3p post-transcriptionally regulates the expression of F3, the human tissue factor gene, and TF expression in acute coronary syndrome

A. Siegbahn, C. Christersson2, J. Alfredsson, L. Uppsala University, Department of Medical Sciences, Clinical Chemistry, Uppsala, Sweden; 2Uppsala University Hospital, Department of Medical Sciences, Cardiology, Uppsala, Sweden

Background: Tissue Factor (TF), the main initiator of blood coagulation, initiates thrombosis on disrupted atherosclerotic plaques which plays an essential role during the onset of acute coronary syndromes (ACS). TF mRNA transcripts are rapidly turned-over (half-life 45–90 minutes), though in ACS patients the levels of circulating TF are elevated for months after the first cardiac event, proving that the molecular regulation of F3, the human TF gene, is complex and needs to be explored further.

Purpose: To investigate if microRNAs (miRNAs) post-transcriptional regulate the TF expression as its 3'UTR contains predicted binding-sites for several miRNAs. Methods: TaqMan Array Human MicroRNA A+B Cards were used to screen for differentially expressed miRNAs in a cell based system where TF can be down-regulated. We explored the effect of Endothelial microparticles on neointima formation in a model of acute vascular injury in vivo and on VSMC proliferation and migration in vitro.

Methods: VSMCs treated with EMP displayed significantly reduced proliferation and migration capacities in vitro with critical steps in neointima formation. Following experiments revealed a time-dependent uptake of EMP into VSMCs in vitro and into the media of perfused vessels in vivo. To dissect the underlying mechanisms of EMP-promoted inhibition of VSMC proliferation, Taqman microRNA-array was performed and microRNA (miR)-126 was identified as the predominantly expressed miR in EMP. Furthermore, miR-126 was transported into recipient VSMC by EMP. Expression of miR-126 target protein LRP6, regulating VSMC proliferation, was reduced in VSMCs after EMP treatment. Genetic knockdown of miR-126 in EMP abrogated EMP-mediated inhibition of LRP6 expression and subsequently VSMC migration and proliferation in vivo and neointimaformation in vivo, suggesting a crucial role of miR-126 in EMP-mediated neointima formation reduction. Finally, expression analysis of miR-126 in circulating MPs in 176 patients with coronary artery disease revealed that patients with high level of miR-126 within circulating MPs have a significantly reduced MACE- and revascularization rate in a 6-year follow up period, supporting a role for miR-126 in the regulation of MACE in patients with coronary artery disease.

Conclusions: EMP reduce neointima formation and decrease proliferation and migration of vascular smooth muscle cells in a microRNA-126-LRP6-dependent mechanism

1954 | BENCH

Differential effects of microRNAs from patients with coronary artery disease as compared to healthy subjects on endothelial cell functions: critical role of miR-222

N. Kraenkel1, S. Briand2, E. Straessler2, T.F. Luescher3, U. Landmesser1. 1Charité - Universitätsmedizin Berlin, Berlin, Germany; 2University of Zurich, Center for Molecular Cardiology, Zurich, Switzerland; 3University Hospital Zurich, Heart Center, Zurich, Switzerland

Background: Shed microvesicles (SMV) within the circulation might originate from various cell types. We hypothesized that SMV release from leukocytes is enhanced in coronary artery disease (CAD), an inflammatory condition, and might affect the molecular composition (e.g. microRNA content) of SMVs and their effect on the vascular endothelium.

Methods: SMVs were isolated from plasma of healthy subjects with patients with CAD. Flow cytometry was used to quantify platelet, endothelial cell and leukocyte-derived SMVs. The capacity of SMV-to-endothelial cell MV-s for SMV-to-endothelial cell survival, inflammatory activation and re-endothelialisation was assessed following ex vivo exposure. Content of pro-apoptotic, pro-angiogenic and pro-inflammatory miR species was quantified by RT-qPCR. SMVs of H or CAD donors were transfected with electroporation with mirco or PowerInhibitor of miR-222 or with scramble control oligonucleotide (con) prior to washing and exposure to endothelial cells.

Results: While SMV of healthy donors (H) supported in vitro re-endothelialisation (27.7±1.3% increase vs. PBS), SMVs from CAD patients had lost this capacity (0.8%±8.5% decrease vs. PBS; p<0.05). Leukocyte-derived and endothelial cell-derived SMVs, but not overall SMVs or platelet-derived SMVs were increased in patients with CAD. The number of leukocyte-derived SMVs

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475/1/163330974757/guest on 07 February 2019
among the overall SMV population negatively correlated with the SMV ability to support in vitro re-endothelialization and to counteract endothelial cell apoptosis. SMVs of CAD patients contained higher levels of miR-222 (163.5±%±7.2% increase vs. H; P<0.05). Transfection of SMV from H donors with mimic of miR-222 impaired SMV capacity to stimulate in vitro re-endothelialization (SB431542) to 14.8% decrease vs. control transfection (con; P<0.05) as well as proliferation (16.0%±6.3% decrease vs. con; P<0.05), with proliferation reaching (25.6%±1.1% increase vs. con; P<0.05).

Conclusions: In CAD, increased circulating levels of leukocyte SMVs may contribute to the impairment of endothelial dysfunction. Leukocyte SMVs might feature a different molecular composition to SMVs from other cell types, including the pro-inflammatory miR-222. In vitro modulation of miR content might improve SMV effects on the endothelium.

1955 | BENCH

TGFβ triggers miR-143/145 transfer from smooth muscle cells to endothelial cells through tunneling nanotubes

L. Elia, M. Climent Salarich, G. Condorelli, M. Quintavalle. Clinical Institute Humantitas IRCCS, Razzano, Italy

Rationale: The miR-143/145 cluster is highly expressed in smooth muscle cells (SMCs), where it regulates phenotypic switch and vascular homeostasis. Whether it plays a role in neighboring endothelial cells (ECs) is still unknown.

Objective: To determine whether SMCs control EC functions through passage of miR-143 and miR-145.

Methods and results: We used co-cultures of SMCs and ECs under different conditions as well as intact vessels to assess the transfer of miR-143 and miR-145 to ECs and vice versa. We found that the two miRNAs are transferred from SMCs to ECs through membrane protrusions known as tunneling nanotubes. Furthermore, we show that this transfer is modulated by the transforming growth factor beta (TGFβ) pathway, since a specific TGFβ inhibitor (SB431542) suppresses the passage of miR-143/145 to ECs. Moreover, miR-143 and miR-145 modulated angiogenesis by reducing the proliferation index of ECs and their capacity to form vessel-like structures when cultured on matrigel. We also identified hexokinase II (HKII) and integrin beta 8 (ITGb8)—two genes essential for angiogenic potential of ECs—as targets of miR-143 and miR-145, respectively. The inhibition of these genes modulated EC phenotype similarly to miR-143 and miR-145 overexpression in ECs. These findings were confirmed by ex vivo and in vivo approaches, in which respectively TGFβ and vessel stress markers miR-143 and miR-145 were tested. Conclusion: Our results demonstrate that miR-143 and miR-145 act as communication molecules between SMCs and ECs to modulate the angiogenic and vessel stabilization properties of ECs.

Acknowledgement/Funding: Italian Ministry of Health (MIUR #GR2010- 2302354) and Marie Curie Action (PIRGP08-GA-2010-276993)

1956 | BENCH

MicroRNA-155 exerts cell-specific anti-angiogenic but pro-arteriogenic effects during adaptive neovascularization

F. Pankratz1, X. Bentgen1, R. Zeiser2, I. Hilgendorf1, C. Smolka1, T. Helbing1, I. Hoefler1, M. Moser1, C. Bode1, S. Grundmann1, 1 University Heart Center Freiburg, Cardiology and Angiology I, Freiburg, Germany; 2 University Hospital Freiburg, Internal Medicine I, Freiburg, Germany; 3 University Medical Center Utrecht, Utrecht, Netherlands

Background: Adaptive neovascularization after arterial occlusion is an important compensatory mechanism in cardiovascular disease and includes both the remodeling of pre-existing vessels to collateral arteries (arteriogenesis) as well as angiogenic capillary growth. We now aimed to identify regulatory microRNAs (miRNAs) involved in the modulation of neovascularization after femoral artery occlusion in mice.

Methods and results: Using miRNA-transcriptome analysis, we identified miR-155 as a downregulated miRNA during hindlimb ischemia. Correspondingly, inhibition of miR-155 in umbilical vein endothelial cells (HUVECs) had a stimulatory effect on proliferation and angiogenic tube formation via de-repression of its direct target gene angiotensin II type 1 receptor. Surprisingly, miR-155 deficient mice showed an unexpected phenotype in vivo with a strong reduction of blood flow recovery after femoral artery ligation (arteriogenesis) and a decreased number of infiltrating circulating cells as well as an attenuated expression of the pro-angiogenic cytokine TGFα-alpha in ischemic muscle tissue. Following these results, we found a weakened endothelial-leukocyte interaction in a model of intravital microscopy as well as a reduced migration capacity of bone marrow derived macrophages (BMMDC) compared to wildtype controls. Consistent with these results, we also found an impaired pro-angiogenic cytokine/chemokine production profile of BMDM lacking miR-155, mediated by a direct targeting of suppressor of cytokine signaling (SOCS-1) by miR-155. These data implicated that the defective phenotype of miR-155 deficient mice following hindlimb ischemia was mainly mediated by circulating cells. However, transplantation experiments showed that wildtype mice transplanted with miR-155−/− bone marrow cells displayed a comparable phenotype to global miR-155−/− mice, indicating that miR-155 also affected vascular inflammatory properties, independent of circulating cells. Indeed, we found that this miRNA regulates endothelial adhesion molecule expression in murine endothelial cells by suppressing ASTR1.

Conclusion: Our data demonstrate a divergent role of miR-155 in regulation of the different forms of vascular growth via the suppression of different target genes. Its expression in both endothelial and bone marrow derived cells is essential for arteriogenesis in response to hindlimb ischemia in mice.

1957 | BENCH

EMMPRIN is a major pro-angiogenic component of cardiac progenitor cell derived exosomes

J.A. van der Boom1, K.R. Vrijen2, V. Verheugen1, P.A.F.M. Doevendans3, S.H. Charefu1, M.J. Goumans1, J.P.G. Sluiter1, 1 Leiden University Medical Center, Molecular Cell Biology, Leiden, Netherlands; 2 University Medical Center Utrecht, Utrecht, Netherlands

Background: Exosomes are small nano-sized vesicles carrying cell-specific content including miRNAs, miRNAs and proteins. Exosomes secreted by human cardiomyocyte progenitor cells (CMPs) are able to induce endothelial cell migration and sprout formation in vitro, and can therefore be considered an important mediator in the angiogenic process during tissue repair. Several pro-angiogenic factors are present in CMP-derived exosomes, of which one is the extracellular matrix metalloproteinase inducer (EMMPRIN). EMMPRIN plays an important role in angiogenesis by inducing the production of for example MMPs and VEGF, thereby promoting extracellular matrix modulation and activation of endothelial cells. Here, we investigated the role of exosome-derived EMMPRIN in angiogenesis.

Purpose: To elucidate the role of EMMPRIN in the pro-angiogenic effect of exosomes from CMPs.

Methods: Exosomes were isolated from CMP-conditioned medium by differential centrifugation. The presence of EMMPRIN was assessed by nanosight, sucrose-gradient separation and Western Blotting. The angiogenic potential of CMP exosomes was assessed by accepted assays for endothelial cell migration (in vitro and in vivo). The functional involvement of EMMPRIN was assessed by using an EMMPRIN neutralizing antibody and by knockdown of EMMPRIN in the donor CMPs and their secreted exosomes.

Results: CMPCs release exosomes that are characterized by traditional sizes (30–100nm) and marker expressions (CD9, CD63, CD81). Moreover, they are enriched for EMMPRIN and able to induce endothelial cell migration, tubule formation and sprouting and are therefore pro-angiogenic. Incubation of endothelial cells with EMMPRIN antibody-neutralized exosomes resulted in an abrogation of exosome stimulated endothelial cell migration. Knockdown of EMMPRIN in CMPs sufficiently reduced the migration of endothelial cells (45.1% vs 61.8% scratch closure) in vivo. In vivo matrigel plug assays, migration of endothelial cells with EMMPRIN knockdown exosomes was markedly reduced compared to migration with controlCMP exosomes.

Conclusion: EMMPRIN is enriched in CMP derived exosomes, and is a major component of their pro-angiogenic activity. Reduction of EMMPRIN levels on exosomes inhibits their pro-angiogenic effects in vivo and in vitro angiogenesis assays.

1958 | BENCH

Exosomes secreted from dentritic cells enhance tube formation in cardiac microvascular endothelial cells after myocardial infarction

H. Liu1, J. Yuan1, W. Gao1, C. Wu1, K. Yao1, L. Zhang1, X. Guo2, W. Yu2, Y. Zou1, J. Ge1, 1 Zhongshan Hospital, Fudan University, Shanghai Institute of Cardiovascular Diseases, Shanghai, China; People’s Republic of; 2 Yinzhou People’s Hospital Affiliated to Medical school of Ningbo University, Clinical Laboratory Center, Ningbo, China, People’s Republic of

Introduction: The infiltration of dentritic cells (DCs) significantly increased in infarcted myocardium and DCs ablation impaired angiogenesis after myocardial infarction (MI) in mice. However, the mechanism of how DCs exert effects on MI is still not completely understood. Exosome (EX) has been known as the messenger between cells, we therefore hypothesize that DCs could enhance myocardial angiogenesis post-MI by secretion of EXs.

Purpose: To clarify whether EXs derived from DCs induce angiogenesis via paracrine signaling post-MI.

Methods: Mouse bone marrow-derived DCs (BMDCs) suspensions were incubated with normal or infarcted hearts for 24 hr respectively (as necrosis or control group). EXs were isolated from the supernatant of necrotic or normal HL-1 myocardial cells for 24 hrs as an exosome source. Normal and necrosis BMDCs derived exosomes (EXs) were collected and transfected with mimic or inhibitor of miRNA-222, miR-143 and miR-145. Transfection of SMV from H donors with mimic or inhibitor of miR-143 or miR-145 impaired SMV capacity to stimulate in vitro re-endothelialization (46.1%±13.1% increase vs. con; p<0.05). Transfection of SMV from H donors with inhibitor of miR-143 or miR-145 impaired SMV capacity to stimulate in vitro re-endothelialization (25.6%±7.1% increase vs. con; p<0.05), with proliferation reaching (25.6%±1.1% increase vs. con; p<0.05).

Conclusions: In CAD, increased circulating levels of leukocyte SMVs may contribute to the impairment of endothelial dysfunction. Leukocyte SMVs might feature a different molecular composition to SMVs from other cell types, including the pro-inflammatory miR-222. In vitro modulation of miR content might improve SMV effects on the endothelium.
significantly lower amounts of miR-222 and showed reduced anti-inflammatory
strated that miR-222 was transported into recipient endothelial cells by EMP and
lated miR between EMP and endothelial cells. Following experiments demon-
was performed and microRNA (miR)-222 was identified as the strongest regu-
plaques. In order to explore the underlying mechanisms, Taqman microRNA-array
endothelial ICAM-1 expression and infiltration of macrophages into atherosclerotic
systematic treatment of ApoE−/− mice with EMP significantly reduced murine en-
there was no effect on VCAM-1 expression. Reduced ICAM-1 expression af-
induced endothelial ICAM-1 expression on mRNA and protein level, whereas
In vitro, EMP treatment significantly reduced TNF-
Methods and results: In vitro, EMP treatment significantly reduced TNF-α-
induced endothelial ICAM-1 expression on mRNA and protein level, whereas
there was no effect on VCAM-1 expression. Reduced ICAM-1 expression af-
ter EMP treatment resulted in diminished monocyte adhesion in vitro. In vivo,
A: DEXs uptake by CMECs  b: the enlarge imaging of A  c: the 3D imaging
recognised that DEXs is highly enriched in DEXs from necrosis group compared to those from control group.

Conclusions: These results suggest that exosomal miRNA especially angio-
genetic miRNA could be secreted from DCs and promote angiogenesis post-MI. Our study may present a potent and novel DEXs-based therapeutic approach for MI treatment.

Acknowledgement/Funding: National Natural Science Funds of China (Grant No 81230007, 81200147, 81400263, 81470386)

1959 | BENCH
Endothelial microparticles reduce ICAM-1 expression in a microRNA-222-dependent mechanism

F. Jansen, K. Baumann, G. Nickenig, N. Werner. University Hospital of Bonn, Medical Clinic II, Bonn, Germany

Objective: Endothelial microparticles (EMP) are released from activated or apop-
totic endothelial cells (ECs) and can be taken up by adjacent endothelial cells, but their effect on vascular inflammation after engulfment is largely unknown. We sought to determine the role of EMP in endothelial cell inflammation.

Methods and results: In vitro, EMP treatment significantly reduced TNF-α-induced endothelial ICAM-1 expression on mRNA and protein level, whereas there was no effect on VCAM-1 expression. Reduced ICAM-1 expression after EMP treatment resulted in diminished monocyte adhesion in vitro. In vivo, systemic treatment of ApoE−/− mice with EMP significantly reduced murine endothelial ICAM-1 expression and infiltration of macrophages into atherosclerotic plaques. In order to explore the underlying mechanisms, Taqman microRNA-array was performed and microRNA (miR)-222 was identified as the strongest regulated miR between EMP and endothelial cells. Following experiments demonstrated that miR-222 was transported into recipient endothelial cells by EMP and functionally regulated expression of its target protein ICAM-1. Interestingly, after simulating diabetic conditions, EMP derived from glucose-treated ECs contained significantly lower amounts of miR-222 and showed reduced anti-inflammatory capacity in vitro and in vivo.

Conclusions: Endothelial microparticles promote anti-inflammatory effects in vitro and in vivo by reducing endothelial ICAM-1 expression via the transfer of functional microRNA-222 into recipient cells. In pathological hyperglycaemic conditions, EMP-mediated miR-222-dependent anti-inflammatory effects are reduced.

1961 | BENCH
Mir-33 antagonism increase cholesterol efflux and atheroma regression by increasing caveolin-1 expression in hypercholesterolemia rabbits

W.W. Lin1, M.F. Lee2, W.T. Chao3, K.Y. Wang1. 1 Taichung Veterans General Hospital, cardiovascular center, Taichung, Taiwan, ROC; 2 Taichung Veterans General Hospital, medical research center, Taichung, Taiwan, ROC; 3 Tunghai University, life science department, Taichung, Taiwan, ROC

Introduction: Mir-33 embedded within introns of the SRBEP gene, inhibits the expression of ABCA1, thereby attenuating cellular cholesterol efflux to nascent HDL. Antagonism of miR-33 promotes reverse cholesterol efflux (RCT) and regression of atherosclerosis in both mice and non-human primates. Caveolin-1 also regulates cellular cholesterol homeostasis and promotes RCT. However the relation between miR-33 and caveolin-1 remain unknown.

Purpose: We aimed to clarify the interaction between miR-33 and caveolin-1 on HDL-mediated cholesterol efflux in J774 macrophage and hypercholesterolemia rabbits.

Methods: Rabbits (N=5 per group) were fed with 2% high cholesterol diet. At the end of 5 weeks, rabbits were injected subcutaneously with 5 mg/kg antisense miR-33 or mismatch anti-miR-33 or saline twice weekly for 2 weeks and then weekly for another 3 weeks, than sacrificed at end of 8 weeks. In vitro study, J774 cells were loaded with 100 μg/ml cholesterol in DMEM, incubating the cells for 24–48 h at 37°C, then transfected with 60nM miR33 antagonist.

Results: Hypercholesterolemia rabbits treated with anti-miR-33 showed increase plasma HDL level and atheroma regression in aortic arch (figure 1). ABCA1 and caveolin-1 expression were increased in both aortic endothelial cell and J744 cell after anti-miR-33 treatment. Cholesterol efflux was also increased in J744A cells after treatment. On the contrary, the expression of ABCA1, caveolin-1 decreased and cholesterol efflux reduced after caveolin-1 siRNA transfection. MiR-33 expression were increased after caveolin-1 siRNA treatment.

Conclusion: These findings demonstrate that caveolin-1 play an important role in miR33 regulated lipid metabolism, and may identify a new target for enhance cholesterol efflux and atherosclerosis treatment.

1960 | BENCH
Inflammasome-induced intercellular signalling mechanisms via microparticles

P. Pfeifer1, F. Jansen1, S. Zimmer1, K. Baumann1, E. Latz2, B. Franklin2, G. Nickenig1, N. Werner1. 1 University Hospital Bonn, Department of Internal Medicine II Cardiology, Pneumology, and Angiology, Bonn, Germany; 2 University Hospital Bonn, Institute of Innate Immunity Biomedical Center, Bonn, Germany

Background: The inflammasome has been shown to be an important mediator in the development of atherosclerosis. Microparticles (MPs) are small membrane vesicles, which are released from apoptotic cells. Whether inflammasome activation leads to the release of MPs by vascular cells is unknown.

Methods and results: Human coronary artery endothelial cells (HCAEC) and monocytes were primed with 1 μg/ml LPS 4h and subsequently stimulated with either 5μM ATP or 20 μM Nigericin, two established inflammasome activators. MP release was quantified by flow cytometry using TruCount tubes. Stimulation of HCAEC and monocytes with both Nigericin and ATP resulted in a time-dependent release of MPs. Highest MMP-release by THP-1 cells was detected after stimulation with ATP for 24h (Mean: 14682±2477 MMP/μl) and Nigericin for 8h (Mean: 37107±6727 MMP/μl). Highest EMP-release by HCAEC was detected after stimulation with ATP for 8h (Mean: 79121±1074 EMP/μl) and Nigericin for 4h (Mean: 46586±6594 EMP/μl). Inflammasome activation in THP-1 cells using ATP and Nigericin was confirmed by the release of IL-1β into the cell supernatant (ATP: Mean: 43±2 pg/ml; Nigericin: Mean: 80±2.6 pg/ml). While there was much less release of IL-1β detectable in supernatant of HCAEC treated with 100ng/ml TNF-α for 24h, subsequent treatment with 1μg/ml LPS for 4h followed by treatment with 20μg/ml Nigericin (Mean: 2.16±0.32 pg/ml). Inflammasome activation in HCAEC treated for 24h with 100ng/ml TNF-α and subsequently for 24h with 5μM ATP could be shown by Caspase-1 Assay (Activity: 2.02 fold of control), while treatment of these cells with Nigericin, TNF-α or LPS alone did not lead to an activation of Caspase-1. Inoculation of HCAEC for 2h with EMP derived from HCAEC treated with 100ng/ml TNF-α for 24h, subsequent treatment with 1μg/ml LPS for 4h followed by inoculation with 20μg/ml Nigericin for 48h lead to significant cell death shown by Viability Assay (Mean: 72% ± 6.86%; Cell Viability). Furthermore, treatment of HCAEC with EMP derived from HCAEC treated with 1μg/ml LPS for 4h and subsequent treatment with 20μg/ml Nigericin for 48h lead to reduced cell migration and proliferation shown by Scratch Assay (73% cell free area after 24h).

Conclusions: We show for the first time that Nigericin and ATP, two established inflammasome activators, lead to inflammasome activation and release of mi-
croparticles by vascular cells. Furthermore, we could demonstrate that these mic-
roparticles, when given to other vascular cells, cause cell death accompanied with reduced cell migration and proliferation.

Conclusion: These findings demonstrate that caveolin-1 play an important role in miR33 regulated lipid metabolism, and may identify a new target for enhance cholesterol efflux and atherosclerosis treatment.
1970 | BEDSIDE
Predicting intracranial bleeding risk in patients with atrial fibrillation using several bleeding risk scores
L. Faucher1, A. Banerjee2, I. Lagrenade3, N. Clemmey4, D. Angoulvant4, A. Bernard4, D. Babuty5, G.Y.H. Lip5, 1 Tours Regional University Hospital, Hospital Toussaint, Tours, France; 2 Birmingham City Hospital, Birmingham, United Kingdom

Several clinical risk factors have been incorporated into clinical risk stratification scores to identify the risk of bleeding in patients with atrial fibrillation (AF). However, intracranial hemorrhage (ICH) is a life-threatening complication of anti-coagulation and clinicians need to weigh the risk of ICH far more than the risk of all major hemorrhages. The purpose of this study was to evaluate the predictive value of current bleeding risk stratification schemas for ICH and gastrointestinal (GI) bleeding in a cohort of unselected patients with AF.

Methods: Patients with AF were identified in a database and followed up between 2000–2010 for mortality, stroke and bleeding events. We evaluated the predictive value of several risk stratification schemas in this cohort whether patients were treated with anticoagulation or not. Among 8962 patients with AF, 789 severe bleeding events, 126 ICH and 141 GI bleeding events were recorded during a follow-up of 877±1052 days. We compared the predictive value of the HAS-BLED score with 2 other bleeding risk schemes (HEMORR2HAGES, ATRIA) using continuous and categorical (low, moderate and high risk subgroups of patients) analyses.

Results: Severe bleeding, ICH and GI bleeding events occurred more commonly in patients with higher HAS-BLED, HEMORR2HAGES and ATRIA scores. However, HEMORR2HAGES and ATRIA scores as categorical variables were not able to identify a higher risk of ICH. Of the 3 tested schemas, the HAS-BLED score performed best in multivariate analysis, with a stepwise increase in rates of major bleeding (Hazard ratio (HR) 1.17 95% CI 1.07–1.27, p<0.0003) and of ICH (HR 1.26 95% CI 1.03–1.55, p<0.002) with increasing HAS-BLED risk category. HEMORR2HAGES and ATRIA scores were not independent predictors of ICH and gastrointestinal (GI) bleeding in a cohort of unselected patients with AF.

Methods: We included 1,226 patients in the study; 37% in the dabigatran- and 63% in the warfarin group. Median time to cardioversion was 4.0 (interquartile range [IQR] 2.7–6.1) and 7.0 (IQR 4.0–12.1) weeks in the dabigatran- and warfarin group respectively. The odds ratio of cardioversion within the first 4 weeks was 2.9 (95% Confidence Interval [CI] 2.3–3.8; p<0.005) in favor of dabigatan. The cumulative incidences of stroke, bleeding or death were 0.8% and 1.7% at 30 in the dabigatran and warfarin groups respectively with a hazard ratio of 2.5 (95% CI 0.5–12.5; p=0.257).

Background: Dabigatran is an alternative to warfarin as anticoagulation therapy in cardioversion of patients with non-valvular atrial fibrillation.

Purpose: Examine the time to cardioversion and risk of subsequent cardiovascular complications in patients treated with dabigatran or warfarin.

Methods and results: Time to cardioversion was used as the primary outcome in ARISTOTLE.

Results: Of the 1,226 patients included in the study, 37% were on dabigatran and 63% on warfarin. Median time to cardioversion was 4.0 weeks in the dabigatran group and 7.0 weeks in the warfarin group. The odds ratio of cardioversion within the first 4 weeks was 2.9 (95% CI 2.3–3.8; p<0.005) in favor of dabigatran. The cumulative incidences of stroke, bleeding or death were 0.8% and 1.7% at 30 days in the dabigatran and warfarin groups respectively with a hazard ratio of 2.5 (95% CI 0.5–12.5; p=0.257).

Conclusion: Anticoagulation treatment with dabigatran allows shorter time to cardioversion than warfarin, and appears to be an effective and safe alternative treatment strategy.

Acknowledgement/Funding: The study was supported by an unrestricted research grant from Boehringer-Ingelheim.

1973 | BEDSIDE
Less non-major bleeding with apixaban versus warfarin among patients with atrial fibrillation: insights from the ARISTOTLE trial
M.C. Bath1, R.D. Lopes2, D.M. Wold3, C. Heldt4, M. Hannars5, D. Vinereanu6, S. Goto7, J.H. Alexander2, L. Wallentin8, G.B. Granger9, 1INECO Neurociencias, Rosario, Santa Fe, Argentina; 2Duke Clinical Research Institute, Duke University Medical Center, Durham, United States of America; 3Uppsala Clinical Research Center, Uppsala University, Uppsala, Sweden; 4Bristol-Myers Squibb, Princeton, United States of America; 5University of Medicine and Pharmacy Carol Davila, Bucharest, Romania; 6Tokai University School of Medicine, Isehara, Japan

Background: Minimizing the risk of major bleeding is an important objective in using antithrombotic therapy, but less is known about non-major (NM) bleeding.

Purpose: We describe the cumulative incidence and location of NM bleeding, as well as how it was managed, in ARISTOTLE.

Methods: In ARISTOTLE, 18,201 patients with AF were randomized to apixaban vs. warfarin; median follow-up was 22 months. 18,140 patients who received at least 1 dose of study drug were included in this analysis. NM bleeding was defined according to ISTH criteria and included the first bleeding event of both clinically relevant and minor bleeding, not preceded by a major bleeding event.

Results: NM bleeding was 3 times more common than major bleeding (12% [n=2204] vs 3.9% [n=692]). Like major bleeding, NM bleeding was less frequent with apixaban (10.1% [918/9088]) than warfarin (14.2% [n=1286/9052]) (HR [apixaban vs. warfarin] 0.69 [95% CI 0.62–0.74] (Figure). The most frequent sites of NM bleeding were: hematuria (16.4%), epistaxis (14.8%), hematomata (11.5%), and bruising/ecchymosis (10.1%). Clinically relevant NM bleeding was associated with an increased risk of overall death (HR 1.70 [1.32–2.18]). Medical
Conclusion: In ARISTOTLE, NM bleeding was common, associated with adverse outcomes, and less frequent with apixaban than warfarin. When NM bleeding occurred, apixaban was less frequently discontinued than warfarin. These findings reinforce the safer profile of apixaban than warfarin for patients with AF.

Acknowledgement/Funding: The ARISTOTLE trial was supported by Bristol-Myers Squibb and Pfizer

1974 | BEDSIDE

Efficacy and safety of apixaban compared with warfarin in relation to renal function over time in patients with atrial fibrillation: Insights from the ARISTOTLE trial

Z. Hijazi1, S.H. Hohnloser2, U. Andersson3, J.H. Alexander4, C.B. Granger4, M. Hannn4, R.D. Lopes4, A. Siegbahn5, L. Wallentin1, 1Uppland University, Dep. of Medical Sciences, Cardiology, and Uppland Clinical Research Center, Uppsala, Sweden; 2W. Goethe University, Dep. of Cardiology, Frankfurt, Germany; 3Uppland University, UCR-Uppland Clinical Research Center, Uppsala, Sweden; 4Duke University Medical Center, Durham, United States of America; 5Bristol-Myers Squibb, Princeton, United States of America; 6Uppland University, Dep. of Medical Sciences, Clinical Chemistry, and Uppland Clinical Research Center, Uppsala, Sweden

Background: Renal impairment confers an increased risk of stroke, death, and bleeding in antiocoagulated patients with atrial fibrillation (AF). In the ARISTOTLE trial, apixaban as compared with warfarin reduced the risk of stroke, mortality, and major bleeding regardless of renal function at baseline.

Purpose: This study evaluated renal function over time and its interactions with outcomes during apixaban vs. warfarin treatment throughout follow-up.

Methods: In the ARISTOTLE trial 16,971 patients had repeated creatinine measurements available after randomization. For each patient estimated glomerular filtration rate (eGFR) according to CKD-EPI was assessed from randomization to 18 months using linear regression with eGFR measurements and time from randomization. Patients were divided into categories according to if eGFR during the follow-up was stable or deteriorated more than 20%. The relations between treatment outcomes, and renal function were investigated using Cox regression.

Results: Median eGFR only slightly declined, 0.6 mL/min per year. A total of 1647 (9.7%) declined ≥20% in eGFR. The rate of stroke or systemic embolism events in patients with AF.

Conclusions: In anticoagulated patients with AF, declining renal function is associated with a higher risk of cardiovascular events. Regardless of renal function over time apixaban is consistently associated with a lower risk of stroke, death and major bleeding.

1975 | BEDSIDE

Real-world comparison of bleeding risks among non-valvular atrial fibrillation patients on apixaban, dabigatran, rivaroxaban: cohorts comprising new initiators and/or switchers from warfarin

P. Tepper1, J. Mardekan2, C. Masseria2, H. Phatak3, S. Kamble3, Y. Abdulla3sart2, W. Petkun3, G.Y.H. Lip4, 1University of Pittsburgh, Epidemiology, Pittsburgh, United States of America; 2Pfizer, Inc., New York, United States of America; 3Bristol-Myers Squibb, Princeton, United States of America; 4University of Birmingham, Birmingham, United Kingdom

Background: Limited information is available about the safety of non-Vitamin K antagonist oral anticoagulants (NOACs) in the real-world setting.

Purpose: To compare bleeding risks among non-valvular atrial fibrillation (NVAF) patients treated with apixaban vs. dabigatran and rivaroxaban in a large US database.

Methods: Using MarketScan Earlyview insurance claims database, NVAF patients ≥18 years who received NOAC or switched from warfarin to NOAC from 01/2013–31/10/2014 were identified. Patients were followed up to 6 months until bleeding, discontinuation/switch of therapy, disenrollment, or end of the study. Hazard ratios (HRs) of major bleeding, clinically relevant non-major bleeding (CRNM) as well as any bleeding for rivaroxaban and dabigatran compared to apixaban were estimated.

Results: We studied 8,785 NVAF patients on apixaban, 20,963 on dabigatran and 30,529 on rivaroxaban. Compared to dabigatran or rivaroxaban users, apixaban users were more likely to have switched from warfarin, to use antiplatelet agents, to have more comorbidities, and to have slightly higher CHADS2 and HAS-BLED scores. Multivariable Cox regression showed that compared to apixaban users, rivaroxaban users were more likely to have major (HR: 1.36), CRNM (HR: 1.43) or any bleeding (HR: 1.41); and dabigatran users were more likely to have gastrointestinal (GI) related CRNM bleeding (HR: 1.24).

Impact of the environment on anticoagulation in non-valvular atrial fibrillation

C.-Y. Hsu, P.-H. Huang, H.-B. Leu, J-W. Chen, S.-J. Lin, Taipei Veterans General Hospital, Division of Cardiology, Taipei, Taiwan, ROC

Background: Atrial fibrillation (AF) is associated with increased risks of several neurological complications, such as stroke and dementia. However, the independent association between AF and seizure disorder has never been evaluated in longitudinal cohort studies. Moreover, the CHADS2 score is a useful scheme for risk stratification of thromboembolism events in patients with AF.

Purpose: The aim of this study was to investigate the combined role of AF and the CHADS2 Score for risk stratification of NVAF patients for the first 6-month after treatment initiation.

Methods: In the CHADS2 Score, on the risks of development of seizure disorder in a nationwide, population-based cohort database in Taiwan.

Conclusions: Using real-world administrative data, rivaroxaban appears to increase the risk of major, CRNM, and any bleeding while dabigatran appears to increase the risk of GI related CRNM bleeding compared to apixaban for NVAF patients for the first 6-month after treatment initiation.

Acknowledgement/Funding: Research grant was received by Dr. Tepper from Pfizer, Inc
Conclusion: AF was associated with an increased risk of future seizure events, and the CHADS2 score is a useful scheme for predicting the risk of seizure occurrence in patients with AF.

1977 | BEDSIDE
Severity of renal impairment in patients with heart failure and atrial fibrillation: implications for novel oral anticoagulant dose adjustment

Background: The novel oral anticoagulants (NOACs) have varying degrees of renal elimination, and plasma concentrations are associated with bleeding risk. This may be particularly problematic in patients with heart failure (HF) and atrial fibrillation (AF).

Purpose: To examine the severity and variation in renal impairment in patients with HF and subsequent AF, and the proportion of patients requiring NOAC cessation or dose reduction according to prescribing guidelines.

Methods: Retrospective analysis of renal function in North American patients enrolled in the Candesartan in Heart Failure Assessment of Reduction in Mortality and Morbidity program. This randomized controlled trial investigated candesartan in 7599 patients with New York Heart Association class II to IV symptoms, of whom 2058 had AF possibly requiring anticoagulation. We examined temporal trends and the proportion of patients with varying degrees of renal impairment over 26 months defined using Cockcroft-Gault (CG), simplified Modification of Diet in Renal Disease (MDRD), and Chronic Kidney Disease Epidemiology Collaborative (CKD-EPI) equations. The proportion of patients requiring cessation or dose reduction of individual NOACs was estimated.

Results: Mean eGFR was worse at every time point in patients with AF compared to those without AF, the difference being approximately 11 ml/min (CG), 9 ml/min (CKD-EPI) and 7 ml/min (MDRD). As renal function declined, CG classified a greater proportion of patients as having moderate or severe chronic kidney disease and agreement with MDRD/CKD-EPI declined. At least moderate renal impairment was present in one quarter of patients with AF at baseline, one third by study completion, and approaching one half at least once during follow-up. Using FDA prescribing guidance, apixaban had the lowest requirement for dose reduction (7% baseline and 3% of patients during follow-up) and rivaroxaban the greatest (27% and 16% respectively).

Conclusion: Renal impairment in patients with HF and AF is common, fluctuates, and increases, and would frequently mandate dose reduction or cessation of NOACs. Baseline renal function, the method of estimating GFR, and intensity of anticoagulation were associated with subsequent bleeding risk.

Risk vs. benefit of anticoagulation therapy in elderly patients with atrial fibrillation and documented ground-level falls
A. Bohm 1, P. Michalek 2, P. Slezák 2, J. Stěvlik 2, P. Jackulík 2, M. Stevová 2, T. Uher 3, C. Comenius University, Bratislava, Slovak Republic; 2 University Hospital Hradec Králové, Czech Republic; 3 Medical University of Science, Brno, Czech Republic

Introduction: Patients with atrial fibrillation have a five-fold increased risk of stroke, which can be effectively reduced with oral anticoagulant therapy. How- ever, the elderly population is at greater risk of falls, and associated injuries are often detrimental to the treatment of fear of bleeding. Clinicians prescribing oral anticoagulants often face a dilemma in these situations.

Purpose: Previous studies on this issue typically used “risk of falls” rather than documented falls or they got data about falls from hospital registries which usually provide unreliable information, because of the tendency not to record those events. This was the reason that led us to our “real world” research with personally acquired data.

Methods: Our study included elderly patients from 2 medical institutions hospitalized for atrial fibrillation between the years 2008–2011 and treated with warfarin for at least 3 years. They were personally interviewed on the number of falls, episodes of spontaneous bleeding and bleeding outcomes, which were correlated with their medical reports. The Chi-square test was used for the two-sided confidence intervals for single proportion, and the Fisher’s exact test for 2 by 2 contingency table analysis

Results: Of the 204 patients monitored during 3 years, 23% (n=47) had a total of 94 falls. In both cohorts of patients with and without falls, the average CHA2DS2VASc score was 5 and HASBLED score was 3. Incidence of bleeding in the cohort with falls was significantly higher by 86.6% (95% confidence interval [CI] = 78.7% to 91.1%, p < 0.0001), than in the cohort without falls. Incidence of minor bleeding (WHO grade 1) was also significantly higher in the cohort with falls by 16.9% [CI = 1.20% to 38.5%, p = 0.0419], than in the cohort without falls. However, the incidence of severe bleeding (WHO grade 4) was significantly higher by 17.3% [CI = 6.17% to 37.8%, p = 0.0023] in the cohort without falls, than in the cohort with falls. Incidence of severe bleeding (WHO grade 4) after a fall was 1.06% [CI = 0.03% to 5.79%].

Conclusions: Our study showed that the incidence of minor bleeding in patients on warfarin and documented falls is higher, but surprisingly incidence of severe bleeding is lower, than in patients without falls. This suggests that spontaneous bleeding is more dangerous than bleeding after a fall, indicating that HASBLED
This study. PLF-LGAS and HGAS were present in n=484 (41.8%; MPG: 27.1±8.3 mmHg) based on data of a clinical registry from three independent institutions.

Methods and results: A total of 1260 patients undergoing TAVI were included in this study. PLF-LGAS and HGAS were present in n=484 (41.8%; MPG: 27.1±8.3 mmHg; SVI ≤ 35 ml/m²) and n=776 (58.2%; MPG: 54.8±20.8 mmHg; SVI = 37.5±11.3 ml/m²) patients, respectively. EuroScore I (27.6±15.7 vs. 24.0±9.13.5; p<0.05), EuroScore II (48.0±15.3 vs. 82.5±6.1; p<0.017) were significantly different between groups. TAVI was performed transfemorally in the majority of patients (overall 71.4%) with a high procedural success rate (> 98%).

Patients with PLF-LGAS had a significantly higher in-hospital mortality (10.9% vs. 6.7%, p<0.011) and 1-year mortality (32.0% vs. 24.1%, p=0.008) compared to patients with HGAS. The rate of VARC-defined secondary endpoints was without significant differences between the groups: new pacemaker: 13.2% vs. 17.3%; bleeding: 8.0% vs. 11.8%; stroke: 1.4% vs. 2.5%; length of hospital stay: 31.1±13.9 vs. 28.5±6.1 (p=0.017) were significantly different between groups. TAVI was performed transfemorally in the majority of patients (overall 71.4%) with a high procedural success rate (> 98%).

Conclusions: Both mean and peak baseline AVGs are directly associated with improved survival post TAVI, independent of EF or the presence of LEF-LGAS. A higher rate of LEF-LGAS, suggesting that AVG can be used to select patients most likely to benefit from TAVI.

Impact of transcatheter aortic valve replacement (TAVI) on severity of concomitant mitral regurgitation, pulmonary artery pressure and tricuspid regurgitation

A. Launet1, A. Selle1, M. Franz1, A. Hamadachi1, B. Goebel1, M. Ferrari2, T. Sandhaus1, T. Doenst1, H.R. Figulla1, 1Universitätsklinikum Jena, Jena; 2Kerckhoff Clinic, Bad Nauheim; 3University Hospital Bonn, Bonn, Germany

Background: The effect of transcatheter aortic valve replacement (TAVI) on severity of mitral regurgitation (MR) and right ventricular afterload is still a matter of debate. The aim of this study was to analyze the short- and mid-term impact of TAVI on MR as well as consecutive changes of pulmonary artery (PA) pressure and tricuspid regurgitation (TR).

Methods: 516 patients undergoing TAVI were enrolled into a prospective institutional registry. The present analysis focuses on patients with MR≥ II. Pa
tients with severe aortic stenosis (AS) may present with a mean AV gradient mean 1.79±0.65 at hospital discharge (n=86; p<0.001) and remained significantly below baseline after 1 (n=52: 1.61±0.58), 3 (n=37: 1.70±0.59) and 6 months (n=35: 1.61±0.58) month. This was associated with a significant reduction of PA-pressure from 47.6±13.8mmHg to 37.9±11.8mmHg (p<0.05) and a decrease of TR-severity from 1.85±0.79 to 1.59±0.8 (p<0.05) after 1 month. Post-operative NYHA-class (3.0±0.5 vs. 2.50±0.55; p<0.01) as well as 6-minute walking distance (94.18±94.1m vs. 162.4±114.4m at 1 month vs 249.0±132.94m at 3 months; p<0.001) improved, demonstrating a functional benefit in patients with MR≥ II at 30 days after TAVI. In-hospital-mortality was 3.7% (n=4). At 1, 3, 6 and 12 month after TAVI, mortality was 6.6% (n=7), 15.09% (n=16), 17% (n=18) and 22.6% (n=24), respectively.

Conclusions: Transcatheter aortic valve replacement results in LV-afterload reduction with a significant and sustained improvement of ≥ grade II MR, pulmonary artery pressure and tricuspid regurgitation. These hemodynamic changes are associated with a significant functional benefit with improvement of NYHA-class and increased 6-min-walking distance.

Impact of diabetes mellitus on short- and midterm mortality after transcatheter aortic valve implantation

F. Schlötzer1, N. Mangner1, F. Wolte1, K. Stachel1, A. Lindner1, J. Wilde1, D. Holzhey2, F.W. Mohr2, C. Schulze1, M. Linke1, 1Heart Center of Leipzig, Department of Internal Medicine/Cardiology, Leipzig, Germany; 2Heart Center of Leipzig, Department of Cardiologic Surgery, Leipzig, Germany

Background: Diabetes mellitus (DM) is an established risk factor of cardiovascular disease. The role of DM as a predictor of complications and outcomes after transcatheter aortic valve implantation (TAVI) remains to be further clarified. Therefore, it was aim of the study to evaluate the impact of DM on short- and mid-term mortality after TAVI.

Methods and results: Consecutive TAVI patients treated between 01/2006 and 10/2013 were prospectively stratified according to the presence of DM and DM treatment. All-cause-mortality at 30 days and one-year mortality were defined the primary endpoints and periprocedural stroke, bleeding and access-site-related complications as secondary end points. All end point definitions were subject to the Valve Academic Research Consortium-II (VARC-II) definitions. Overall, 1450 patients were included: 614 patients (42.3%) had DM at admission (dietary treatment (oDM) n=142 (23.1%); oral medication (iDM) n=220 (35.8%); insulin treatment (sDM) n=252 (41.0%)). The presence of DM did not differ between patients with DM compared with patients without DM (noDM: 8.0%; DM: 7.5%; p=ns) and according to diabetes treatment status (noDM: 8.0%; oDM: 8.0%; sDM: 5.1%; iDM: 9.4%; p=ns). One-year mortality after TAVI was not significantly different in patients with DM compared with patients without DM (noDM: 24.0%; DM: 26.3%; p=ns). Diabetes treatment had no significant influence on one-year survival after TAVI (noDM: 24.0%; oDM: 28.8%; iDM: 23.7%; sDM: 27.3%; p=ns). Periprocedural stroke (major/minor/TIA), periprocedural bleeding (life-threatening/fatal/major/minor/access-site-related complications) were not significantly different between diabetics and non-diabetics. A higher rate of VARC-2 acute kidney injury was observed in the subgroup of diabetics.

Conclusions: The presence of DM did not significantly affect periprocedural rates
of stroke, bleeding, access-site related complications as defined by VARC-II cri-
teria. 30-day and one-year mortality after TAVI were unaffected by the presence
of DM at baseline, questioning its use in contemporary risk prediction models.

1984 | BEDSIDE
Determinants and prognostic value of B-type natriuretic peptide in
patients with aortic valve stenosis

V. Nguyen, C. Cinadevilla, D. Arangalage, M. Dehoux, J. Dreyfus, I. Codogno,
X. Duval, V. Huart, A. Vahanian, D. Messika-Zeitoun, AP-HP - Hospital
Bichat-Claude Bernard, Department of Cardiology, Paris, France

Background: Usefulness and prognostic value of natriuretic peptides in aortic
stenosis are largely unknown.

Methods: Patients with AS enrolled between 2006 and 2013 in 2 ongoing
prospective studies constituted our cohort. Clinical, biological measurements in-
cluding Nt-proBNP and echocardiographic evaluations were performed at study
entry for all patients. Asymptomatic patients were contacted every 6 months and
seen at our research center every year. The occurrence of AS related events (sud-
den death, congestive heart failure, or new onset of symptoms) within 2 years was
 prospectively recorded.

Results: 809 patients were included. Nt-proBNP increased with AS severity
(p < 0.0001) and symptomatic status (p < 0.0001) but there was a wide overlap
between groups and Nt-proBNP had a poor sensitivity (61%) and a modest
specificity (77%) for the diagnosis of severe symptomatic AS (area-under-the-
curve = 0.74). Nt-proBNP was the results of complex interaction of multiple factors
including AS severity and symptoms but also age (p = 0.0008), history of coro-
nary artery disease (p < 0.03), rhythm (p < 0.007) and diastolic function (p < 0.0001).
Consequently, in asymptomatic patients with moderate/severe AS with normal left
ventricular ejection fraction and in sinus rhythm, Nt-proBNP was associated to AS-
related events in univariate (p = 0.009) but not after adjustment for AS severity
(p = 0.12). Finally, repeated Nt-proBNP measurements at 1 year did not improve
its predictive value (p = 0.43).

Conclusion: The present study clearly shows the limits of Nt-proBNP in AS and
raises caution regarding its use, at least as a single factor, in the decision-making
process of asymptomatic patients with AS.

1985 | BEDSIDE
Pre-existing and new-onset atrial fibrillation: a meta-analysis of
mortality outcomes and cerebrovascular events in 13,795 patients
undergoing transcatheter aortic valve implantation

A. Sannino, G. Gargiulo, G.G. Schiattarella, C. Perrino, E. Stabile, M.A. Losi,
M.A. Galderisi, G.G. De Simone, B. Tramarco, G. Esposito. University Hospital
Federico II, Naples, Italy

Background: Atrial fibrillation (AF) and new-onset atrial fibrillation (NOAF) pre-
dict morbidity and mortality in several conditions but little is known about their
role in transcatheter aortic valve implantation (TAVI).

Methods and results: Twenty-five studies, enrolling 13,795 patients under-
going TAVI, with a 28.8% of patients with pre-existing AF and 15.5% with NOAF,
were analyzed for early and long-term all-cause mortality; a further meta-analysis
was performed to assess the occurrence of cerebrovascular events (CVE). In pa-
tients with baseline AF, 30-day all-cause mortality was similar to patients in sinus
rhythm. Conversely, long-term all-cause mortality was significantly greater in AF
patients than in patients with baseline sinus rhythm (HR: 1.66, 95% CI: [1.43 to
1.92], p < 0.0001). Surprisingly, baseline AF was not predictor of CVE at long-term
follow-up (HR: 1.68, 95% CI: 0.86 to 3.30, p = 0.131). NOAF patients showed a similar
short- and long-term all-cause mortality, when compared to patients in sinius
rhythm, whereas experienced significantly higher incidence of CVE at short-
term follow-up (HR: 2.54, 95% CI: 1.51 to 4.25, p < 0.0001). Only a trend towards a
higher incidence of CVE was observed at long-term follow-up (HR: 1.44; 95%
[CI]: 1.00 to 2.40, p = 0.30).

Conclusions: Pre-existing AF, but not NOAF, is predictor of all-cause mortality in
patients undergoing TAVI. Moreover, NOAF is related to the occurrence of CVE at
short-term follow-up. Similar to SAVR, the optimal management and risk strat-
ification of these patients need to be further investigated in ad-hoc trials.

1986 | BEDSIDE
Predictors of mortality in patients with aortic stenosis: the role of
myocardial fibrosis

V. Vassiliou1, C.E. Raphael1, A. Perperoglou2, E. Nyktari3, C.W.L. Chinn4, A. Ali5,
F. Alpendurada6, D.J. Pennell1, M.R. Dweck1, C.K. Prasad1,2, Royal Brompton
Hospital, Biomedical Research Unit, Imperial College London, London, United
Kingdom; 3 University of Essex, Department of Mathematical Sciences, Essex,
United Kingdom; 2 Biomedical Research Unit of Royal Brompton London,
London, United Kingdom; 4 University of Edinburgh, Edinburgh, United Kingdom

Purpose: Myocardial tissue characterization with cardiovascular magnetic reso-
nance (CMR) late gadolinium enhancement (LGE) is associated with worse short
term prognosis in patients with aortic stenosis (AS). We investigated the long term
effect of myocardial fibrosis in AS patient survival.

Methods: Consecutive patients with moderate or severe AS underwent CMR
between 2003 and 2008. They were characterized by blinded observers into 3
groups based on the CMR LGE findings: those with midwall fibrosis, those with
infarction fibrosis and those with no fibrosis. Each patient was followed for 5 years.
The end-point was all-cause mortality.

Results: Overall 143 patients (68±14 years; 97 male) were followed prospec-
tively. 81 patients had significant coronary disease and 80 underwent aortic valve
replacement during this time. 44 died during the follow up period: 21/54 (39%) in
the midwall fibrosis group, 16/40 (40%) in the infarction group and 7/49 (14%) in
the no fibrosis group. Patients with either midwall fibrosis [HR 2.6 (95% CI 1.3–5.2,
p = 0.005)] or infarction [HR 2.7 (95% CI 1.3–5.6, p = 0.004)] showed increased all-
cause mortality when compared to patients with no fibrosis (HR 1, no LGE/fibrosis
in black, midwall fibrosis in red, infarction in green). On multivariate analysis, only
age, ejection fraction (EF), wall thickness and midwall fibrosis were significantly
associated with prognosis.

Conclusion: Patients with moderate or severe AS with midwall fibrosis on CMR
have a worse 5 year survival when compared to patients with no fibrosis. Mid-
wall fibrosis remained an independent adverse predictor of survival at 5 years
providing incremental predictive value to EF.

Acknowledgement/Funding: NIHR Cardiovascular Biomedical Research Unit
of Royal Brompton & Harefield NHS Foundation Trust and Imperial College London

1987 | BEDSIDE
Overestimation of bicuspid aortic stenosis severity by
echocardiography

C.W.L. Chinn, E. Luo, J. Hwan, A. White, D. Newby, M. Dweck. University of
Edinburgh, Centre for Cardiovascular Science, Edinburgh, United Kingdom

Objectives: Current guidelines for classifying aortic stenosis (AS) severity are
established without differentiating between bicuspid and tricuspid AS. We inves-
tigated the relationship between mean pressure gradient (MPG) and aortic valve
area (AVA) between bicuspid and tricuspid AS, and assessed the impact of stroke
volume (SV) estimation on classification.

Methods: Patients with mild to severe AS (100 tricuspid and 48 bicuspid) under-
went comprehensive echocardiography and cardiovascular magnetic resonance
imaging (MRI). The relationship between AVA and MPG was modeled using non-
linear regression, and thresholds were compared between tricuspid and bicuspid
AS. We further compared the effects of Doppler- and MRI-derived stroke volume
(SV) on severity classification of bicuspid and tricuspid AS. We inves-
tigated the relationship between mean pressure gradient (MPG) and aortic valve
area (AVA) between bicuspid and tricuspid AS, and assessed the impact of stroke
volume (SV) estimation on classification.

Results: Thresholds for severe AS (AVA < 1.0 cm²) in tricuspid and bicuspid were
similar with Doppler-derived SV (MPG of 26 versus 27 mmHg respectively), but
there was >10 mmHg difference with CMR-derived SV (MPG of 30 versus 42
mmHg respectively; see Figure). Compared to MRI, echocardiography underesti-
mated the left ventricular outflow tract area (LVOTarea) and consequently the SV,
to a greater extent in bicuspid compared to tricuspid AS (LVOTarea: 0.99±0.84
versus 0.20±0.73 cm³ respectively; SV: 6.6±12.5 versus 2.9±11.4 mL/mm² re-
spectively). Indeed, planimeted LVOTarea on MRI was larger in bicuspid com-
pared to tricuspid AS (4.82±1.6 versus 3.60±0.69 cm³, P < 0.001).
Conclusions: Echocardiography overestimates aortic stenosis severity in patients with bicuspid aortic stenosis due to inaccuracies in the measurement of LVOT area and stroke volume consequently, the AVA.

Acknowledgement/Funding: British Heart Foundation

1988 | BEDSIDE
Identification of peri-procedural myocardial infarction in patients undergoing transcatheter aortic valve implantation by using a high-sensitivity troponin I assay
1 Kerckhoff Heart and Thorax Center, Bad Nauheim, Germany; 2 Kerckhoff Heart and Thorax Center, Department of Cardiology, Bad Nauheim, Germany; 3 Kerckhoff Heart and Thorax Center, Cardiac Surgery, Bad Nauheim, Germany; 4 Justus-Liebig University of Giessen, Cardiology, Giessen, Germany.

Background: Transcutaneous aortic valve implantation (TAVI) is a standard procedure for high-risk patients. The peri-procedural myocardial infarction (MI) has been linked to worse prognosis. According to the VARC-2, MI is defined by a rise in cardiac troponin (cTn) and creatine kinase MB (CK-MB); however, many patients have elevated cTn levels without clinical evidence of MI.

Purpose: The aims of this study were to establish reference values of cTn levels, measured with a high-sensitivity assay, in TAVI patients and to assess its peri-procedural diagnostic and prognostic value.

Methods: hs-cTnI and CK-MB levels were assessed prior to, and up to 3 days after transfemoral (TF) or transapical (TA) TAVI in 505 patients. Patients were followed up for 12 months.

Results: In total, 47.9% of patients had elevated hs-cTnI concentrations at baseline. According to VARC-2 nearly all TA-AVI patients (99.5%) showed a MI based on hs-cTnI compared with 4.2% based on CK-MB. In TAVI patients, 81.1% had a MI based on hs-cTnI compared with 9.0% based on CK-MB. A total of 10 patients showed a type 1 MI. The TAVI cohort 99th percentile for hs-cTnI was 855.4 ng/L. The frequency of MI was lower using the TAVI-specific 99th percentile (TF-AVI: 5% vs. 81.1%, P<0.001; TA-AVI: 22.2% vs. 99.5%, P<0.001). In TF-AVI patients, every 1000 ng/L hs-cTnI rise after TAVI increased the risk of in-hospital death by 6.5% (CI 95% 0.3–13%, P=0.03), and every 10 μg/L rise in CK-MB increased the risk of in-hospital death by 2.9% (CI 95% 0.2–5.5%, P=0.02). These biomarkers were independent predictors of major adverse cardiac events (MACE) and all-cause death.

Conclusion: The VARC-2 definition leads to an overestimation of peri-procedural MI. TAVI specific reference values yield a more realistic estimation of the myocardial ischemic risk. Further, serial measurement of hs-cTnI levels might be helpful for short-term risk stratification in TF-AVI patients.

1989 | BEDSIDE
Anticoagulation therapy of patients with atrial fibrillation after TAVI - Dresdner DOAK Register-TAVI (DDRT)
G. Enke, L. Sichting, C. Pfluecke, S. Quick, L. Schoener, R.H. Strasser, K. Ibrahim. Technische Universität Dresden, Department of Medicine and Cardiology, Heart Center Dresden, University Hospital Dresden, Dresden, Germany.

Background: Up to now transcatheter aortic valve implantation (TAVI) represents an established therapy for older patients with symptomatic aortic stenosis and several comorbidities. After implantation an inhibition of the blood coagulation is necessary. This could be done by inhibition of platelet aggregation, anticoagulation or a combination of both. Currently, there is no generally accepted anticoagulation standard for patients with atrial fibrillation who received TAVI. Additionally, the possible use of direct oral anticoagulants, like Xa- or IIa-inhibitors after TAVI for patient with atrial fibrillation remains unclear at the moment.

Methods and results: The aim of this register study was to analyze the inhibition of blood coagulation and antithrombotic therapy in patients with atrial fibrillation and TAVI. Therefore the compatibility, compliance, thromboembolic and hemorrhagic complications were registered. Overall data of 101 patients after TAVI with additive indication for anticoagulation were collected. Taken together, 32 patients were treated with vitamin K antagonists (VKA), 94% of them received one platelet inhibitor in addition (20 patients ASS, 10 patients clopidogrel). In 69 patients anticoagulation was done with direct oral anticoagulants (DOAC), 24 of them received a single therapy with DOAC (34.8%), 43 of them received DOAC in combination with one platelet inhibitor (62.3%) and only two patients received a triple therapy. Overall 2 patients died within the first 30 days after TAVI. There were no differences in stroke and bleeding frequency between the VKA and DOAC group within the first 30 days after implantation. But, 3 months after TAVI, patients who were treated with DOAC showed less bleeding, thrombosis and mortality in comparison to VKA-patients. Furthermore, no differences were seen between DOAC single therapy or DOAC with one platelet inhibitor.

Summary: Until now, no universal standard for anticoagulation strategies for patients with atrial fibrillation undergoing TAVI exists. In this registry study patients with DOAC had a lower risk for bleeding, thrombosis and death. There were no differences in stroke and bleeding frequency between the VKA and DOAC group within the first 30 days after implantation. But, 3 months after TAVI, patients who were treated with DOAC showed less bleeding, thrombosis and mortality in comparison to VKA-patients. Furthermore, no differences were seen between DOAC single therapy or DOAC with one platelet inhibitor.

PREMATURE CARDIOVASCULAR AGING

2013 | BEDSIDE
Glycemic excursions trigger senescence-associated pathways and vascular ageing features in patients with type 2 diabetes
F. Paneni1, S. Costantino1, R. Battista1, G. Capretti1, S. Chiandotto1, M. Volpe1, F. Cosentino1, G. Capretti1, S. Chiandotto1, M. Volpe1. 1 Karolinska Institute, Cardiology Unit, Stockholm, Sweden; 2 Clinical Hospital, Diabetology, Sora, Italy; 3 Sapienza University of Rome, Sant’Andrea Hospital, Rome, Italy

Background: Type 2 diabetes (T2D) is associated with reduced life expectancy and increased cardiovascular disease (CVD) risk, even after intensive glycemic control targeting glycated haemoglobin (HbA1c) levels.

Purpose: In the present study we aimed to assess if glycemic excursions (GE) may affect senescence-related pathways and vascular ageing in T2D patients with target HbA1c values.

Methods: Twenty-four T2D patients with optimal glycemic control (HbA1c<7%) and no previous history of CVD were consecutively recruited in an outpatient setting. All patients gave written consent for their participation. Based on 3-day continuous glucose blood monitoring, the study population was divided according to the presence (n=12) or absence (n=12) of GE, defined by median values of amplitude of glycemic excursions (AMGE) and post-prandial incremental area under the curve (AUCpp). Pulse pressure (PP), a well-established marker of vascular age, was calculated as the difference between systolic and diastolic blood pressure. Expression profile of senescent genes was determined by real-time PCR array in peripheral blood monocytes, and expressed as fold change (FC).

Results: Patients with and without GE did not differ for age (62±8 vs. 61±14 years, p<0.05, respectively), gender (F,M: 7.5 vs. 6.6, p<0.05, respectively), BMI (27±3 vs. 29±5 kg/m², p<0.05, respectively), diabetes duration (13±11 vs. 15±10 years, p<0.05, respectively), CV risk factors and glucose-lowering medications. PP was significantly higher in patients with GE (27±3 vs. 24±2 mmHg, p<0.05). The expression profile of senescent genes showed that Telomerase Reverse Transcriptase (TERT), responsible for telomere ends maintenance, was markedly downregulated in T2D patients with GE (FC=−21, p<0.05). Subjects with glucose perturbations also showed upregulation of DNA damage gene Ataxia Telangiectasia Mutated (ATM, FC=10.4, p<0.01) and ATM-dependent oncosuppressor p53 (FC=5.6, p<0.01). Subjects with glucose perturbations also showed upregulation of DNA damage gene Ataxia Telangiectasia Mutated (ATM, FC=10.4, p<0.01) and ATM-dependent oncosuppressor p53 (FC=5.6, p<0.01).

Conclusions: Our findings show that glucose fluctuations are associated with premature cardiovascular ageing in T2D patients with near-normal HbA1c values. Targeting glycemic variability might contribute to prevent senescent features, thus reducing CVD burden in people with diabetes.
Results: The main new findings were 2-fold: First, premature vascular ageing persisted in ART adolescents, as evidenced by decreased FMD (P < 0.01), and increased CRP, Hcy, fibrinogen, and hs-CRP, which significantly differed in mean 10-year ambient air pollution levels: PM2.5 (22.4 vs. 41.7 μg/m³) and PM10 (29.4 vs. 56.9 μg/m³), respectively. Data regarding BMI, lifestyle, ethnics and family history was collected. We found no significant differences in BP parameters, pulse pressure (PP) among subjects differing in exposure to air pollution. Lublin vs. Krakow: DBP: 70.3; IQR 10.5 vs. 69.7; IQR 9.3 mmHg; SBP (122.3; IQR 16.3 vs. 121.3; IQR 16.6 mmHg); PP (50.8; IQR 12.8 vs. 51.3; IQR 12.7 mmHg). Moreover we found lower PP (51.0; IQR 13.0 vs. 53.1; IQR 12.0 mmHg) in subjects drinking energy drinks more frequent than several times a week. We found significantly higher inflammatory parameters in inhabitants of highly polluted city. Lublin vs. Krakow: CRP (4.0; IQR 0.5 vs. 0.7; IQR 0.6 mg/ml, p < 0.0001), hs-CRP (0.35; IQR 0.4 vs. 0.50; IQR 0.6 mg/ml, p < 0.0001), Hcy (9.03; IQR 4.6 vs. 10.3; IQR 4.4 μM, p < 0.0001) and fibrinogen (244; IQR 57.7 vs. 263; IQR 87.8 mg/dl, p < 0.0001). Rhinitis was more frequent in subjects living in Krakow (16.12% vs. 5.82%, IQR 0.35), Hcy levels were in overweight subjects living in Cracow.

Conclusions: This study shows, that young adolescents living in a city with high air pollution show increased levels of cardiovascular risk biomarkers including inflammatory response.

2023 | SPOTLIGHT

Could occupational determinants impact on changes in blood pressure over a five-year follow-up? Results from the VISAT study

S. Huo Ying Kai1, Y. Esquiv2, V. Bongard1, J.-B. Ruidv4et1, J.-C. Marqu3, J. Ferries1 on behalf of VISAT GROUP.

- CHU, Epidemiology, Toulouse, France;
- UMR 1027 Paubat Sabater University
- CHU, Occupational health, Toulouse, France;
- UMR 1027 Paubat Sabater University
- Cardiology, Toulouse, France;
- UMR 5263 CNRS, Toulouse, France

Background: Among many factors involved in increased Blood Pressure (BP), environmental and temporal factors have been shown to be associated with cardiovascular risk in this exponentially growing population.

Purpose: To assess the impact of a large panel of occupational factors exposures on changes of BP over a 5-year follow-up period.

Methods: Data from VISAT (Vieillissement SAnté Travail), a South French cohort study, 790 volunteer participants were recruited in 2001 and available to participate in 2006. Data were collected through self-questionnaires and medical examination during these two gatherings. Four categories of occupational factors were investigated: physical, organizational, psychosocial and employment-related factors, thus exploring thirty occupational exposure determinants (assessed in 2001). Changes in Systolic BP (SBP) and Diastolic BP (DBP) between the two surveys were dichotomized into increased BP versus decreased or unchanged BP. Logistic regressions were performed to explain how each occupational factor interacts with changes in BP after adjustment on age, gender, education level, change of occupational sector, social-occupational status, body mass index, leisure physical activity, behavioural lifestyle and treatment for hypertension.

Conclusion: Psychosocial factors appear as the major determinants of changes of BP over time with a dual effect, whereas biomechanical occupational factors play a minor role. Because occupational factors are potentially modifiable, a targeted preventive strategy could be implemented.

2024 | BEDSIDE

Hypertension population science

Hypertension prevalence, awareness, treatment and control in four states in India: the DISHA study baseline results

K. Kohli1, P. Jeonoom1, D. Kondal1, A. Purty1, A. Bhardwaj4, J. Sanghvi1, P. Negi3, S. Ladhani6, G. Toteja3, D. Prabhakaran1 on behalf of DISHA Study.

1Centre for Chronic Disease Control, New Delhi, India;
2Pondicherry Institute of Medical Sciences, Pondicherry, India;
3Rajendra Prasad Medical College, Ranchi, India;
4Sri Aurobindo Medical Sciences, Pune, India;
5Gandhi Medical College, Shimla, India;
6Agar Khan Health Services, Mumbai, India;
7Indian Council of Medical Research, New Delhi, India

Background: Hypertension prevention and control, a national public health priority as it affects more than 110 million adults in India. Awareness, treatment and control are reported to be very low in Indian setting.

Purpose: To describe prevalence, awareness, treatment and control of hypertension in four states in India using baseline risk factor survey of DISHA study.

Methods: DISHA study, a cluster randomized control trial of hypertension prevention and control in India. There were 12 villages randomly identified each from
five different districts of states of Puducherry, Gujarat, Madhya Pradesh, and Haryana Pradesh. Villages were randomly assigned into intervention and control, if distance between them was less than 10KM one was replaced with another randomly selected village. A detailed baseline survey of risk factors of CVD was completed. Approximately 300 participants were selected from each village.

**Results:** Baseline survey results of 24 intervention (n=6663) and 24 control (n=7150) clusters in four sites are presented here. Mean age of study population was 39.0 years (SD=14.8 years). Nearly half (46%) of studied population was males. Prevalence of hypertension was 23.1% (95% CI: 22.4–23.8). One in four of hypertensive individuals were aware about hypertension and one in seven of them achieved blood pressure control status (Figure 1)

### Conclusion:
Hypertension affects one in four individuals in India and awareness, treatment and control rates are very low in Indian settings. This calls for innovative methods for prevention and control. DISHA study tests effectiveness of task-shifting of front-line health workers for imparting lifestyle education for prevention and control of hypertension in both rural and urban settings in India.

### ANTICOAGULATION IN NON-VALVULAR ATRIAL FIBRILLATION

#### 2031 | BEDSIDE
Rivaroxaban vs. warfarin with concomitant aspirin use in patients with atrial fibrillation: findings from the ROCKET AF trial


**Background:** The safety and efficacy of concomitant aspirin use (ASA) use in patients with atrial fibrillation (AF) treated with rivaroxaban, compared with warfarin, for stroke and systemic embolism prevention are not known.

**Methods:** In the double-blind ROCKET AF study, 14,264 patients with nonvalvu- lar AF were randomized to rivaroxaban 20 mg (15 mg for CrCl<60 mL/min) once daily or dose-adjusted warfarin. Concomitant ASA use was left to investigator discretion and assessed at baseline. Outcomes including stroke and systemic embolism, myocardial infarction (MI), vascular death, and major or non-major clinically relevant (NMCR) bleeding were compared between groups. Multiivariate modeling was done to adjust for baseline risk factors.

**Results:** A total of 5205 (36.5%) patients had ASA use at baseline (mean dose 92 mg), 30.6% of whom had known coronary artery disease. Patients receiving concomitant ASA were more likely to have prior MI (22% vs. 14%, p<0.001) and heart failure (68% vs. 59%, p<0.001). Relative efficacy of rivaroxaban versus warfarin was similar with and without ASA use for stroke prevention/systemic embolism (p=0.95 for interaction), and major or NMCR bleeding (p=0.76 for interaction) (Figure). Irrespective of ASA use, fatal bleeding was less frequent with rivaroxaban (0.4% vs. 0.8%, p=0.003) compared with warfarin.

**Conclusion:** Rivaroxaban was non-inferior to warfarin for the prevention of stroke or systemic embolism, and was associated with less fatal bleeding, irrespective of concomitant ASA use.

### Acknowledgement/Funding:
ROCKET AF was funded by Janssen Pharmaceuticals and Bayer

---

### Abstract 2031 – Figure 1

### 2032 | BEDSIDE
Stroke and bleeding outcomes with apixaban versus warfarin in patients with high creatinine, low body weight or high age receiving standard dose apixaban for stroke prevention in atrial fibrillation

J. Alexander1, U. Andersson2, R.D. Lopes1, Z. Hijazi3, S.H. Hohnloser4, J. Ezekowitz5, S. Halvorsen6, M. Hanna7, C.B. Granger1, L. Wallentin2, id1 Duke Clinical Research Institute, Durham, United States of America; 2 Uppsala Clinical Research Center, Uppsala, Sweden; 3 Department of Medical Sciences, Cardiology, and Uppsala Clinical Research Center, Uppsala University, Uppsala, Sweden; 4 Division of Cardiac Electrophysiology, J.W. Goethe University, Frankfurt, Germany; 5 University of Alberta, Edmonton, Canada; 6 Oslo University Hospital, Department of Cardiology, Oslo, Norway; 7 Bristol-Myers Squibb, Princeton, United States of America

**Background:** In the ARISTOTLE trial comparing apixaban with warfarin in pts with AF, apixaban 2.5 mg was used in pts with 2 or more dose reduction (DR) criteria: age ≥80 years, creatinine ≥1.5 mg/dL, weight ≤60 kg. Pts assigned 2.5 mg of apixaban vs. warfarin (n=831) had similar reductions in stroke/SE and major bleeding to pts assigned 5.0 mg of apixaban vs. warfarin (n=17,370).

**Methods:** We compared pts assigned to apixaban 5.0 mg or warfarin with 1 of 3 DR criteria with pts with 0 of 3 criteria. Stroke/SE and major bleeding rates, hazard ratios and 95% CIs were evaluated, and interactions between treatment and the presence of 1 vs. 0 DR criteria were determined.

**Results:** Among pts assigned 5.0 mg of apixaban or warfarin, 4046 (23%) had one DR criterion. These pts were older (77 vs. 69 years), lighter weight (86 vs. 70 kg), and had worse renal function (creatinine 1.00 vs. 1.07 mL/min) than pts with no DR criteria. Pts with one DR criteria had more stroke/SE and major bleeding but had similar benefits of apixaban vs. warfarin on stroke/SE (p=0.41) and major bleeding (p=0.06). Similar patterns were seen for individual DR criteria.

**Conclusion:** Pts with isolated advanced age (>80 years), low body weight (<60 kg), or renal dysfunction (CrCl<1.5 mg/dL) had slightly more stroke/SE and significantly more major bleeding but similar benefits with apixaban 5.0 mg BID compared with warfarin to pts with none of these characteristics. Apixaban 5.0 mg BID is a safe and efficacious dose for these pts.

### Acknowledgement/Funding:
The ARISTOTLE trial was funded by Bristol-Myers Squibb and Pfizer.

---

### Abstract 2032 – Table 1. Stroke/SE and major bleeding by DR criteria and apixaban vs. warfarin

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Subgroup</th>
<th>Apixaban</th>
<th>Warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Events (%)</td>
<td>n</td>
</tr>
<tr>
<td>Stroke/SE</td>
<td>5.0 mg BID with 0 DR criteria</td>
<td>6675</td>
<td>137 (1.00)</td>
</tr>
<tr>
<td></td>
<td>5.0 mg BID with 1 DR criteria</td>
<td>2032</td>
<td>64 (3.17)</td>
</tr>
<tr>
<td></td>
<td>5.0 mg BID with age DR criteria</td>
<td>452</td>
<td>14 (1.73)</td>
</tr>
<tr>
<td></td>
<td>5.0 mg BID with weight DR criteria</td>
<td>733</td>
<td>27 (2.30)</td>
</tr>
<tr>
<td></td>
<td>5.0 mg BID with creatinine DR criteria</td>
<td>847</td>
<td>23 (1.50)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>5.0 mg BID with 0 DR criteria</td>
<td>6658</td>
<td>204 (1.77)</td>
</tr>
<tr>
<td></td>
<td>5.0 mg BID with 1 DR criteria</td>
<td>2020</td>
<td>108 (5.40)</td>
</tr>
<tr>
<td></td>
<td>5.0 mg BID with age DR criteria</td>
<td>448</td>
<td>30 (6.68)</td>
</tr>
<tr>
<td></td>
<td>5.0 mg BID with weight DR criteria</td>
<td>731</td>
<td>26 (2.28)</td>
</tr>
<tr>
<td></td>
<td>5.0 mg BID with creatinine DR criteria</td>
<td>841</td>
<td>50 (6.02)</td>
</tr>
</tbody>
</table>

---

### 2033 | BEDSIDE
Level of kidney function predicts risk of stroke and bleeding in patients with atrial fibrillation

A. Nissen Bonde1, A-L. Kamper2, N. Carlsson1, E.L. Fosbø2, L. Staerk3, G.H. Gislason1, J.B. Olsen1, Gentofte University Hospital, Gentofte; 2 Rigshospitlet - Copenhagen University Hospital, Dept. of Nephrology, Copenhagen; 3 Hvidovre Hospital - Copenhagen University Hospital, Hvidovre, Denmark

**Purpose:** To determine the risk of stroke and bleeding according to level of kidney function in non-anticoagulated patients with atrial fibrillation (AF).

---

**Abstract 2033 – Table 1. Stroke/SE and major bleeding by DR criteria and apixaban vs. warfarin**

**HR (95% CI)**

- Stroke/SE: 0.77 (0.62–0.97), 0.92 (0.56–1.50), 1.08 (0.51–2.30).
- Major bleeding: 0.72 (0.60–0.86), 0.67 (0.52–0.86).

---

**Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475/9777257 on 07 February 2019**
Advances in Basic Science: State of the Art on Plaque Vulnerability

2058 | BEDSIDE

Plaque Morphology in Patients with Type 2 Diabetes Mellitus

K. Takata, A. Iwata, S. Imai, B. Zhang, S. Miura, K. Saku, J. Fukuo, University of Department of Cardiology, Fukuoka, Japan; Fukuoka University, Department of Biochemistry, Fukuoka, Japan

Background: Plasma high-density lipoprotein (HDL) cholesterol concentration is inversely correlated with the risk of coronary artery disease (CAD), and HDL has several anti-atherosclerotic actions. However, little is known about the relationship between functional property of HDL and vulnerability of coronary plaque.

Purpose: We examined the association between anti-oxidative capacity of HDL with the presence of high vulnerability coronary plaques using integrated backscatter intravascular ultrasound (IB-IUS) in patients with type 2 diabetes mellitus (T2DM).

Methods: Thirty-three consecutive T2DM patients with CAD who underwent percutaneous coronary intervention (PCI) under IB-IUS guidance were included. IB-IUS analysis on the target lesion was performed to determine two-dimensional (at the most diseased cross-section) and three-dimensional IVUS parameters including each plaque component before PCI. HDL inflammatory index (HII), higher HII indicates lower anti-oxidative capacity of HDL, was measured from diluted plasma with pathological studies, subsequently supported by imaging techniques. The high definition of optical coherence tomography (OCT) provides new opportunities to explore STEMI culprit stenosis characteristics in real patient populations.

Purpose: To describe and quantify the characteristics of the culprit plaque in STEMI patients, in order to establish a pathological mechanism.

Methods: We report on the findings made in a prospective series of patients undergoing primary PCI for STEMI in whom OCT was used as a guidance tool. OCT assessment was performed after achieving reperfusion with thrombus aspiration, but before balloon or stent PCI. Plaque was categorized as fibroatheroma (thin cap [TCFA] if minimum cap thickness <70 μm), fibrous or fibrocalcific. The presence of microchannels and macrophages was noted and the content in thrombus, calcium and lipid was quantified (as suggested by Prati F et al EHJ 2010). The most likely mechanism for vessel occlusion was inferred by the morphologic findings.

Results: A total of 47 patients were analyzed. 3 of them excluded due to insufficient quality of OCT pictures. The most frequent plaque morphology was fibroatheroma (33.75%), 22 of which fulfilling TCFA criteria. The most frequent mechanism was plaque rupture (25.57%). None of the cases suggested a calcium nodule as the pathological mechanism. In a significant proportion of patients (16% 36%), an unequivocal mechanism could not be established. In the cases where plaque erosion or other feature not detected by OCT technique. Microplaque channels (26.59%) and macrophages (26.59%) were frequently found features, as were an intimal layered appearance (26.59%). It is noteworthy that evidence for intra-plaque hemorrhage (IPH) (walled spherical void suggesting hematoma or darkened area associated to microchannels) was a frequent finding (22.50%), even in cases without clear rupture (9 cases).

Conclusions: The pathological substrate of STEMI, as assessed with OCT during primary PCI, is highly variable. Overlaid, ulcerated lipid-rich plaques were the dominant finding in vessel thrombosis site, frequently with signs suggesting prior episodes of subclinical thrombosis, and many times with evidence of IPH and inflammation. This information may be useful to formulate specific treatment strategies during or after primary PCI and supports the value of OCT use in the acute STEMI setting.
CURRENT AND FUTURE APPLICATIONS OF COMPUTED TOMOGRAPHY CORONARY IMAGING

2099 | BEDSIDE
Combined score of clinical risk parameters and coronary CT angiography findings improves prediction of death: an analysis based on 15219 patients with 5.3 years of follow up from the CONFIRM registry

S.D.C. Deseive1, M. Hadamitzky2, S. Massberg1, J. Hausleiter1 on behalf of CONFIRM.
1 Ludwig-Maximilians University, Medizinische Klinik und Poliklinik I, Munich, Germany; 2German Heart Center of Munich, Klinik für Radiologie und Nuklearmedizin, Munich, Germany.

Background: Various multicentre studies have proven coronary CT angiography’s (CCTA) value for long-term outcome prediction in patients. A combined score of clinical risk factors and CCTA parameters (CONFIRM score) has shown improved prediction of all-cause mortality compared to clinical risk scores alone in a large cohort of patients with a 2 year follow-up.

Purpose: The aim of this analysis was to investigate the performance of the CONFIRM score for prediction of all cause mortality during clinical follow-up of 5.3 years.

Methods: The CONFIRM (Coronary CT Angiography Evaluation For Clinical Outcomes: An Intenational Multicenter) registry is an international multicentre registry including patients with suspected coronary artery disease undergoing CCTA. Our analysis is based upon 15219 patients. The primary endpoint was all-cause mortality. The Framingham risk-score, the Morise score and the NCEP ATP III score were calculated and correlated to the primary endpoint. The CONFIRM score implemented the number of proximal segments containing calcified or mixed plaque tissue and the number of obstructed coronary segments to the NCEP ATP III score.

Results: During follow-up, 982 patients died. Figure 1 shows receiver-operating curves for all 4 scores. Prediction of the primary endpoint was significantly higher for the combined CONFIRM score (c-index 0.7, green curve) compared to the Framingham risk score (c-index 0.67, p<0.0001, red curve) and the NCEP ATP III score (c-index 0.68, p<0.0001, dark blue curve).

Conclusion: The CONFIRM score, based on CCTA parameters and clinical risk factors, demonstrates a significantly improved prediction of all-cause mortality risk than traditional risk scores over a 5 year follow-up period.

2100 | BEDSIDE
Characterization of coronary plaques in patients with acute coronary syndrome by multidetector computed tomography

Russian Cardiology Research and Production Center, Moscow, Russian Federation

Purpose: To assess morphological features of atherosclerotic plaques in culprit and non-culprit coronary lesions in patients with acute coronary syndrome without persistent segment ST elevation (NSTE-ACS) by multidetector spiral computed tomography (MDCT).

Methods: 70 patients with NSTE –ACS underwent 64-MDCT and invasive angiography. 64-slice MSCT was performed using CT scanner with 64 detector rows (Aquilion, Toshiba, Japan; gantry rotation time 400 ms; 64 x 0.5 mm detector collimation, retrospective ECG gating, intravenous administration of 100 - 150 mg of non-ionic iodinated contrast agent) before invasive coronaryography. We evaluated plaque type (soft, mixed and calcified), minimum CT density (HU), contour, length as well as presence of spotty calcium, ring-like sign and positive remodeling in all culprit lesions and in non-culprit segments, if stenosis was >50% (Figure1). We included in the analysis 214 coronary segments (70 culprit and 144 non-culprit).

Results: In culprit lesions (n=70) compared to non-culprit lesions (n=144) frequency of soft plaques (60% vs. 43%, p<0.003), positive remodeling (70.2% vs. 45.3%, p=0.03) and uneven contour (19.1% vs. 68.7%, p<0.0002) was significantly higher in the culprit coronary segments (40.1±25.3 HU vs 74.1±16.8 HU, p=0.02 and 16.8±13.4 mm vs 13.2±6.9 mm, p=0.01, respectively). Uneven contour was the most sensitive sign of plaque’s vulnerability (91.7%), and ring-like sign, such as spotty calcium – the most specific (78.3% and 72.9% respectively). Receiver-operator characteristic curve analysis identified the optimal cutoff value of minimum plaque density and length for discrimination between culprit and non-culprit lesion as 40 Hounsfield units (HU) and 13.5 mm respectively. The combination of soft plaque with a minimum density <40 HU and uneven contour occurred in a third of cases in culprit lesions and almost two times less in non-culprit (31.67% vs 17.91%, p=0.04) and was characterized by a high specificity (82.1%) and negative predictive value (72.7%).

Conclusions: Thus, the most specific features of culprit lesions in patients with ACS include positive vascular remodeling, length > 13.5 mm, minimum CT-density <40 HU, soft plaque’s type and presence of uneven contour, as well as a combination of the last three features.

2101 | BEDSIDE
Cardiac CT versus functional testing in suspected coronary artery disease - a randomised multicentre study

M.M. Lubbers1, T.W. Galena1, P. Musters1, J.M. Akkerhuis2, A. Lien2, T. Bruning3, B. Krenning4, M. Ouhlous4, A. Nizeen5, K. Nieman1. 1Erasmus Medical Center, Rotterdam, Netherlands; 2Sint Franciscus Gasthuis, Rotterdam, Netherlands; 3Maassstad ziekenhuis, Rotterdam, Netherlands; 4Haven ziekenhuis, Rotterdam, Netherlands

Background: Cardiac CT has the potential to improve the diagnostic workup of patients with stable chest pain, mainly because of its high accuracy.

Objective: The aim of this study was to compare the effectiveness and efficiency of an angiographic driven workup of suspected coronary artery disease using cardiac CT compared to that of the current standard of care based on functional testing.

Methods: We conducted a prospective randomised controlled trial in 350 patients with stable chest pain who had been referred for evaluation of possible coronary artery disease to the outpatient clinic of four hospitals in the Netherlands between August 2009 and July 2013. Patients were randomly assigned to cardiac CT (n=175) or to the current standard of care based on functional testing or a diagnostic strategy with cardiac CT (1:2 ratio) using a computer-generated block randomisation sequence, stratified by centre.

Main outcome measures: The study’s three main endpoints were reduction of chest pain and improved quality of life (effectiveness); major adverse events (safety); and costs (efficiency) after one year of follow up.

Results: We included 350 patients with a mean age of 55±8 years (55% women). The angiography frequency measured with the SAQ questionnaire after one year was lower after cardiac CT (p=0.012). The remaining SAQ subscales after one year were similar for cardiac CT and functional testing. There was no difference in quality of life (EQol 0.759, SF-36 p=0.569). A trend towards a better diagnostic yield was observed for the cardiac CT versus standard care group (72% and 58%, p=0.469) and there was no increase in the overall number of invasive angiographic procedures or interventions (12% and 11%, p=0.843). After cardiac CT, as compared with functional testing, the final diagnosis was sooner established (7 vs 26 days; p<0.0001), there was less downstream testing (25% vs. 53%, p<0.0001) and the total diagnostic costs were lower ($369 vs $440; p<0.0001). The cumulative radiation exposure was higher in the cardiac CT group (6.6±8.7 mSV versus 6.1±9.3 mSV; p<0.0001) At an average of 446 days (1.2 years) of follow up, MACE-free survival was 96.7% for patients randomized to cardiac CT and 99.0% for patients randomized to the standard care approach (P=0.011).

Conclusion: A cardiac CT approach provides at least equally and perhaps more effective and safe care. Despite the modest size in our setting, the cardiac CT approach is associated with fewer tests, faster diagnosis and lower costs.

2102 | BEDSIDE
Coronary atherosclerosis features for the prediction of ischaemic events (CAPE-PF study): a CT scan integrated score from a bi-center registry

A.I. Guaricci1, N.D.B. Brunetti1, F.D.R. De Rosa1, M.S. Mustadip2, D.A. Andreini2, M.P. Pepi2, M.D.B. Di Biase1, G.P. Pontone2. 1University of Foggia, Cardiology Department, Foggia, Italy; 2Cardiology Center Monzino IRCCS, Milan, Italy

Aim: To date it is unclear how to implement the information on coronary artery disease (CAD) features as evaluated by coronary computed tomography angiography (CCTA) in order to better predict the occurrence of major adverse cardiac events (MACE). The aim of this study is to validate the prognostic role of a comprehensive CCTA - derived score in consecutive symptomatic patients evaluated for suspected CAD.

Methods and results: We enrolled 277 consecutive symptomatic intermediate-risk patients undergoing CAD for clinical indications. For each patient we evaluated in primary prevention a score based on CCTA findings (plaque remodeling and plaque type) correlated with outcomes. All patients were followed for 49±15 months. The endpoint was the occurrence of MACE defined as the composite endpoint including non-fatal myocardial infarction and cardiac death. The mean CT score was 11.3±12.0 and the prevalence of MACE was 11.3% in overall population. CT score was significantly related to the incidence of MACE at univariate (HR: 2.77; CI 95%; 2.13–3.61) and multivariate analysis (HR: 2.78; CI 95%; 1.91–4.03). At ROC curve analysis, CT-score was the best predictor of incidence of MACE (AUC: 0.83, CI 95%; 0.80–0.87) as compared to Diamond and Forrester score (p<0.001), segment stenosis score (p<0.05) or segment involved score (p<0.001).

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475 by guest on 07 February 2019
Conclusions: The main message of this study is that increasing values of CT-score were significantly related to the incidence of MACE even after correction for age, gender, risk factors, Diamond and Forster score and CAD features. The clinical implications of a score that reflects the coronary atherosclerotic features is related to its direct application to a more reliable prediction of MACE as compared to clinical and CT scores applied individually. A specific consideration regards those patients without obstructive CAD and in which both the extent and the features of non-obstructive CAD could lead to a reclassification to a higher risk profile and thereby to a different cardiovascular treatment.

Acknowledgement/Funding: no funding

2103 | BEDSIDE
Cardiac spectral CT scan to diagnose acute myocarditis
G. Baudry1, C. Boulet1, B. Jung1, G. Ducrocq2, S. Zarka1, J.P. Laisy3, G. Steg3, A. Vahanian3, P. Ou1, 1AP-HP - Hospital Bichat-Claude Bernard, Cardiology, Paris, France; 2Hospital Bichat-Claude Bernard, Radiology, Paris, France; 3Hospital Bichat-Claude Bernard, Emergency Department, Paris, France; 4Hospital Bichat-Claude Bernard, Radiology, Paris, France

Background: The diagnosis of acute myocarditis is difficult because of the wide range of clinical symptoms. Noninvasive diagnosis relies on cardiac MRI, but its availability remains limited. CT spectral imaging has recently been proposed in this setting.

Purpose: The aim of this study is to compare cardiac spectral CT scan to MRI for the diagnosis of myocarditis.

Methods: Between 2012 and 2013, 17 consecutive patients had an acute myocarditis according to cardiac MRI in our institution. All underwent a CT scan during the same time to compare with the MRI considered the gold standard. A coronary CT angiography was performed during the early enhancement and spectral CT imaging was performed 5 min after injection of iodine contrast agent, with late hyperenhancement defining inflammation. Using the 17 segments classification, we compared each myocardial segment using the 2 methods (McNemar and concordance kappa tests).

Results: Mean age was 39±16 years with 82% of men. Symptoms were chest pain (94%) and dyspnea (12%), and 71% of patients had a recent history of viral infection. Mean CRP was 69±73 mg/l and troponin levels were 6±6 ng/ml (normal <0.04). In Cardiac MRI, mean LVEF was 53±8%. The number of inflammatory myocardial segments was 4±3 in MRI and 3±2 in CT scan. When comparing each of the 17 segments using cardiac MRI or CT scan, no significant difference was found and the concordance was good with kappa coefficients between 0.60 and 1.0 (Figure). There was no false positive using the CT scan compared to cardiac MRI.

Conclusion: Spectral CT scan appears valid compared to myocardial MRI for the diagnosis of acute myocarditis. Since CT scan is more easily available than MRI and can also rule out a coronary syndrome, it appears as an interesting option to diagnose myocarditis.

2104 | BEDSIDE
Prevalence, distribution and predictive value on all-cause mortality of clinical relevant extracardiac findings from cardiac CT in the general population: The Heinz Nixdorf Recall Study
E. Tezgh1, A.A. Mahabadi1, K. Kara1, N. Pundt1, L. Eisele1, A. Stang1, S. Moebus3, K.H. Joekoe1, R. Erbel1, H. Kaelsch1 on behalf of The Investigative Group of the Heinz Nixdorf Recall Study. 1University of Duisburg-Essen, West German Heart and Vascular Center Essen, Essen, Germany; 2University Hospital St. Josef, Department of Cardiology, Bochum, Germany; 3University of Duisburg-Essen, Institute for Medical Informatics, Biometry and Epidemiology, Essen, Germany

Objective: Aim of this study was to assess the prevalence and distribution of extracardiac findings (ECF) on cardiac CT in the general population and to investigate their predictive value on all-cause mortality (ACM).

Methods: Participants aged 45–75yrs from the prospective population-based Heinz Nixdorf Recall Study were studied by non-contrast enhanced cardiac CT performed 5 min after injection of iodine contrast agent. The median HR was 70/min [IQR: 66–76] in HTX group and 70/min [IQR: 62–75] in the control group (p = 0.265). We have analyzed 282 coronary segments basis on a four point scale in the proximal and mid segments of the coronary arteries (0=no motion, 1= mild motion, 2= moderate motion, 3= severe motion, not evaluable). For the comparison of the two groups we used Mann-Whitney U and Fisher exact tests.

Results: The median HR was 70/min [IQR: 66–76] in HTX group and 70/min [IQR: 62–75] in the control group (p = 0.265). We have analyzed 282 coronary segments in the HTX group and 281 segments in the control group. In the HTX group 98.6% (278/282) and in the control group 86.3% (248/281) of the segments were diagnostic (SMS=3), p<0.0001. Excellent image quality (SMS=0) was present in 83.0% (234/282) of HTX and 51.6% (145/281) of control group's coronary segments, p<0.0001.

Conclusion: The coronary CT exams of HTX patients had a better image quality as compared to the control group with similar heart rate, coronary dominance, age and BMI. The loss of autonomous neural control results in a regular, steady HR in HTX patients, which seems to be beneficial for coronary CT imaging. Coronary CT provides diagnostic image quality in HTX recipients, therefore it might be utilized as a non-invasive alternative to ICA during the follow-up exams for CAV.

2107 | BEDSIDE
Different effects of statin only or statin + ezetimibe on non-calcified coronary plaque (NCCP) assessed by computed tomography coronary angiography (CTA) with and without metabolic syndrome (MetS)
K. Watanabe, K. Sekiya, Y. Suzuki, S. Shigemi, H. Saeki, T. Tachibana, T. Asami. Saiseikai Matsuyama Hospital, Matsuyama, Japan

To examine changes in plaque composition and morphology by lipid lowering with statin only or statin + ezetimibe, we evaluate coronary plaques from stable angina pectoris with and without MetS before and 12 months after lipid lowering by CTA. 83 patients with non-calcified coronary plaques (Definition Flash, SIEMENS), we enrolled 144 patients with NCCP whose low-density lipoprotein cholesterol (LDLC) ≥100 mg/dl. We divided the patients into two groups according to preceding statin therapy (SO, n=72) and statin + ezetimibe.
Effects of heart imaging radiation on dna double-strand break levels in blood lymphocytes: the Heart-Break study

M. Cheezum1, C. Redon2, A. Burrell2, A. Kaviratne1, J. Bindeman1, D. Maeda2, P. Wisniewski3, P. Delacruz4, W. Bonner2, T. Villines1. 1Walter Reed National Military Medical Center, Dept. of Medicine, Cardiology Service, Bethesda, United States of America; 2National Institutes of Health, Lab. of Molecular Pharmacology, Center for Cancer Research, National Cancer Institute, Bethesda, United States of America; 3F. Edward Hebert School of Medicine, Bethesda, United States of America; 4San Antonio Military Medical Center, Dept. of Internal Medicine (Cardiology Service), San Antonio, United States of America

Background: Potential genotoxic effects from ionizing radiation have raised safety concerns with increasing utilization of cardiac imaging. Purpose: We aimed to compare levels of DNA double-strand breaks (DSBs) in human blood lymphocytes before and after coronary computed tomographic angiography (CTA), single-photon emission computed tomography (SPECT) and digital angiographic invasive coronary angiography (ICA).

Methods: 137 patients were prospectively examined by clinically indicated cardiac imaging methods (n=49 CTA, n=29 SPECT, n=39 ICA), with 10 controls. ICA patients included those with concomitant right heart catheterization (n=12), FFR (n=7), IVUS and aortography (n=1). Blood samples were obtained before and 30 min after imaging, and DSBs were analyzed in lymphocytes by gamma-H2AX immunofluorescence (Figure 1a). SPECT was performed with 1-day low/high dose (10/30 mCi) technetium, 64-slice single source CTA was acquired by prospective-trigger, and ICA was performed in accordance with guidelines.

Results: Median radiation exposure was highest in ICA patients (18.3 mSv [IQR 9.7–27.4] vs SPECT 12.3 [11.9–15.2] vs CTA 3.2 [2.8–4.2] [p < 0.001]). A significant increase in excess foci levels was observed 30 min after ICA compared to SPECT and CTA (Figure 1b-c). There was no difference in DSB levels between CTA and SPECT, and all modalities had significantly more DSBs compared to a control group with no testing (Figure 1c).

Conclusion: ICA is associated with a significant increase in DSB levels compared to CTA and SPECT, attributed to increased radiation exposure. CTA demonstrated the lowest radiation dose, with no observed difference in DSBs between CTA and SPECT despite higher radiation exposure with SPECT. This may reflect differences between radiation sources, and requires further study.
with SSS standard right atrium appendage pacing prolongs atrioventricular conduction resulting in higher percentage of ventricular pacing.

P2112 | BEDSIDE
ECG criteria for right ventricular lead positioning. An analysis from the right pace study
G.L. Botti1, V. Calvi2, G. Maglia2, D. Pecora3, G. Ciaramilia4, M. Cancillio4, F. Detorri1, A. Lili3, M. Campari3, C. Muto15, 1 Sant’Anna Hospital, Como, Italy; 2 University Hospital Vittorio Emanuele, Catania, Italy; 3 Pugliese-Ciacco Hospital, Catanzaro, Italy; 4 Poliambulanza Foundation Hospital Institute of Brescia, Brescia, Italy; 5 University Hospital Paolo Giaccone, Palermo, Italy; 6 Santa Maria di Loreto Mare Hospital, Naples, Italy; 7 Sant Martino Hospital, Oristano, Italy; 8 Azienda USL 12, Viareggio, Italy; 9 Boston Scientific Italy, Milan, Italy; 10 St. Maria della Pietà Hospital, Nola, Italy

Introduction: Pacing on right ventricular (RV) septum could allow more physiologic activation than RV apical pacing. Recently, ECG criteria were proposed to accurately define RV lead position. The aim of this study was to assess the agreement between fluoroscopic and ECG criteria for RV lead positioning in a population of patients who underwent RV lead implantation.

Methods: The RIGHT PACE study enrolled patients with indications for cardiac pacing. Following device implantation, fluoroscopic radiographs were recorded in 3 views (posterior-anterior, 40°RAO, 40°LAO) and analyzed by an independent observer who categorized lead position. A 12-lead ECG was performed during ventricular pacing and following criteria for RV septal positioning were considered: a negative or isoelectric QRS in lead I; a paced QRS duration <140ms; an absence of notching in the inferior leads; early preordial QRS transition (earlier than V4).

Results: Complete data were available for 409 patients. The analysis of radiofluoroscopic and ECG criteria for RV lead placement in the lead position was performed in 170 patients (17 high-, 65 mid-, 88 low-septum) and apical placement in the remaining 239 patients. According to ECG analysis, a negative or isoelectric QRS in lead I identified septal leads with sensitivity of 11% and specificity of 89%, a paced QRS duration <140ms; an absence of notching in the inferior leads; early preordial QRS transition (earlier than V4).

Conclusions: None of the proposed ECG criteria, when considered alone, permitted to accurately identify septal sites. Nonetheless, the verification of multiple criteria increases specificity of septal identification, but markedly worsens sensitivity.

P2113 | BENCH
MRI-induced lead heating of an MRI conditional pacemaker system
G. Mouchawar1, S. Sison1, S. Chen1, X. Min1, J. Chen2, J. Nyerhuis3, R. Peitz1, 1 St. Jude Medical, Inc., Sylmar, United States of America; 2 University of Houston, Houston, United States of America; 3 Purdue University, West Lafayette, United States of America

Introduction: We utilized the ISO/IEC JWG 10974 Tier 3 (ED2) approach to evaluate lead heating under normal (2 W/kg) and 1st level control mode (4 W/kg) of the St. Jude Medical Accent Tendril MRI lead and Accent MRI pacemaker. Models were simulated in 170 patients (17 high-, 65 mid-, 88 low-septum) and various lead pathways in commercial scanners. Electric fields were extracted at both normal operation mode and 1st level control mode. Single lead testing was used as it typically experiences higher heating than that from dual lead testing. Clinically relevant lead states of various levels of fluid ingress were studied, and the lead transfer function (TF) with the highest ingress heating was selected. The TF was validated through ED2 Annex M pathways. It was then integrated with the extracted electric fields to estimate in-vitro temperature rises. A validated thermal model scaled the in-vitro temperature estimates to in-vivo results. The thermal model simulated the worst case conditions using an extreme level of tissue encapsulation of the pacemaker with cardiac tissue. Uncertainties from measurements, TF, and in vivo simulations were assessed with the Monte Carlo (MC) method. Safety was assessed based upon the accepted 43 °C standard (Mehrotra, 1983) for cardiac tissue interfacing with the lead tip helix electrode and lead MRI filter inductor.

Results: Over 400 different patient and MRI system permutations were simulated. When combined with exhaustive lead pathways, and MC analysis, over 14 million simulations were simulated. The risk associated with MRI scans was based upon the number of these 14 million simulations exceeding the safety criterion. For 2 W/kg scans, none of the 14 million scans exceeded the safety criterion at the lead tip helix or the MRI filter inductor, and so is estimated as <1 in 14 million. For 4 W/kg scans, the risk was <1 in 15,000 at the lead tip helix and <1 in 14 million at the MRI filter inductor.

Conclusions: Our results indicate that the risk associated with MRI scans of patients with an Accent MRI pacemaker system due to cardiac damage at the lead helix or MRI filter inductor is extremely low for 4 W/kg scans, and miniscule for 2 W/kg scans, even taking into account worst case considerations into every modeling step.

P2114 | BEDSIDE
Clinical impact of new-onset left bundle branch block after CoreValve implantation: long term follow-up

Background and purpose: New-onset rhythm conduction disturbances are frequently observed after transcatheter aortic valve implantation (TAVI). The most frequently observed is the left bundle branch block (LBBB). The clinical impact of the new-onset LBBB (NO-LBBB) after TAVI remains controversial. The aim of this study was to determine the impact of new-onset LBBB in terms of mortality and morbidity.

Methods: NO-LBBB was defined as pacemakers and admissions for heart failure) at long-term follow-up. Methods: From April 08 to December 14, 220 patients with severe aortic stenosis were treated by implantation of a CoreValve prosthesis. Sixty-seven were excluded for analysis: 22-patients with preexisting LBBB and 45-patients with frequent pacemaker, whether it was implanted before or immediately after implantation of CoreValve prosthesis. The remaining 153 patients were divided into two groups: those with persistent NO-LBBB and those without conduction disturbances after treatment (WCDAT). Patients were followed-up at 1-month, 6-month, 12-month, and yearly thereafter.

Results: Persistent NO-LBBB occurred in 83-patients (37.7%) immediately after TAVI, and 70-patients (31.8%) did not develop any conduction disturbances. The mean follow-up time of both patient groups was 32±22 months (range 3 to 82). There were no differences in mortality rate between the NO-LBBB and WCDAT groups (39.4%vs.45.0%, p=0.59). In NO-LBBB group there were no differences between groups in re-hospitalizations for heart failure (31%vs.32%, p=0.55). The NO-LBBB group did not require more frequently late implantation of permanent pacemaker at follow-up (31%vs.26%, p=0.38).figure-1.

Conclusions: New-Onset-LBBB was not associated with a higher incidence of late need of pacemaker after CoreValve implantation. In addition, there was not a higher risk for late mortality or rehospitalization rates.

P2115 | BEDSIDE
Time course of detection of new atrial fibrillation (AF) and AF burden in patients with cardiac implanted electronic devices
G. Boriani1, T.V. Glotzer2, M. Santin3, T.M. West4, M. De Mels5, M. Sepesi6, M. Gasparini7, T. Lewalter8, J.A. Camm9, D. Singer10, 1 Institute of Cardiology, Univ. of Bologna, Bologna, Italy; 2 Hackensack University Medical Center, Hackensack, United States of America; 3 San Filippo Neri Hospital, Rome, Italy; 4 Bakken Research Center, Maastricht, Netherlands; 5 University Hospital Brno, Brno, Czech Republic; 6 Clinical Institute Humanitas IRCCS, Rozzano, Italy; 7 Isar Heart Center, Munich, Germany; 8 St Georges Medical School, London, United Kingdom; 9 Massachusetts General Hospital, Boston, United States of America

Background: In patients with a cardiac implantable electronic device (CIED), continuous monitoring, through an atrial lead, allows detection and quantification of new atrial fibrillation (AF). New onset AF is associated with an increased risk of stroke. Several different thresholds of AF burden (5 minutes, 1, 6, 12 and 23 hours) have been studied to quantify the increase in stroke risk, which has been correlated with CHA2DS2-VASc scores to determine need for oral anticoagulation (OAC).

Methods: A pooled analysis of individual patient data from three prospective studies (TRENDS, Italian Clinical Service, and PANORAMA), part of the SOS AF project, was performed. 6990 patients (mean age 69 years, 72% male), were identified who had no history of AF and no OAC use at baseline. Time to each AF burden threshold was evaluated with Kaplan-Meier curves.

Results: During follow-up (mean 2.4 years), 2244 patients (34%) had device detected AF burden ≥5 mins, 1558 (24%) had AF burden ≥1 hour, 1041 (16%) ≥6 hours, 774 (12%) ≥12 hours, and 547 (8%) had AF burden ≥23 hours. The thresholds of AF burden were respectively attained at 6 months by 20%, 13%, 8%, 5% and 3% of patients, and at 1 year respectively by 26%, 17%, 11%, 7% and 5% of patients (Figure).

Conclusion: A substantial amount of patients with CIEDs and no prior AF, develop new AF over time, with the attainment of different AF burden thresholds. The potential candidates to be considered for OAC according to risk stratification,
can vary up to 5–6 fold, indicating that the threshold of AF burden plays a pivotal role for decision making.

**IMPROVING ANTIPLATELETS REGIMEN AND CARDIOPROTECTION IN CORONARY PATIENTS**

P2116 | BEDSIDE

**Efficacy of antiplatelet agent usage for primary and secondary prevention in dialysis patients: a nation-wide data survey and propensity analysis**

Y.H. Lin¹, C.K. Wu¹, Y.H. Yang², J.W. Huang¹, V.C. Wu¹, J.K. Lee¹, P.C. Chen³, L.Y. Lin¹
¹National Taiwan University Hospital, Department of Internal Medicine, Taipei, Taiwan, ROC; ²Chang Gung Memorial Hospital, chia-Yi, Taiwan, ROC; ³National Taiwan University, Institute of Occupational Medicine and Industrial Hygiene, Taipei, Taiwan, ROC

**Objective:** Although cardiovascular (CV) disease is the leading cause of mortality and morbidity in dialysis patients, there is little evidence to guide the use of antiplatelet agents in dialysis patients. The objective of this study is to assess the efficacy of the use of antiplatelet agents in dialysis patients.

**Methods:** A nation-wide database (Registry for Catastrophic Illnesses) for Taiwan, which has data from nearly all patients who received dialysis therapy from 1995 to 2008, was used. This is a population-based cohort study with time to event analyses to estimate the relation between antiplatelet agent use and outcomes. Hazard ratios were calculated to evaluate the effect of antiplatelet agent use on the risk of major CV events and mortality. Baseline characteristics were matched by propensity score (PS).

**Results:** A total of 108,954 were enrolled and 16,075 (14.8%) patients received an anti-platelet agent. After PS-based matching, 11,259 patients who used an antiplatelet agent and 11,259 non-users were included. Compared to the non-users, those using an antiplatelet agent were significantly associated with fewer CV events and less overall mortality.

Discussion: In dialysis patients, an antiplatelet agent usage is significantly associated with fewer CV events and less overall mortality.

P2117 | BEDSIDE

**Advanced age and high-residual platelet reactivity in patients receiving dual antiplatelet therapy with clopidogrel or ticagrelor**

M. Verdoia¹, L. Barbieri¹, A. Schaffer¹, M. Nardin¹, P. Marino¹, H. Suryapranata², Y.H. Lin¹, C.K. Wu¹, Y.H. Yang², J.W. Huang¹, V.C. Wu¹, J.K. Lee¹, P.C. Chen³, L.Y. Lin¹
¹National Taiwan University Hospital, Department of Internal Medicine, Taipei, Taiwan, ROC; ²Chang Gung Memorial Hospital, chia-Yi, Taiwan, ROC; ³National Taiwan University, Institute of Occupational Medicine and Industrial Hygiene, Taipei, Taiwan, ROC

**Background:** Elderly still represent a challenging subset of patients for the management of antithrombotic strategies, due to the complex balance between an increased frailty and risk of bleedings and enhanced platelet reactivity.

**Purpose:** Aim of present study was to evaluate the impact of age on platelet function and the occurrence of high residual on treatment platelet reactivity (HRPR) in patients treated with dual antiplatelet therapy with ASA and clopidogrel or ticagrelor.

**Methods:** Patients treated with DAPT were scheduled for platelet function assessment at 30–90 days post-discharge. By Multiplate aggregometry, HRPR was considered for ASPI test > 862 AU·min for (ASA) and ADP test values > 417 AU·min (for ADP-antagonists). Elderly were defined for age ≥ 70 years old.

**Results:** Among 494 patients on DAPT, 224 (45.3%) were ≥70 years old. Advanced age was associated with female gender, a higher prevalence of major es-

Discussion: In conjunction with other risk factors of ST, WBV as the major determinant of ESS, seems to be an independent predictor of ST after acute STEMI and may obtain additional data for risk categorization.

P2119 | BEDSIDE

**Impact of intravenous lysine acetylsalicylate versus oral aspirin on prasugrel inhibited platelets: results of a prospective, randomized, crossover study**


**Background:** Prasugrel and ticagrelor, new P2Y12-ADP receptor antagonists, are associated with greater pharmacodynamic inhibition and reduction of cardiovascular events in patients with an acute coronary syndrome. However, evidence is lacking about the effects of achieving faster and stronger cyclooxygenase inhibition with intravenous lysine acetylsalicylate (LA) compared to oral aspirin on prasugrel inhibited platelets.

**Purpose:** The objective was to assess the pharmacodynamics effect of combined established cardiovascular risk factors and an elevation of inflammatory parameters. ADP-mediated platelet aggregation increased with decades of age (279.3±148.6 vs 319.6±171.1 vs 347.3±190.1 vs 345.7±169.2, p=0.03) with a linear relationship between aggregation levels and age (r=0.15, p=0.001), while no difference was observed for other aggregation tests and for ASA response.

A reduced effectiveness of ADP-antagonists was observed among the elderly. In fact, among the 117 patients displaying HPRR (23.7%), a higher prevalence was observed among patients above 70 years old (30.4% vs 18.1%, p=0.02, adjusted OR [95% CI]=2.14 [1.26–3.63], p=0.005). Similar results were obtained among the 266 clopidogrel treated patients (HRPR prevalence: 38.5% vs 27.9%, p=0.09, adjusted OR [95% CI]=2.85 [1.42–5.7], p=0.003) and in the 228 patients receiving ticagrelor (HRPR rate: 19.1% vs 8.1%, p=0.03, adjusted OR [95% CI]=2.93 [1.01–9.45], p=0.049).

Conclusion: In patients receiving dual antiplatelet therapy, advanced age is independently associated with a reduced effectiveness of ADP-antagonists and a higher rate of high-on treatment platelet reactivity with both clopidogrel and ticagrelor.
administration of oral prasugrel and intravenous LA versus prasugrel and aspirin orally on platelet aggregation.

Methods: This was a randomized, single-center, open, two-period crossover platelet function study conducted in 30 healthy volunteers. Subjects were randomly assigned to receive a loading dose (LD) of intravenous LA 450mg plus oral prasugrel 60mg, or LD of aspirin 350mg plus prasugrel 60mg orally in a crossover fashion after a 2-week washout period between treatments. Platelet function was evaluated at baseline, 30 min, 1h, 4h, and 24h using light transmission aggregometry and vasodilator-stimulated phosphoprotein phosphorylation.

Results: The primary endpoint of the study, inhibition of platelet aggregation after type I collagen (0.8 μg/ml) was significantly increased when platelets were preincubated with gluca (25 mM) while RAC1 inhibitor (30 μM) reduced aggregation, and this effect was improved at highest glucose concentrations. Finally, platelets from diabetic patients (n=20) showed higher levels of Rac-1, correlated to percentage of glycated hemoglobin, when compared to control subjects (n=11); consistently, a higher dose of NSC23766 (60 μM) was necessary to obtain a significant reduction in DM platelets aggregation compared to control subjects. NSC23766 treatment was also able to potentiate antiplatelet effects of aspirin in patients with DM.

Conclusions: This study is the first to demonstrate the role of Rac-1 in glucose-induced platelet hyperaggregation and endothelium dysfunction. We also found that NSC23766 was able to protect from endothelial alteration, rescue NO release from platelets and abolish glucose-induced platelets hyperaggregation.

P2121 | BENCH

Rac-1 as a new target to modulate endothelial function and platelet aggregation in diabetes mellitus

F. Iliard1, A. Carrizzo2, G.G. Schiattarella1, A. Damato2, M.T. Ambrosio2, V. Trimarco1, C. Perrino1, B. Trimarco1, C. Vecchione2, G. Esposito1. 1 Federico II University Hospital, Advanced Biomedical Sciences, Naples, Italy; 2 Neuroned Institute IRCCS, Pozzilli, Italy; 3 Federico II University Hospital, Hypertension Research Center, Naples, Italy

Background: Vascular injury and abnormal platelet function are major contributors of increased thrombotic events of diabetes mellitus (DM) population. Rac-1 protein, a small GTP-binding protein, has been involved in platelet aggregation and vascular damage induced by high glucose levels, but no studies have evaluated its role in the enhanced platelet aggregation in DM.

Purpose: We investigate whether Rac-1 inhibitor, named NSC23766, could reduce human platelet hyperaggregation induced by high glucose stimulation, and also whether it could modulate vascular and platelet functions in vitro and in a in vivo mouse model of DM.

Methods and results: Mesenteric arteries (n=4 for each group) from C57BL/6 mice were exposed to low (5mM) and high (25mM) glucose concentrations. At high glucose levels arteries showed a significant reduction to acetylcholine-evoked vasorelaxation (p<0.01 vs. Glu 5mM), which was restored by pretreatment with NSC23766 (30 μM). To evaluate the in vivo effects of hyperglycemia on Rac-1 regulation of vascular function, diabetes was induced in C57BL/6 mice with single intraperitoneal injection of streptozotocin (STZ - 40 mg/kg). Vascular studies revealed the abolition of endothelial dysfunction up to 96 hours after a single injection of Rac-1 inhibitor. Studies on human platelets revealed that high glucose levels (25mM) induced the activation of Rac-1 and the reduction of nitric oxide (NO) release, which was restored after the treatment with NSC23766. Treatment with NSC23766 also restored vasorelaxation evoked by supernatant from stimulated platelets close to basal condition. Aggregation induced by type I collagen (0.8 μg/ml) was significantly increased when platelets were preincubated with glucose (25 mM) while RAC1 inhibitor (30 μM) reduced platelet aggregation, and this effect was improved at highest glucose concentrations. Finally, platelets from diabetic patients (n=20) showed higher levels of Rac-1, correlated to percentage of glycated hemoglobin, when compared to control subjects (n=11); consistently, a higher dose of NSC23766 (60 μM) was necessary to obtain a significant reduction in DM platelets aggregation compared to control subjects. NSC23766 treatment was also able to potentiate antiplatelet effects of aspirin in patients with DM.

Conclusions: This study is the first to demonstrate the role of Rac-1 in glucose-induced platelet hyperaggregation and endothelium dysfunction. We also found that NSC23766 was able to protect from endothelial alteration, rescue NO release from platelets and abolish glucose-induced platelets hyperaggregation.

P2122 | BEDSIDE

Temporal trend in incidence of acute myocardial infarction and the effect of baseline cardioprotective therapy on initial clinical presentation: a nationwide study

L. Smedegaard, M.G. Charlot, G.H. Gislason, P.R. Hansen. Gentofte Hospital - Copenhagen University Hospital, Department of Cardiology, Hellerup, Denmark

Purpose: Changes over time in incidence, initial presentation and preceding use of cardioprotective medication in patients presenting with first time myocardial infarction (MI) have not been characterized in detail. The present study aimed to investigate temporal trends in incidence of MI with or without ST-segment elevation (STEMI) and the effect of prior cardioprotective medication on the initial clinical presentation.

Methods: A nationwide study (STE) and the effect of prior cardioprotective medication on the initial clinical presentation. Patients with the first hospitalization for ST-elevation MI from platelets and abolish glucose-induced platelets hyperaggregation.

Introduction: Beta-blockers reduce mortality after acute myocardial infarction (MI). Whether beta-blockers exert a class effect in the era of coronary reperfusion therapy is unknown.

Methods: We identified patients with the first hospitalization for STEMI through January 2003 to December 2010 from the National Health Insurance claims database, Taiwan. Patients receiving carvedilol, bisoprolol or propranolol were analyzed. Treating the carvedilol group as the common reference, simultaneous three-group comparison approach was used to compare the relative risks of outcomes included all-cause death, cardiovascular death and recurrence of MI.

Results: Among 16836 patients, 7591 were prescribed with carvedilol, 5934 with bisoprolol and 352 with propranolol. The mean follow-up was 1.0 years. After accounting for baseline differences, patients treated with bisoprolol (adjusted hazard ratio [HR] 0.87, 95% confidence interval [CI] 0.72–1.05, p=0.14) or propranolol (adjusted HR 1.07, 95% CI 0.84–1.36, p=0.64) had a similar risk of all-cause death in comparison with those with carvedilol. There was no significant difference among the three beta-blocker groups in risks of cardiovascular death and recurrence of MI.

Conclusions: Beta-blockers have class effect in the modern era of acute MI treatment.
P2124 | BENCH
Rapid endovascular moderate hypothermia before reperfusion provides more cardioprotection than mild hypothermia in a porcine model of myocardial infarction

R. Dash1, F. Dawoud2, F. Ikeino1, A. Tachibana1, J. Lyons1, Y. Mitsuoka1, W.B. Pyun1, M. McConnell1, U. Illindala2, A. Yeung1. 1 Stanford University Medical Center, Stanford, United States of America; 2Zoll Circulation, San Jose, United States of America

Background: Cardiac protection of mild hypothermia during acute myocardial infarction (AMI) yielded equivocal results in recent clinical trials.

Purpose: We investigated dose-response relationship between myocardial salvage and depth of rapid therapeutic hypothermia.

Methods: Swine (n=24, 46±3 kg) were randomly assigned to 3 groups: normothermia (38C), mild hypothermia (35C) and moderate hypothermia (32C). AMI was induced by 1-hour ischemia-reperfusion of mid LAD. Then an endovascular balloon catheter controlled temperature to either 32C or 35C. Cooling started 30 minutes before reperfusion, target temperature was reached in 9±5 (35C) and 29±8 (32C) minutes, and maintained for 1 hour followed by slow rewarming. Infarct size (IS) was assessed on day 6 with in vivo cardiac magnetic resonance (CMR) imaging and ex vivo TTC staining.

Results: TTC area-at-risk (AAR) was equivalent in all groups (p=0.473). Both the 35C and 32C groups showed significant IS reduction (62% and 91%) per AAR compared to 38C (IS%AAR 45±12, 17±10, 4±4, p<0.001) and a similar reduction per LV mass (IS%LV: 14±5, 5±3, 1±1, p<0.001). Additionally, 32C group showed significant IS per AAR reduction compared to 35C (p=0.013) suggesting further tissue salvage from deeper cooling.

Delayed-enhancement CMR of IS per LV also showed significant reduction at 32C (10±4*, 8±3, 3±2*, *p<0.001). Cardiac output (CO) change at follow up relative to baseline was less affected in the 32C group only (−30%±16*, −24%±7, −17%±18*, p<0.041).

Using linear regression, the predicted TTC IS reduction was 7% of AAR and 2% of LV per 1°C drop at reperfusion.

Conclusion: Pre-reperfusion moderate therapeutic hypothermia shows a strong dose-dependent infarct size reduction as well as favorable hemodynamic outcome more consistently than mild hypothermia.

P2125 | BENCH
P2Y12-receptor knockout leads to reduced myocardial ischemia/reperfusion injury in mice

A. Maier1, D. Duerschmidt1, D. Von Ellenriede2, M. Mauler1, M. Moritz2, T. Witsch1, J. Neudorfer1, K. Peter1, C. Bode1, C. Von Zur Muehlen1, 1University of Freiburg, University Heart Center Freiburg, Freiburg, Germany; 2University of Freiburg, Freiburg, Germany; 3Baker IDI Heart and Diabetes Institute, Melbourne, Australia

Introduction - Microvascular obstruction and inflammation play a substantial role for the extent of myocardial IR injury. Platelets and platelet-neutrophil-complexes are critically involved in this and can be affected pharmacologically by P2Y12-receptor inhibitors. Therefore, we investigated in this study the influence of a simulated therapy with thienopyridine-class antithrombotic agents on IR injury in an in vivo mouse model with an innovative molecular MRI imaging strategy and compared these findings with established infarct size read-out methods.

Methods: C57BL/6N and P2Y12−/− mice were subjected to a 50 minute ligation of the LAD, MRI of activated platelets and necrosis in the reperfused myocardium was performed two hours after reperfusion. Activated platelets were targeted with monoclonal antibodies linked to anti-lipid-induced binding sites of the activated platelet GPIIb/IIIa (LIBS-MPIO). In comparison, a control antibody was applied (control-MPIO). Necrosis was detected via late gadolinium enhancement (LGE). All imaging results were correlated to findings in histology for platelets, platelet-neutrophil-complexes (PNCs), and necrosis. Ejection fraction and infarct size of the area at risk in wildtype vs. P2Y12−/− mice were quantified by echocardiography and Monolite blue/TTC staining.

Results: In MRI short axis images a significant signal decrease in the area of LAD occlusion occurred after injection of LIBS-MPIO in WT mice, whereas in P2Y12−/− mice no signal decrease was found. In parallel, gadolinium allowed the detection of myocardial necrosis in both groups. The extent of necrosis was significantly lower in P2Y12−/− mice quantified by LGE (p<0.01) as well as in histological HE staining (p<0.001). Significantly less accumulation of microthrombi in P2Y12−/− mice was counted in the reperfused myocardium (p<0.001). The amount of bound MPIOs was significantly reduced to the level of WT mice (p<0.01). Moreover, the amount of PNCs was reduced in P2Y12−/− mice (p<0.001). In Monolite Blue/TTC staining, infarct size of the area a risk was significantly lower in P2Y12−/− mice (p<0.05). A strong tendency toward a better preserved EF in P2Y12−/− compared to WT mice was found in echocardiography (p<0.1).

Conclusions: A simulated therapy with P2Y12-receptor inhibitors leads to reduced inflammation and myocardial necrosis after coronary vessel occlusion and reperfusion in mice. This was evident in histology and echocardiography as well as in a novel dual in-vivo MR imaging technique and is of great clinical and prognostic interest.

P2126 | BEDSIDE
Presence of myocardial scar does not prevent improvement in myocardial perfusion and left ventricular function in refractory angina patients undergoing intramyocardial bone marrow cell injection

I. Mann, S.F. Rodrigo, J. Van Ramshorst, S.L.M.A. Beeses, H.J. Lamb, H.M. Siebelink, R.J. Van Der Geest, W.E. Fibbe, M.I. Schalij, D.E. Atsma. Leiden University Medical Center, Cardiology, Leiden, Netherlands

Background: We previously showed that myocardial perfusion and left ventricular function in refractory angina patients improve after intramyocardial bone marrow cell injection. However, the treatment response varies between patients.

Purpose: The aim of this study is to evaluate whether the presence of myocardial scar influences the treatment effect.

Methods: A total of 93 refractory angina patients, with stress-inducible ischemia as assessed by single photon emission tomography (SPECT) and left ventricular ejection fraction (EF) of >25% was assessed using magnetic resonance imaging (MRI) were treated with intramyocardial cell injection using the NOGA system. Late gadolinium enhancement on MRI was used to assess presence of myocardial scar at baseline. At 3 months, perfusion and function were re-evaluated.

Results: At baseline, presence of myocardial scar was associated with more perfusion defects upon stress (assessed by summed stress score (SSS) (R²=0.348, P<0.001)) and with a lower baseline EF (R²=0.188, P<0.001), but not with stress-induced ischemia (assessed by summed difference score (R²=0.002, P=0.708)). Baseline myocardial scar was not associated with improvement in summed stress score (R²=0.003, P=0.607), summed difference score (R²=0.006, P=0.487) or EF (R²=0.007, P=0.462) at 3 months after cell injection.

Conclusion: Myocardial scar does not prevent improvement in myocardial perfusion and ejection fraction after cell therapy. Thus, presence of myocardial scar in this patient group is not a contra-indication for cell injection.

P2127 | BEDSIDE
Ultrasound superparamagnetic particles of iron oxide-enhanced magnetic resonance imaging in the assessment of cellular inflammation after myocardial infarction


Background: Optimal levels of early “proinflammatory” and late “reparative” macrophages after myocardial infarction (MI) are crucial to the recovery of cardiac function. Ultrasound superparamagnetic particles of iron oxide (USPIO) are engulfed by resident macrophages in infarmed tissues and can be detected using magnetic resonance imaging (MRI). We aimed to determine the duration of USPIO-enhancement following acute MI, and examine their association with functional recovery.

Methods: Thirty-one patients with acute MI were studied in the 3-month period following acute MI. Repeated T2-weighted 3T MRI was performed immediately before and 24 h after USPIO (ferumoxytol, 4 mg/kg) administration at 2±1, 5±2, 13±3, 21±4 and 89±11 days. Regions of interest (ROIs) were categorised into infarct, peri-infarct, and remote myocardial zones by co-registration with late gadolinium enhancement (LGE). R2* values (1/T2*) within ROIs were determined to assess the duration of USPIO uptake.

Results: Compared to remote myocardium, increased USPIO uptake in the infarct zone is seen at days 2±1 (p<0.0001), days 5±2 (p<0.01), and days 13±3 (p<0.01) (Figure 1). No difference in USPIO uptake is seen at later time points (21±4, 89±11 days; p>0.05, not shown). USPIO uptake within the infarct zone is significantly less accumulation of microthrombi in P2Y12−/− mice was counted in the reperfused myocardium (p<0.001). The amount of bound MPIOs was significantly reduced to the level of WT mice (p<0.01). Moreover, the amount of PNCs was reduced in P2Y12−/− mice (p<0.001). In Monolite Blue/TTC staining, infarct size of the area a risk was significantly lower in P2Y12−/− mice (p<0.05). A strong tendency toward a better preserved EF in P2Y12−/− compared to WT mice was found in echocardiography (p<0.1).

Conclusions: A simulated therapy with P2Y12-receptor inhibitors leads to reduced inflammation and myocardial necrosis after coronary vessel occlusion and reperfusion in mice. This was evident in histology and echocardiography as well as in a novel dual in-vivo MR imaging technique and is of great clinical and prognostic interest.
at days 4–13 post MI correlated with improved ejection fraction (EF) at 3 months (not shown).

Conclusion: USPIO-enhanced MRI can detect and quantify infarct-related cellular inflammation after MI and in other inflammatory cardiac conditions.

P2129 | BEDSIDE
T1 mapping by cardiac magnetic resonance imaging: from histological validation to clinical implication
A. Kammerlander, S. Pfaffenerberger, C. Zotter-Tufaro, A. Bachmann, S. Aschauer, F. Duca, K. Knechtedsleger, M. Wiesinger, D. Bönderman, J. Mascherbauer. Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria

Background: Diffuse myocardial fibrosis/extracellular matrix expansion is a landmark feature of heart failure. Cardiac magnetic resonance (CMR) T1 mapping has recently been developed as a non-invasive technique to estimate the extracellular volume (ECV). However, the prognostic and diagnostic validity of extracellular matrix expansion by CMR T1 mapping is not well established. In particular, validation data against myocardial biopsy and prospective prognostic data are sparse.

Methods: 531 consecutive patients without hypertrophic cardiomyopathy (49% female, 57±18 years old) referred to CMR were prospectively enrolled. The ECV was measured using the Modified Look-Locker Inversion Recovery (MOLLI) sequence, excluding myocardial infarction.

39 patients (26 with heart failure, 9 with cardiac amyloidosis and 4 with valvular heart disease) underwent myocardial biopsy. Myocardial specimens were stained using Modified Trichrome. The ECV was histologically quantified using TissueFAXS analysis (TissueFAXS-ECV) and correlated with ECV by CMR T1 mapping (MOLLI-EVC).

For the assessment of the prognostic value of MOLLI-EVC, we investigated its association with outcome in the 531 patients (hospitalization for heart failure or cardiovascular death) by multivariable Cox-regression analysis.

Results: In myocardial specimens TissueFAXS-ECV was 33±16% and showed excellent correlation with MOLLI-EVC (r=0.915, p<0.001). MOLLI-EVC was 29±7% on average. When patients were divided into quartiles according to ECV (quartiles: 18.3–25.1%, 25.2–27.1%, 27.2–29.7% and <29.8%), those with higher MOLLI-EVC had a reduced event-free survival (log-rank: p<0.001). By univariable Cox-regression, patients with higher MOLLI-EVC were at significantly higher risk for a cardiac event (hazard ratio 1.095 per 1% increase, p<0.001). Including cardiovascular risk factors, comorbidities, age and NT-proBNP in a multivariable Cox-regression model, MOLLI-EVC still was independently associated with outcome (p<0.001), in addition to age (p<0.001) and NT-proBNP level (p=0.016).

Conclusion: MOLLI-EVC allows accurate non-invasive quantification of extracellular matrix expansion and is independently associated with event-free survival.

DIET, LIPIDS AND THE VASCULARITY

P2130 | BENCH
Dyslipidemia impairs high-density lipoprotein cardioprotective effects leading to larger infarcts. HDL-characterization by lipid analysis and differential proteomics
V. Vilahur1, J. Cubedo1, M. Gutierrez2, L. Casani2, A. Capdevila1, G. Pons-Lladó1, F. Carreras1, A. Hidalgo2, L. Badimon1, Barcelona Cardiovascular Research Center (CSIC-ICCC), IIB-Sant Pau, Hosp Sant Pau, UAB, Barcelona, Spain; 2Hospital de la Santa Creu i Sant Pau, Radiology Unit., Barcelona, Spain; 3Hospital de la Santa Creu i Sant Pau, Cardiology Unit, Barcelona, Spain

Purpose: We investigated whether the presence of dyslipidemia diminishes HDL-induced cardioprotective effects in a pre-clinical animal model.

Methods: Pigs (n=12) were randomized to 2 intravenous infusions 3 days apart of HDL (15mg/kg) either isolated from allogenic pigs fed a normocholesterolemic diet or fed a Western-type hypercholesterolemic diet (NC-HDL; cholesterol: 76±4 mg/dL) or fed a Western-type hypercholesterolemic diet (HyperC-HDL; cholesterol: 296±34 mg/dL) diet (p<0.0001). One day after the last dose all pigs underwent 1h closed-chest coronary balloon occlusion followed by reperfusion (MI). Cardiac function, myocardium-at-risk, no-reflow and necrosis were quantified by 3T-cardiac magnetic resonance 3 days post-MI. Lipid analysis and differential proteomics of NC-HDL and HyperC-HDL were performed prior infusion. NC-HDL and HyperC-HDL antioxidant potential was assessed.

Results: Despite similar extent of myocardium-at-risk in all animals after MI those having received infusion of HyperC-HDL resulted in an almost 50% reduction in myocardial salvaged index (P<0.05) and 37% larger scar size (P<0.05) as compared to those having received NC-HDL. HyperC-HDL-treated animals showed increased no-reflow (P<0.05) which correlated with the extent of necrosis (P<0.05; R=0.7). Although no differences were detected in global contractility (P<0.05), left ventricle volumes were worsened by ≈20% in HyperC-HDL recipient pigs (p<0.001 vs NC-HDL). HDL characterization revealed that neutral lipids were increased in HyperC-HDL vs NC-HDL (P<0.05). Proteomic analysis indicated that HyperC-HDL had significantly reduced content of lipid- (ApoB and arylsulfatase-G-isofrom1), lipocerins- and vitamin A-transporters and metabolic compounds (RBP4, ApoM and CRABP-II). No changes were observed in ApoA-I profile. Antioxidant activity of HyperC-HDL was 18% lower than that of NC-HDL (P<0.05).

Conclusions: We demonstrate, for the first time, that the presence of hyper-
hypocholesterolemia modifies HDL and its potential to induce cardioprotection during MI. Increased extent of infarct size and worsening of cardiac perfusion and performance are major findings in this study. Hypercholesterolemia induces HDL remodeling and shifts HDL towards a less anti-oxidant profile.

P2131 | BEDSIDE
Association between epicardial fat thickness and circulating endothelial progenitor cell levels in patients with coronary arterial disease.

C.-C. Chiu, C.-Y. Hsu, P.-H. Huang, T.-C. Wu, H.-B. Lee, J.-W. Chen, S.-J. Lin, Taipei Veterans General Hospital, Division of Cardiology, Taipei, Taiwan, ROC

Objectives: Epicardial fat tissue is associated with advanced atherosclerosis and several studies revealed thicker epicardial fat thickness (EFT) is associated with higher risk of cardiovascular disease. Increasing evidence suggests that injured endothelial monolayer is regenerated by circulating bone marrow derived-endothelial progenitor cells (EPCs), and levels of circulating EPCs reflect vascular repair capacity. However, the relation between EFT and EPC remains unclear. Here, we tested the hypothesis that patients with thicker EFT might have decreased EPC levels and attenuated EPC function.

Methods: A total of 101 consecutive patients undergoing elective coronary angiography because of suspected coronary artery disease (CAD) were screened and received examinations of echocardiography between November 2013 and November 2014. Flow cytometry with quantification of EPC markers (defined as CD34+/CD133+/KDR+, CD34+/KDR+/Lin− and CD34+/KDR+/Lin−/CD133+/Lin−) in peripheral blood samples was used to assess circulating EPC numbers. The adhesive function, migration, and tube formation capacities of EPCs were also determined. Syntax scores were calculated according to the coronary angiography.

Results: Patients with thicker EFT (≥5mm) had significantly decreased circulating EPC levels (table), attenuated EPC functions, and enhanced systemic inflammation compared to patients with thinner EFT. In addition, higher Syntax score was found patients with thicker EFT (21.32 vs 24.69, p=0.009).

Conclusions: Patients with CAD and thicker EFT have decreased circulating EPC numbers and functions and higher Syntax score than those with thinner EFT.

P2132 | BENCH
ATF3 regulates high fat diet induced adipocytes hypertrophy and obesity by repression of ChREBP signaling pathway.

C.-F. Cheng, H.-C. Ku, T.-L. Tseng, H. Lin, Tzu Chi General Hospital, Hualien; 2 Taipai Medical University, Institute of Physiology, Taipei, Taiwan, ROC

Background: Obesity is a severe and complicated health issue related to lifestyle and dietary modifications, and is highly associated with metabolic syndrome and diabetes. Activating transcription factor 3 (ATF3) is a member of the ATF/CREB response element-binding protein family of transcriptional factors. It can be induced by stress condition in a variety of tissues, including the adipocytes. However, the physiology and mechanism of ATF3 in adipocytes and obesity regulation is not clear.

in vivo are not clear. ever, the physiology and mechanism of ATF3 in adipocytes and obesity regulation is induced by stress condition in a variety of tissues, including the adipocytes. How-

Results: ATF3−/− mice were given HFD for 16 weeks, with decrease body weights were observed as compared to ATF3−/− mice then received AAV8-mediated gene transfer of ATF3 (AAV8-ATF3) at 16 weeks, in which decrease body weights were observed as compared to AAV8-ATF3 mice. Histology demonstrated increased adipocyte cell diameter in ATF3−/− mice, whereas the expression of ATF3 did not repress both PPARg2 and adipogenic markers (including C/EBPa, PPARg, adiponectin, leptin and resistin), FABP4 promoter activities.

Conclusions: These results suggest that ATF3 inhibits 3T3-L1 preadipocyte differentiation and lipid droplet formation in murine adipocytes through attenuating cellular inflammation and inhibiting both adipogenic and lipogenic processes; likely through repressing the ChREBP-ACC1 pathway. Therefore, our results confirm that ATF3 regulates high-fat diet-induced adipocytes hypertrophy and lipid metabolism in mice via ChREBP repression.

P2133 | BEDSIDE
Arginase inhibition improves endothelial function in patients with familial hypercholesterolemia.

O. Kovanee, A. Shemyakin, M. Eriksson, B. Angelin, J. Pernow, Karolinska Institute, Department of Medicine, Stockholm, Sweden

Background: Elevated low density lipoprotein cholesterol (LDL-C) is an important risk factor for coronary artery disease. An important mechanism is endothelial dysfunction characterized by reduced bioavailability of nitric oxide (NO) which permits vascular uptake of LDL-C. Arginase has emerged as a key regulator of endothelial function and is activated by oxidized LDL. Therefore we aimed to study the effect of arginase inhibition on endothelial function in patients with familial hypercholesterolemia (FH) and healthy subjects.

Methods: Twelve patients with FH (age 32±3) on lipid-lowering medication and twelve healthy subjects (30±2) were recruited. Venous occlusion plethysmography with intra-arterial infusion of serotonin and nitroprusside was used to assess forearm endothelium-dependent (EDV) and —independent (EIVD) vasodilation, respectively, before and after 120 min administration of the arginase inhibitor AIF-4 (5 mmol/L) (Sigma-Aldrich). HDL in soluble form was added both while on lipid-lowering medication and 4 weeks after medication withdrawal.

Results: In FH patients LDL-C increased from 3.4±0.6 mmol/L at the initial examination to 7.6±0.5 mmol/L at follow-up (p<0.001). In control subjects LDL-C was 2.9±0.3 mmol/L. Baseline EDV and EIVD did not differ between the examinations and the groups. Arginase inhibition enhanced EDV both in control subjects and FH patients. However, the improvement in EDV evoked by arginase inhibition was significantly higher in FH patients with high LDL-C levels as compared to the respective control group.

Conclusions: Arginase inhibition results in greater improvement in endothelial function in patients with FH compared to LDL-C levels compared to healthy controls, suggesting an up-regulation of arginase activity regulating NO bioavailability.

P2134 | BEDSIDE
Vasculoprotective effects of dietary flavanols in hemodialysis patients: a double-blind, randomized, placebo-controlled trial.

C. Rammos, 1 U.B. Hendgen-Cotta, 1 C. Heiss, 2 W. Kleoghas, 2 F. Dellanna, 1 O. Kovamees, 2 A. Shemyakin, 1 M. Eriksson, 2 C. Heiss 1, 1, 2 C. Rammos, 1, 2 C. Heiss 1, 1 German University of Dusseldorf, Department of Cardiology, Dusseldorf, Germany; 2Nephrology Practice, Dusseldorf, Germany; 2University of California, Department of Nutrition, Davis, United States of America

Background: Patients with end-stage renal disease (ESRD) are characterized by increased cardiovascular morbidity and mortality. Hemodialysis per se entails endothelial dysfunction characterized by impaired flow-mediated dilation (FMD). Intervenational data show that flavanol-rich supplements improve cardiovascular functions.

Objective: To investigate the effects of a flavanol-rich dietary supplement on endothelial function in patients with ESRD. Endothelial dysfunction is the key step in atherosclerosis and characterized by impaired flow-mediated dilation (FMD). Interventional data show that flavanol-rich supplements improve cardiovascular functions.

Methods: This trial was conducted in a randomized, double-blind, placebo-controlled manner (Clinicaltrials.gov NCT01412320). In a safety and efficacy study we determined acute effects of flavanoids on endothelial function and hemodynamics. In a subsequent study following a 30-day ingestion period, we studied the effects of flavonoids on hemodialysis-mediated vascular dysfunction as compared to a nutrient-matched control. Primary and secondary outcome measures included safety and changes in FMD and plasma flavanol metabolites, respectively.

Results: 57 patients with ESRD were included (mean±SD, 42% male, age 65±13 years, BMI 29.5±5 kg/m2, dialysis vintage 41±32 months). Flavanol ingestion was well tolerated. Acute ingestion was associated with an increase in circulating epicatechin metabolites and increased FMD by 53% (p<0.0001) with no effects on blood pressure or heart rate. A 30-day ingestion of flavanoids led to an increase of baseline FMD by 18% (p<0.001) with increased heart rate (70±2 to 74±3 bpm; p=0.007) and reduced diastolic blood pressure (74±2 mmHg to 70±5 mmHg; p=0.004). No effects were observed for placebo. Acute ingestion of flavonoids during hemodialysis alleviated hemodialysis-induced vascular dysfunction (Delta FMD flavanols 0.7±1.0 vs. placebo 1.4±0.5, p<0.001).
P2135 | BENCH
Occurrence of coronary lipid deposits and myocardial fatty dystrophy in dabigatran etexilate-treated diabetic rats
A. Scridon1, D. Gheban2, A. Marginean2, M. Perian1, R.C. Serban3, D. Dobreanu1.
1 University of Medicine and Pharmacy of Tirgu Mures, Physiology Department, Tirgu Mures, Romania; 2 University of Medicine and Pharmacy of Cluj Napoca, Pathology Department, Cluj Napoca, Romania; 3 University of Medicine and Pharmacy of Tirgu Mures, Tirgu Mures, Romania

Background: Besides its role in the coagulation cascade, thrombin has also been shown to interfere with lipid metabolism and to play a role in the initial development of atherosclerotic plaques.

Purpose: The present study aimed to assess the impact of direct thrombin inhibition with dabigatran etexilate (DE) on coronary, aortic, and myocardial lipid deposits in diabetic and control rats.

Methods: Thirty-two 11-wk-old Wistar rats were randomized into 4 groups: control (C; n=6), control treated with DE (CD; n=8), diabetes (D; n=8), and diabetes treated with DE (DD; n=10). In a cascade by bilateral diabetes was induced with an injection of Streptozotocin (60 mg/kg). CD and DD rats were treated with DE via chow (50 mg/kg body weight) for 12 wks. At 38 wks of age, all rats were euthanized; blood and tissue samples were collected. Atherosclerotic lesion formation in aorto-cervical, coronary, and myocardial lipid deposits were evaluated with Oil Red staining. A 3-point scoring system was used to assess lipid burden within the 3 examination sites.

Results: Three D and 2 DD rats died during the study and were excluded from the study. At the 3 examination sites, in CD and DD rats compared to C and CD rats (all p<0.02), while there was no significant difference between C and CD rats (all p>0.05), nor between D and DD rats (all p>0.05). Coronary atherosclerotic lesion formation in DD rats were absent in C and D rats, while 4 CD rats (50%) and 7 DD rats (87.5%) presented myocardial fatty dystrophy. None of the C rats presented aortic lipid deposits, while 6 CD rats (75%), 4 D rats (80%), and 6 DD rats (75%) presented mild aortic lipid deposits. Coronary lipid deposits were only present in CD rats, and in none of the other rats. Coronary lipid deposits were found in 6 DD rats (80%), including grade 2 (moderate) deposits in 2 DDs and grade 3 (gross) deposits in 1 DD rat.

Conclusions: Regardless of the diabetic status, DE administration was associated with myocardial fatty dystrophy. Administration of DE in control rats was associated with aortic lipid deposits similar to those seen in age-matched, untreated diabetic. More importantly, although DE administration in controls did not influence coronary lipid content, 80% of DE-treated diabetics developed coronary lipid deposits, including moderate-gross deposits. These results suggest that interfering with the coagulation cascade by blocking thrombin in diabetic rats may promote coronary atherosclerosis and myocardial fatty dystrophy.

P2136 | BEDSIDE
HDL functionality in children with type 1 diabetes
C. Nguyen1, E. McLaughlin1, T. Khan1, M. Charakida1, Y. Elia2, E. Sochett2, F. Mahmoud2, J. Deanfield1, 1 University College London, Institute of Cardiovascular Sciences, London, United Kingdom; 2 Hospital for Sick Children, Department of Pediatrics, Toronto, Canada

Background: The prognosis for childhood-onset type 1 diabetes (T1D) remains poor. Apart from poor glycaemic control, microalbuminuria is considered as an early risk marker for the development of cardiovascular (CV) disease in T1D patients. HDL dysfunction has been reported in adults with diabetes and this seems to further increase their CV risk. However it remains unknown whether similar changes can be seen in T1D adolescents.

Methods: We examined HDL function in 40 children (aged 10–16 years) with T1D and 20 age matched controls in relation to Albumin/Creatinine ratio (ACR) in the urine. T1D adolescents were divided into two groups (high ACR and low ACR). HDL endothelial properties were assessed by measuring Nitric Oxide and superoxide production in aortic endothelial cells using ESR spectroscopy. Serum paraoxonase (PON-1) activities were measured by UV spectrophotometry.

Results: Children with high ACR had higher HDL levels than those with low ACR and normal controls (beta per group 0.12 (95% CI 0.025 to 0.22), p-trend: 0.017). HDL from the high ACR group showed reduced Nitric Oxide bioavailability compared to controls (beta +0.73 (95% CI 1.27 – 1.8), p: 0.01) and the low ACR group (beta -0.71 (95% CI -1.26 to -1.7), p: 0.012). Similar trends but no significant change were also seen in endothelial superoxide release and serum PON-1 levels in T1D with high ACR compared to controls. HDL did not influence endothelial properties between T1D with low ACR and controls (p: 0.96).

Conclusion: In this study we demonstrated that T1D adolescents with high ACR had impaired HDL endothelial properties compared to controls. These disturbances were not observed in C and D groups. Our findings show that impaired HDL endothelial properties may contribute to increased CV risk of T1D with high ACR. Further studies are needed to assess whether measuring the endothelial properties of HDL will improve CV risk stratification in T1D adolescents.

P2137 | BEDSIDE
QRS fragmentation is superior to QRS duration in the prediction of death or ventricular tachycardia in adults with tetralogy of Fallot
J.P. Bokma1, M.M. Winter1, H.W. Vliegen2, A.P. Van Dijk2, P.G. Pieper4, F.J. Melboom4, M.C. Post1, B.J. Mulder1, B.J. Bouma1, 1 Academic Medical Center of Amsterdam, Cardiology, Amsterdam, Netherlands; 2 Leiden University Medical Center, Leiden, Netherlands; 3 University Hospital Nijmegen, Nijmegen, Netherlands; 4 University Medical Center Groningen, Groningen, Netherlands; 5 St Antonius Hospital, Nieuwegein, Netherlands

Background: Adults with tetralogy of Fallot (TOF) are at risk for life threatening arrhythmias and early death. Fragmentation of QRS (fQRS) complexes can be easily assessed and has been related with right ventricular fibrosis.

Purpose: To determine if fQRS is predictive for all-cause mortality and/or sustained ventricular tachycardia (VT) in adult TOF patients.

Methods: This multi-center study included TOF patients from a prospective nationwide registry. Notches in the QRS complex in ≥2 contiguous leads on standard 12-lead electrocardiograms (ECG), not related to right bundle branch block (RBBB), were defined as fQRS. The extent of fQRS was classified as none, moderate (<4 leads) or severe (≥5 leads). Clinical data were obtained from the registry.

Results: A total of 794 patients (median age 28 years, 56% male) were included. The extent of fQRS at inclusion was classified as none in 52% of patients, moderate in 32% and severe in 16%. During long-term (median 10.4 years) follow-up, 46 (6%) patients died and 28 (4%) had a sustained VT. Overall 10-year survival was 98% in patients without fQRS, 93% in moderate fQRS and 81% in severe fQRS. In multivariable analysis, the extent of fQRS (HR: 2.38/class, 95% CI: 1.50–3.79, p<0.001) and age (HR: 1.07/year, CI: 1.05 to 1.09, p<0.001) were independently predictive for mortality. QRS duration was no longer predictive for mortality (HR: 1.00/ms, p<0.79) in multivariable analysis. The extent of fQRS was also predictive for sustained VT (HR: 2.41/class, 95% CI: 1.38–4.20, p=0.002) and the combined endpoint (death or VT) (HR: 2.30/class, 95% CI: 1.59–3.11, p<0.001) in multivariable models.

Conclusion: Fragmented QRS complexes are present in about half of adult TOF patients. The extent of QRS fragmentation is superior to QRS duration in predicting death or VT.
tion (r=0.06, p=0.77). There was also no significant correlation between LVEDP or PCWP and RV end-diastolic and end-systolic volumes or RV ejection fraction on MRI. In addition, QRS duration was not significantly related to PCWP or LVEDP, while it was significantly correlated with RV volumes (r=0.56, p<0.001 for RVEDV/indexed) and measures of biventricular function (r=0.64, p<0.001 for RV ejection fraction and RV fractional area, respectively). PCWP was, however, weakly correlated to elevated systemic arterial pressure (r=0.34, p=0.047).

Conclusion: Despite the reported strong prognostic significance of LV filling pressures on outcome, no correlation between PCWP or LVEDP and RV volumes or function in adult patients with repairedToF. Therefore, the current data suggest that elevated LV filling pressures may not merely reflect RV disease but may rather be a marker of intrinsic LV pathology, highlighting the important role of the LV in determining late outcome after repair ofToF.

P2139 | BEDSIDE

Relation between exercise capacity and skeletal muscle metabolism during exercise in patients with repaired tetralogy of Fallot

A. Frigiolia1, K. Bull1, M. Papademetriou2, A. Hoskote1, G. Derrick1, S. Cullen3, P2139 | BEDSIDE

<derwent cardiac magnetic resonance imaging (MRI). Patients had lower peak oxygenation index (TOI), from the right vastus lateralis muscle. Patients also un-near infrared spectroscopy (NIRS) measurement of O2-hemoglobin, and tissue males) underwent maximal cardiopulmonary exercise testing and simultaneous Methods and results: 44 patients with repaired tetralogy of Fallot (ToF; 31±15 years, 25 males) and 26 age and gender matched controls (28±15 years, 13 males) underwent maximal cardiopulmonary exercise testing and simultaneous near infrared spectroscopy (NIRS) measurement of O2-hemoglobin, and tissue oxygenation index (TOI), from the right vastus lateralis muscle. Patients also underwent cardiac magnetic resonance imaging (MRI). Patients had lower peak VO2 than controls (27±8 vs. 32±9 mL/kg/min, p=0.001), lower peak HR (93±8 vs. 100±8% of predicted, p=0.001) and similar VE/VCO2 slope (p=0.286). Right ventricular end diastolic diameter in the ToF population was 100±26 mm2, ejection fraction was 59±7%, and pulmonary regurgitant fraction was 18±4%. Resting to peak exercise changes (Δ) in O2-hemoglobin, total-haemoglobin and TOI were not statistically different between the two groups (p between 0.444 and 0.520). On single linear regression analysis only ΔTOI was predictive of peak VO2 in patients in controls (p=0.007 and p=0.003). To understand the clinical magnitude of these associations in patients, we used the coefficients obtained at multiple regression to calculate the % changes in peak VO2 associated with 1 standard deviation (SD) increase in the variables alternatively peak VO2 and TOI. One SD increase in peak VO2 and TOI caused respectively a +4.5%, and a +25.5% increase in peak VO2.

Conclusions: In ToF patients and in controls, peak VO2 depends more on inter-individual differences in muscle oxygen extraction than on HR response to exercise thus suggesting that “peripheral” factors might be more important than “central” factors in determining exercise capacity. Therapeutic options, including cardiac rehabilitation, should be promoted for patients with CHD.

P2141 | BEDSIDE

Infective endocarditis following pulmonary valve intervention in patients with repaired congenital heart disease: a comparison of surgical and percutaneous procedures

S. Cesna1, M.J. Jones2, F. Walker1, S. Cullen2, P. Bonhoeffer2, V. Tsaing2, T.Y. Hsia2, B. Pandya2, 1University Hospital Santariskiu Klinikos, Vilnius, Lithuania;2 The Heart Hospital, London, United Kingdom

Background: Percutaneous pulmonary valve implantation (PPVI) avoids the risks associated with open heart surgery, including mortality and morbidity. Infective endocarditis (IE) has been described following both percutaneous and surgical procedures.

Purpose: To quantify the incidence and define the clinical course of CHD patients developing either PPVI or PVR.

Methods: Retrospective analysis of patients undergoing either PVR or PPVI at our centre for adults with CHD between 2005 and 2013 and to identify and confirm endocarditis, and clinical course.

Results: During the period 2005–2013, 303 patients underwent pulmonary valve implantation: 209 (69.0%) underwent surgical PVR and 94 (31.0%) underwent. Duration of follow up was 0.1–7.8 years. Endocarditis was confirmed in eight patients with PVR and nine patients with PPVI (3.8% vs 9.6%, p=0.44). Freedom from IE was 1402±273 days in the PVR group (361–2736 days) and 1160±309 days in the PPVI group (58–2500 days, p<0.0001). Three patients in the surgical PVR-IE group were successfully treated with antibiotic therapy, three required early PVR due to failure of medical therapy and two underwent elective PVR following a period of antibiotic sterilization. In the PPVI-IE group, one patient was successfully treated with antibiotic therapy; seven required urgent PVR and one underwent elective surgical PVR. We did not perform repeat PPVI in any patients. There was one death in PPVI-IE group. Three patients in surgical PVR-IE group had recurrent IE after repeat PVR despite antibiotic therapy.

Conclusion: The incidence of IE following PPVI is significantly higher than in patients who have undergone PPVI than those with PVR in our institution. Freedom from IE is significantly longer in the surgical group. Factors such as immune system dysfunction should be considered carefully when planning replacement of the pulmonary valve.

P2142 | BEDSIDE

Early cardiac remodelling post-pulmonary valve replacement in patients with repaired tetralogy of Fallot

E.L. Heng1, M.A. Gatzoulis1, G.C. Smith1, D.F. Shore1, B. Sethia2, H. Uemura2, G.P. Diller2, S.Y. Ho4, D.J. Pennell2, S.V. Babu-Narayan1, 1Royal Brompton Hospital, Department of Adult Congenital Heart Disease & NIHR Cardiovascular Biomedical Research Unit, London, United Kingdom;2Royal Brompton Hospital, Department of Adult Congenital Heart Disease, Faculty of Cardiovascular Science, University of Manchester, Manchester, United Kingdom;3University of Alabama at Birmingham, Birmingham, Alabama, United States;4University Hospital Essen, Essen, Germany

Background: Histological abnormalities of the ascending aorta (AAo) have been described in tetralogy of Fallot (ToF) but the clinical implications are not well known.

Purpose: To determine the extension, prevalence and predictors of aortic dilatation late after ToF repair (rToF) and to assess the aortic strain and stiffness in this context.

Population and methods: Eighty-six consecutive adults after rToF were included and were compared with a sex- and age-matched healthy volunteer group (n=46). The inner diameters of the sinuses of Valsalva (SoV), sinotubular junction (STJ) and AAo were measured using transthoracic echocardiography, in parasternal long-axis view. We defined aortic dilatation as an aortic z-score (AoZ) ≥ 2. The aortic dilatation was assessed by two-dimensional speckle tracking (2D-ST) global peak circumferential ascending aortic strain (CAAS). The aortic stiffness index was calculated according to ln (Ps/Pd)/CAAS and the arterial stiffness as 0.9Pps/SV (Ps and Pd stand for systolic and diastolic blood pressure, respectively and SV for stroke volume).
156.1±11.9mg/dL vs ePVR 104.9±28.4mg/dL, RVEFV1 pPVR 74.9±26.2mg/dL vs ePVR 57.4±22.7ml/m², indexed RV mass pPVR 64.2±13.8g/m² vs ePVR 55.4±15.2g/m² and RVEF pPVR 52.9±7.7% vs ePVR 46.4±8.8%; p < 0.01) in Figure. The improvement in RV volumes was sustained whilst RVEF returns to pre-PVR baseline at mid-term follow-up. PVR produced a continued improvement in corrected cardiac output, pulmonary valve competency, in addition to it's modest but significant improvement of LVEF. Right atrial remodelling was also evident.

**Conclusions:** Cardiac remodelling is generally regarded as a gradual process post-PVR. RVEF monostavas for the first time that the major improvement in RV volumes seen at mid-term follow-up have already taken place within days of surgery. This occurs with an apparent transient impairment of RVEF, although corrected RVEF more easily illustrates the immediate, positive effect of PVR, which continues to improve up to mid-term.

**References**


**Risk factors for prosthetic pulmonary valve failure (PPVF) in patients with congenital heart disease (CHD) are not well known.**

**Methods:** Cumulative freedom from re-intervention due to PPVF after 148 pulmonary valve replacement (PVR) in 114 patients with CHD is analyzed. Six risk factors (age at intervention, underlying cardiac defect, hemodynamic indication for PVR, type of intervention, history of palliative procedures, and number of prior interventions) were analyzed using multivariate Cox proportional hazard models. Receiving operating characteristics (ROC) curves were used for discrimination. Internal validation in subgroups of patients with tetralogy of Fallot (N=81) and patients with severe pulmonary regurgitation as hemodynamic indication for PVR (N=57) was also performed.

**Results:** Median age at intervention was 23 years old. There were 60 reinterventions due to PPVF (41%). Median event-free survival was 14 years (95% CI 12–16 years). The only independent risk factor was the age at intervention (hazard ratio 0.93; 95% CI 0.90–0.97; p < 0.001; area under the ROC curve 0.95; 95% CI 0.92–0.98; p < 0.001). Freedom from re-intervention because of PPVF 15 years after surgery was 70% when it was performed at age > 20.5 years compared with 33% when age at intervention was < 20.5 years (p = 0.004) (figure). Internal validation in patients with tetralogy of Fallot (area ROC 0.98; 95% CI 0.96–1.0; p < 0.001) or severe pulmonary regurgitation (area ROC 0.94; 95% CI 0.86–1.02; p < 0.001) was excellent.

**Conclusion:** Re-intervention risk due to PPVF after 15 years of follow-up is more than two-fold when PVR is performed before the age of 20.5 years.

**WHAT DOES EPIDEMIOLOGY TEACH US ABOUT CARDIOVASCULAR RISK?**

**P2144 | BEDSIDE**

**LDL cholesterol remains an important predictor of coronary heart disease events even in the statin era**

A.M. Navar-Boggan 1, E.D. Peterson 1, D.M. Wojdyla 1, J.E. Eliasassi 2, R.B. D’Agostino 2, R.J. Sanchez 2, M.J. Pencina 2, 1 Duke Clinical Research Institute, Durham, United States of America; 2 Regeneron Pharmaceuticals, Inc., Tarrytown, NY, United States of America; 3 Boston University, Boston, United States of America.

**Background:** One in three adults is estimated to have elevated low-density lipoprotein cholesterol (LDL-C), a known risk factor for coronary heart disease (CHD). In the era of statin therapy, however, the prevalence of elevated LDL-C as well as the overall incidence of CHD events have decreased over time. We investigated whether the association of LDL-C and new onset CHD has changed in the modern era of statin therapy.

**Purpose:** To compare the association between LDL-C and new onset CHD in the pre- and post-statin eras and evaluate the population attributable risk of new onset CHD due to elevated LDL-C.

**Methods:** We combined data from the Cardiovascular Health Study and the Framingham Offspring Study to create two equally sized, age- and sex-matched cohorts of adults aged 40–79 free of cardiovascular disease at baseline, including 1) a ‘pre-statin era’ cohort (data from 1983–1996) and 2) a ‘post-statin’ cohort (1997–2007). The association between LDL-C and new onset CHD, adjusting for standard CHD risk factors, was compared between the two cohorts using Cox proportional hazards modeling. The population attributable risk of LDL-C on CHD risk was determined using LDL-C levels in CHD cases and hazard ratios from the Cox models.

**Results:** We identified 4020 adults aged 40–79 in each cohort. Use of statins increased in the ‘post-statin era’, from 7.1% in 1997 to 30.7% in 2007. The overall CHD event rate declined from 1.35 per 100 patient-years of follow up in the pre-statin cohort to 1.20 in the post-statin cohort. The average baseline LDL-C in CHD cases was lower in the post-statin cohort compared with the pre-statin cohort (140 mg/dL vs 132 mg/dL, p < 0.001). Despite these changes, the association between LDL-C and new onset CHD events was not statistically significantly lower in the post-compared with the pre-statin era (adjusted HR 1.11 (1.06–1.17) versus 1.09 (1.03–1.16) per 20 mg/dL LDL-C increase, p = 0.09). The population attributable risk of CHD due to elevated LDL-C was also numerically lower in the post-versus pre-statin era (13.2% (3.8–22.0%) vs 18.7% (10.0–26.8%), respectively).

**Conclusions:** The use of statin therapy has risen markedly over time and has contributed to a decline in overall CHD event rates. However, the association between elevated LDL-C and CHD remains unchanged in the modern era. Although the population attributable risk of CHD due to elevated LDL-C has declined somewhat over time, 13.2% of CHD cases in the post-statin era are still attributable to elevated LDL-C.

**P2145 | BEDSIDE**

**Relationship between lipoprotein(a) level and mortality in 72766 Korean adults**

B.J. Kim, B.S. Kim, K.C. Sung, J.H. Kang, S.H. Lee, J.Y. Lee. Division of Cardiology, Kangbuk Samsung Hospital, Sungkyunkwan University School of Medicine, Seoul, Korea, Republic of Korea.

**Introduction:** Lipoprotein(a) (Lp(a)) is known as a risk factor of cardiovascular disease. However, the studies about the relation between Lp(a) and cardiovascular mortality have shown the inconsistent results, and most of the studies were limited to western population.

**Objectives:** This study was performed to evaluate the association of Lp(a) with the mortality in Korean adults.

**Methods:** Among individuals enrolled in Kangbuk Samsung Health study, 72766 participants (29469 women; age 41±9 years) between 2003 and 2005 who were free of coronary heart disease, stroke, and cancer and had Lp(a) measurements were followed for a median of 5.5 years. A large number of variables were collected: death from all causes, cardiovascular disease, coronary artery disease, cerebrovascular disease, cancer, and nonvascular disease and noncancer. Participants were divided into three groups (<7.0mg/dL, 7.08–29.99 mg/dL, and ≥30mg/dL) according to the Lp(a) level at baseline.

**Results:** The incidence of each mortality was the following: 347 death from all causes, 49 death from cardiovascular disease, 22 death from coronary artery disease, 27 death from cerebrovascular disease, 164 death from cancer, and 85 death from nonvascular and noncancer. Individuals in the highest Lp(a) tertile had higher unadjusted relative risk (RR) of death from cardiovascular disease (RR [95% CI], 2.52 [1.26, 5.04]) and death from cerebrovascular disease (2.81 [1.14, 6.90]) compared with those in the lowest Lp(a) tertile, whereas there was no significant difference in the risk between the above two groups in terms of mortality from all causes, coronary artery disease, cancer, and nonvascular and noncancer. Multivariate Cox-Hazards regression model adjusted for age, sex, smoking status, body mass index, systolic blood pressure, glucose, total cholesterol, low-density lipoprotein cholesterol, creatinine, and the presence of diabetes and hypertension history showed significantly increased RR of death from car-
diovascular disease (2.34 [1.09, 5.01]) and a trend toward increased RR of death from cerebrovascular disease (2.70 [0.95, 7.84]): meanwhile, the risk of mortality from all causes, coronary heart disease, cancer, and nonvascular disease and noncancer was not different between the two groups.

**Conclusion:** This large cohort study shows that an elevated level of lipoprotein(a) is an independent predictor of cardiovascular mortality, but not all causes mortality and mortality from cancer and mortality from nonvascular disease and noncancer in Korean adults.

**P2146 | BEDSIDE**

**Prevalence and management of familial hypercholesterolaemia in the EUROASPIRE IV project**

G. De Backer1, J. Besseling2, J. Chapman3, G.K. Hovingh2, J.J.P. Kastelein3, K. Kotsia4, K. Ray5, Z. Reiner6, D. Wood7, D. De Bacquer7,1, Ghent University;8 Belgium, Belgium, Belgium, Netherlands;9 Hospital Pitié-Salpêtrière, INSERM Dyslipidemia and Atherosclerosis Research Unit, Paris, France;10 Imperial College London, Cardiovascular Medicine, NHL, London, United Kingdom;11 St George University of Medicine, Dept Internal Medicine, Zagreb, Croatia

**Background:** The prevalence of Familial Hypercholesterolaemia (FH) is estimated in the community by 1:200–500 persons. In patients with established coronary heart disease (CHD) the prevalence is less well documented.

**Purpose:** The aim of this study was to estimate the prevalence of FH among patients with CHD and to compare the management of these patients with the other coronary patients.

**Methods:** In EUROASPIRE IV data were collected from May 2012 to April 2013 in 24 European countries by means of a standardized interview, bioclinical examination and self-reporting. Potenial FH was estimated using an adapted version of the Dutch Lipid Clinic Network Criteria; 85.7% of the patients were on lipid lowering drugs; untreated LDL-cholesterol was estimated using coefficients based on the kind and dosage of lipid lowering drugs that they currently used. Correction was made for reported non-compliance.

**Results:** Among the 7044 patients eligible for analysis, the prevalence of potential FH was 8.3%; 7.5% in men and 11.1% in women. The prevalence was inversely related to age with a putative prevalence of 1:5 in those with CHD -50 yrs of age in females. FH women aged 70 the prevalence was 1:10. Irrespective of age and gender, prevalence differed substantially between European regions; potential FH patients were more likely to smoke, had less low HDL-cholesterol levels but higher triglycerides levels and their blood pressure was less well controlled. The use of cardioprotective drugs and the prevalence of diabetes, obesity and central obesity were similar.

**Conclusion:** The prevalence of potential FH in coronary patients is large; the results underscore the need to promote identification of FH in CHD patients and to improve their risk factor profile.

**P2147 | BEDSIDE**

**Familial hypercholesterolemia is associated with poorer 5-year survival after myocardial infarction. The FAST-MI 2005 registry**


**Background:** The prevalence of potential FH in coronary patients is large; the results underscore the need to promote identification of FH in CHD patients and to improve their risk factor profile.

**Methods:** FAST-MI is a nationwide French registry including consecutive patients with AMI admitted during a one-month period (with a one-month extension for diabetic patients) in 213 institutions at the end of 2005; 5-year follow-up is available in 97% of patients. An algorithm derived from the Dutch lipid clinic criteria, based upon LDL level, personal and family history, and previous use of lipid lowering medications, was used to define probable or definite FH (FH+).

**Results:** From 3670 patients included, 2342 had a lipid profile assessed at admission. There was a greater decrease in high density lipoprotein cholesterol (HDLC) in the subgroup with Rel. In this well-characterised cohort of patients admitted for AMI, patients with FH had 13 years younger on average than non FH patients, but had a similar long-term mortality. After multivariate adjustment, however, 5-year mortality was no longer higher in FH patients, suggesting that specific therapeutic measures may be needed for such patients.

**P2148 | BEDSIDE**

**Impact of a major natural disaster on longitudinal changes in cardiovascular risk factors in the general population**


**Background:** Several recent studies have demonstrated that the incidence of atherosclerotic cardiovascular (ACV) disease increased after the 2011 Japan earthquake and tsunami, especially in the tsunami stricken area. However, no studies have investigated the longitudinal changes in ACV risk factors among survivors of the disaster.

**Methods:** Multiphasic health checkups were performed repeatedly during the post-disaster Phase 1 (8 months after the disaster) and Phase 2 (18 months after the disaster) in the general population living in the tsunami stricken area (n=6,272, mean age = 63 years). Changes in several ACV risk factors between Phase 1 and Phase 2 were compared between subgroups with (n=3,101) and without (n=3,171) relocation (Rel) due to residential property destruction.

**Results:** Body weight and lipoprotein cholesterol levels at Phase 1 (baseline) were similar between the two subgroups with and without Rel. However, changes in weight body weight between Phase 1 and Phase 2 were significantly greater in the subgroup with Rel compared to that without Rel (+0.4 vs. +0.2 kg, p<0.001: Fig-left). There was a greater decrease in high density lipoprotein cholesterol (HDLc) level in the subgroup with Rel, than in the subgroup without Rel (−0.9 vs. +0.1 mg/dl, p<0.001: Fig-right). Changes in other ACV risk factors such as systemic blood pressure, smoking status, non-HDLc and glycosemoglobin did not differ significantly between the two subgroups.

**Conclusion:** Even during the recovering phase more than a year after the disaster, there was a significant body weight gain with decreasing HDLc level in persons directly affected by the tsunami attack. This suggests that long term vigilance for changes in obesity related ACV risk factors is important after any devastating disaster.

**P2149 | BEDSIDE**

**Lipoprotein(a): influence on cardiovascular manifestation**

K.-P. Melwig, M. Schatton, B. Biermann, T. Kottmann, D. Horstkotte, F. Van Buuren. Department of Cardiology, Heart and Diabetes Center North Rhine-Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany

**Background:** The clinical relevance of lipoprotein (a) (Lp(a)) as a cardiovascular risk factor may be underestimated. The aim of our study was to assess the influence of Lp(a) on the development and severity of coronary artery disease (CAD).

**Purpose:** As Lp(a) is a non-normally distributed parameter, we correlated manifestation and severity of CAD in a cohort of 31,274 consecutive first-time-in-hospital survivors of AMI.

**Methods:** The following subgroups were analyzed: Lp(a) <30 mg/dl, Lp(a) 30–60 mg/dl, Lp(a) 61–90 mg/dl, Lp(a) 91–110 mg/dl, Lp(a) >110 mg/dl. Other cardiovascular risk factors (LDL, hba1c) were excluded.

**Results:** Parallel to increasing Lp(a) levels patients demonstrated a significantly higher incidence of advanced CAD (1–3-vessel disease, VD), a significantly more frequent history of myocardial infarction (STEMI) (p<0.001), percutaneous interventions (PCI) (p<0.001) and/or surgical myocardial revascularization (CABG) (p<0.001).

**Subgroups**

<table>
<thead>
<tr>
<th>Lp(a)</th>
<th>1-VD</th>
<th>2-VD</th>
<th>3-VD</th>
<th>STEMI</th>
<th>PCI</th>
<th>CABG</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Lp(a) &lt;30 mg/dl</td>
<td>15.7</td>
<td>50</td>
<td>12.2</td>
<td>39</td>
<td>25.1</td>
<td>80</td>
</tr>
<tr>
<td>Lp(a) 30–60 mg/dl</td>
<td>15.6</td>
<td>35</td>
<td>9.8</td>
<td>22</td>
<td>27.1</td>
<td>61</td>
</tr>
<tr>
<td>Lp(a) 61–90 mg/dl</td>
<td>23.1</td>
<td>53</td>
<td>17.5</td>
<td>40</td>
<td>40.2</td>
<td>92</td>
</tr>
<tr>
<td>Lp(a) 91–110 mg/dl</td>
<td>19.2</td>
<td>30</td>
<td>19.9</td>
<td>31</td>
<td>38.5</td>
<td>60</td>
</tr>
<tr>
<td>Lp(a) &gt;110 mg/dl</td>
<td>14.0</td>
<td>37</td>
<td>18.2</td>
<td>48</td>
<td>50.4</td>
<td>133</td>
</tr>
</tbody>
</table>

**Sex-age adjusted changes in BW and HDLc**

**Conclusion:** Sex-age adjusted changes in BW and HDLc
CAD risk (Odds Ratio) was increased 5.5-fold in patients with a C–M_B mass ≥ 110 mg/dl. Conclusion: A C–M_B mass of 110 mg/dl or above is an independent strong predictor for heart failure and is an adverse prognostic factor.

P2150 | BEDSIDE
Whole exome sequencing combined with integrated variant annotation prediction identifies asymptomatic Tangier disease with compound heterozygous mutations in ABCA1 gene
H. Tada, M. Kawashiri, A. Nohara, A. Inazu, H. Mabuchi, M. Yamagishi. Kanazawa University, Kanazawa, Japan

Background: Molecular diagnosis for the subjects with extremely low HDL cholesterol through candidate-gene approaches has required a huge effort for a long time. Whole exome sequencing (WES) technologies have already accelerated genetic studies of Mendelian disorders, yielding approximately ~30% of successful diagnoses, and there is a great interest in extending this approach to this phenotype. Moreover, a novel in silico prediction software of pathogenicity for novel missense variants named Combined Annotation Dependent Depletion (CADD), which objectively integrating many diverse annotations into a single measure (C-score) for each variant has been recently developed.

Purpose: The aim of our study was to investigate whether a WES combined with integrated variant annotation prediction could facilitate the molecular diagnosis of this rare condition.

Methods: WES was performed on 8 individuals including 2 individuals exhibiting extremely low HDL cholesterol (2 mg/dl and 6 mg/dl), 2 unaffected family members, and 4 unrelated individuals as controls. We have applied 4 independent filters after the standard variant quality controls. We have filtered out the variants as 1) Benign variants predicted by SnpEff, 2) Minor allele frequency < 1%, 3) Segregation unmatched under the assumption of recessive form of inheritance and 4) C-score < 10 calculated using CADD prediction software.

Results: Among 305,202 variants found in those individuals, we found 21,708 nonsense, missense, or splice site variants, of which 5,192 were rare (minor allele frequency < 1% or not reported). Filtering assuming recessive pattern of inheritance combined with the use of integrated variant annotation prediction successfully narrowed down the candidates to the compound heterozygous mutations in ATP-binding cassette transporter 1 (ABCA1) gene (c.7173C>T or p.P2077H/c.6223G>A or p.G948R/c.1130C>T or p.P2077H/c.6223G>A or p.S2046N, and c.2842G>A or p.948R/c.1130C>T or p.P2077H/c.6223G>A or p.S2046N, which may be responsible for the first time even where DNA is available for only one affected individual. Such comprehensive approach is useful to determine true causative variants, especially, in recessive form of inherited cardiovascular diseases.

CURRENT STATUS AND FUTURE DIRECTIONS OF CORONARY ARTERY BYPASS GRAFTING

P2151 | BEDSIDE
Long term follow-up following total arterial versus conventional and hybrid myocardial revascularisation: a propensity-match analysis
C. Muneretto1, G. Bisleri1, L. Di Bacco1, A. Repossini1, M. Tespili2. 1 University of Brescia, Department of Cardiac Surgery, Brescia, Italy; 2 Bologna University Hospital, Department of Cardiothoracic, Italy

Background: The choice of the optimal surgical strategy for myocardial revascularisation in multivessel coronary artery disease (mCAD) has still been widely debated, despite the potential advantages of an extensive use of arterial conduits in addition to the LIMA on LAD grafting. Furthermore, there has been an increased interest towards an hybrid strategy aiming for a transasthmatic revascularisation of non-LAD vessels in addition to the LIMA-LAD graft.

Purpose: To evaluate the impact of the revascularization technique (by means of conventional, total arterial or hybrid myocardial revascularization) in patients with mCAD: primary end-point was overall survival while secondary end-points were cardiovascular death and survival free from major adverse cardiac and cerebrovascular events (MACCEs) defined as myocardial infarction, cardiac death, stroke and repeated target vessel revascularization.

Methods: Among 593 consecutive patients undergoing myocardial revascularisation for coronary artery disease between 2006 and 2012, a propensity-score analysis was performed based on the techniques utilised, either total arterial CABG (Group 1, G1, n=89), conventional CABG/LIMA on LAD plus veins (Group 2, G2, n=89), or hybrid revascularisation (LIMA on LAD plus PTFCA on non-LAD vessels (Group 3, G3, n=89). Matching criteria were: age, sex, left ventricular ejection fraction, number of diseased vessels, NYHA class, logistic EuroSCORE, peripheral vascular disease, chronic obstructive pulmonary disease, previous stroke, chronic renal failure, dyslipidemia, recent STEMI/STEMI.

Results: Early mortality was 0% in all groups. At a mean follow-up of 6.2 years, the use of total arterial myocardial revascularization was associated with a significantly improved overall survival (G1=90.4±3.5% vs G2=82±3.4% vs G3=82±1.5% p=0.049) as well as freedom from MACCEs (G1=95±2.2% vs G2=86±5% vs G3=68±6.9%, p=0.001) while the survival free from cardiac-related death was similar among the groups (G1=97±7.1% vs G2=95±1.2% vs G3=89±5.5%, p=0.08). Finally, at 10 years follow-up, patients undergoing total arterial myocardial revascularisation had a significantly higher freedom from MACCEs (G1=79±8.6% vs G2=72±4.5% vs G3=62±8.7%, p=0.001).

Conclusions: The use of total arterial revascularization is associated with improved outcomes at mid and long term follow-up compared with conventional or hybrid revascularization. In particular, the use of a hybrid strategy is associated with a significantly higher incidence of cardiac-related revascularisation and repeat revascularisation, thereby underlining the need for a careful patients’ selection.

P2152 | BEDSIDE
An evaluation of the incidence and prognosis of post coronary artery bypass grafting myocardial infarction according to different definitions in the CORONARY trial
E.P. Kelley-Cote1, A. Lamy2, G.I. Tagarakis2, Y. Ou3, J. Vincent3, P. Kavask1, M. Zhang2, P.J. Devereaux2, R.P. Whitting1 on behalf of the CORONARY Investigators. 1 McMaster University, Hamilton, Canada; 2 University of Thessaly, Larissa, Greece; 3 Population Health Research Institute. Hamilton, Canada

Background: Over the years, clinical studies in cardiac surgery have used different diagnostic criteria for post coronary artery bypass grafting (CABG) myocardial infarction (MI). These diagnostic criteria, even though widely accepted, are based on arbitrary biomarker thresholds sometimes in association with ECG signs of cardiac necrosis (new pathologic Q waves or new left bundle branch block). The validation of these diagnostic criteria in terms of their association with clinical events is limited.

Methods: Using data from the CORONARY trial (n=4,752), a randomized controlled trial evaluating on-pump versus off-pump CABG, we evaluated the incidence of MI according to five different post CABG MI definitions. To evaluate the clinical relevance of the definitions, we calculated the associated hazard ratio (HR) for 30-day mortality adjusted for the EUROscore.

Results: Depending on the diagnostic criteria used, the incidence of MI after CABG surgery varied from 0.6 to 19% and the associated HR for 30-day mortality ranged from 2.7 to 6.9. On-pump versus off-pump surgery was not a significant interaction term.

Discussion and conclusion: A clinically relevant post CABG MI definition should be independently associated with mortality. Diagnostic criteria that are associated with a 4.0 to 6.9 fold increase in 30-day mortality may lack sensitivity to identify patients at substantial risk of short-term mortality. Our results illustrate the need for a validated post CABG MI diagnostic criteria formulated from its independent association with important clinical outcomes, especially with the movement towards the use of high sensitivity troponin assays.

P2153 | BEDSIDE
Impact of preexisting cerebral ischemia detected by magnetic resonance imaging on clinical outcomes after coronary artery bypass graft in patients without history of stroke
W.-J. Kim, Y.-M. Lim, S.-W. Lim, J.-Y. Moon, D. Min, S.-H. Kim, D.-H. Cha, S.-Y. Cho, W.-I. Yang, I.-J. Kim. CHA Bundang Medical Center, CHA University School of Medicine, Cardiology, Seongnam-si, Gyeonggi-do, Korea, Republic of

Purpose: We sought to assess the impact of preexisting ischemia detected by brain magnetic resonance imaging and angiography (MRI/MRA) on clinical outcomes after coronary artery bypass grafting (CABG).

Background: Limited data existed for long-term clinical outcomes of asymptomatic cerebral ischemia after CABG.

Methods: From January 2003 to May 2009, 3,071 patients underwent CABG in our center. Preoperative brain MRI/MRA was performed in 2,417 patients. Patients with history of stroke were excluded and a total of 2,119 patients were evaluated. Ischemia was detected by brain MRI in 253 patients (Group A), but not in 1,866 patients (Group B). The primary end point was major adverse cardiac and cerebrovascular events (MACCE), defined as the composite of death, myocardial infarction, and stroke.

Results: The baseline characteristics of the two groups were similar except left bundle branch block. There was no significant differences in the primary outcome of MACCE (2.0% vs 1.9% p=0.83). However, stroke was occurred in Group A (0.4%, 95% CI, 0.1–0.8%) and not in Group B (0.0%, 95% CI, 0.0–0.4%, p=0.04).

Conclusions: Our results suggest that asymptomatic cerebral ischemia detected by MRI/MRA may be a risk factor for stroke after CABG.
Results: The group A was older and had higher incidences of diabetes, chronic kidney disease, and peripheral vascular disease. European system for cardiac operative risk evaluation (EuroSCORE) was also higher in group A (4.3±2.3) than group B (3.6±2.2) (p<0.001). After adjustment with weighted Cox model using the inverse probability of treatment weighting, the 3-year risk of death (hazard ratio [HR], 1.72; 95% confidence interval [CI], 1.08–2.72, p=0.02), cardiac death (HR, 2.22, 95% CI, 1.05–4.69, p=0.036), stroke (HR, 2.21, 95% CI, 1.05–4.64, p<0.036), and MACCE (HR, 1.67, 95% CI, 1.09–2.54, p=0.018) were significantly higher in the group A. However, the 3-year risks of noncardiac death was similar between the two groups (HR, 1.49, 95% CI, 0.83–2.68, p=0.195).

Conclusion: Preexisting cerebral ischemic findings on brain MRI in patients who undergoing CABG were related to death, stroke, and MACCE.

P2154 | BEDSIDE

Colchicine treatment to reduce perioperative myocardial damage in patients undergoing on-pump coronary artery bypass grafting: a randomized study

G. Giannopoulou1, C. Angelidiss, V.K. Kouritas2, P. Dedelias2, S. Fotakis3, V. Panagopoulou2, E. Toli1, D. Toussoulis3, S. Defteros1, General Hospital of Athens “G. Genimissas”, Athens, Greece; 2Evangelismos General Hospital of Athens, Cardiac Surgery Department, Athens, Greece; 3Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Objective: The objective of the present study was to test whether a peroperative course of colchicine, in patients undergoing standard coronary artery bypass grafting (CABG), would result in reduced postoperative risk of myocardial injury biomarker levels.

Methods: Patients were prospectively randomized to colchicine or placebo starting 48 hours before scheduled CABG and for 8 days thereafter (0.5 mg twice daily). The primary outcome parameter was maximal high-sensitivity troponin T (hsTnT) concentration within 48 hours after surgery. Secondary outcome measures were maximal creatine kinase myocardial brain fraction (CK-MB) levels and area under the curve (AUC) of hsTnT and CK-MB concentrations.

Results: 59 patients were included. Maximal hs-TnT was 616 [396–988] pg/ml in the colchicine group versus 1613 [732–2587] pg/ml in controls (p<0.002). Maximal CK-MB was 44.6 [36.6–68.8] ng/ml and 93.0 [48.0–182.3] ng/ml, respectively (p<0.002). The median AUC for hsTnT was 40,755 [20,868–79,176] pg/h/ml in controls versus 20.363 [13,891–31,661] pg/h/ml in the colchicine group (p<0.002). AUCs for CK-MB were 2552 ng/h/ml [1564–4791] in controls and 1586 ng/h/ml [1159–2073] in the colchicine group (p=0.003). The main complications associated with colchicine were, as expected, gastrointestinal, with 5 of patients in the colchicine group (16.7%) reporting diarrhea, versus 1 (3.4%) control (p=0.195).

Conclusion: A short peroperative course of colchicine was effective in attenuating postoperative rises of hsTnT and CK-MB compared to placebo. This finding, which needs confirmation in a larger clinical trial powered to assess clinical endpoints, suggests a potential role for this agent in reducing cardiac-surgery-related myocardial damage. Clinical trial registration: ClinicalTrials.gov Identifier: NCT02122484.

P2155 | BEDSIDE

Long-term survival after off-pump coronary artery bypass graft surgery


Background: Randomised controlled trials demonstrate that Off-Pump Coronary Artery Bypass (OPCAB) is equivalent to On-Pump Coronary artery bypass graft surgery (ONCAB) for in-hospital and short-term outcomes. Recent observational data suggests that OPCAB may be associated with increased mid-term mortality although there are several conflicting studies.

Objective: There is little data on the impact of OPCAB on long-term survival. The objective of this study was to determine the impact of OPCAB on long-term survival compared to ONCAB.

Methods: We conducted a retrospective cohort study using the Bristol PATS database of all patients who underwent primary isolated CABG surgery from 1996 to 2011. Mortality data was obtained from the Office of National Statistics. Multivariate regression models were used to estimate the association between OPCAB and long-term survival.

Results: We evaluated long-term survival in 11,881 patients (mean age 65.5±9.3 years, 2202 females) who underwent CABG (OPCAB, n=6133; ONCAB, n=5848). Survival data was complete in 99.2% of patients, with a median follow-up duration of 12 years (interquartile range 8.4 to 11.8 years; maximum 17 years). Both groups were similar in terms of baseline characteristics and intraoperative variables. EuroSCORE (3.7 [0.03] vs 3.8 [0.03], SMD=0.038) was similar between OPCAB and ONCAB groups and mean number of distal anastomoses performed were 2.5 [(0.81) in the OPCAB group and 2.9 (0.78) in the OnCAB group (SMD=0.505). Long-term survival was similar between patients undergoing OPCAB and ONCAB (Log-rank test for equality of survivor functions (τ2 (1) =2.93; Pr: τ>0.087)); HR for death: 0.94, 95% CI [0.87, 1.01], p=0.087).

Conclusion: In patients undergoing CABG surgery, long-term survival is similar using OPCAB and ONCAB strategies.

P2156 | BEDSIDE

Outcome after coronary artery bypass grafting and percutaneous coronary intervention in patients with stage 3B-5 chronic kidney disease

A.K. Lautamaki1, T. Kiviniemi2, F. Biancari2, J.M. Gunn1, Turku University Hospital, Heart Center, Turku, Finland; 2Oulu University Hospital, Oulu, Finland

Introduction: Patients with chronic kidney disease (CKD) are generally considered as having an increased risk for cardiovascular events and cardiac mortality. The prognostic significance of severe renal impairment in patients undergoing coronary revascularization remains mainly unknown because these patients have been excluded from randomized clinical trials. The aim of the present study was to compare the outcome after percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) in patients with an estimated glomerular filtration rate (eGFR) <45 ml/min/1.73 m2.

Methods: This retrospective study includes 110 patients who underwent PCI and 148 patients who underwent isolated CABG between 2007 and 2010. All patients had stage 3B to stage 5 chronic kidney disease (eGFR <45 ml/min/1.73 m2).

Results: The median follow-up time was 26.6±18.7 months. At 30 days and five years, postoperative de novo dialysis was required in 4.7% and 13.2% of CABG patients and in 0% and 7.1% of PCI patients. PCI was associated with significantly higher risk of mortality (at 5 years, 26.3%, vs. 0.8%, adjusted analysis: HR 1.74, 95% CI 1.08–2.78), repeat revascularization (at 5 years, 26.3%, vs. 0.8%, adjusted analysis: HR 16.16, 95% CI 2.01–130.15) and major adverse cardiac and cerebrovascular events (at 5 years, 72% vs. 35%, HR 2.31, 95% CI 1.23–4.33). These findings were confirmed at propensity score matched analysis.

Conclusion: Patients with moderate to severe CKD have a high rate of mortality and morbidity after either PCI or CABG. The fear of postoperative dialysis rates after CABG appears overemphasized since only about 5% of patients needed dialysis during the first 30 days after CABG and long-term survival.

P2157 | BEDSIDE

Outcome after coronary artery bypass grafting and percutaneous coronary intervention in patients with stage 3B-5 chronic kidney disease

S. Nielsen, L. Bjorck, A. Jeppsson, K.W. Giang, T. Zverkova Sandstrom, A. Rosengren, Sahlgrenska Academy, Department of Molecular and Clinical Medicine, Gothenburg, Sweden

Purpose: The aim of the present study was to compare the 4-year mortality in men and women surviving at least 30 days after a first isolated coronary artery bypass graft procedure in 2002-2006, compared to the general population.

Methods: The National Inpatient register was used to identify 22,737 (17,712 men and 5,025 women) >18 years, who survived the first 30 days after CABG during 2002-2006. 4-year mortality rates in the study cohort was calculated and compared with those of the general population using standardised mortality
Conclusions: as shown after induction of unilateral hindlimb ischaemia, and bone marrow
were characterised by higher numbers of CD31-immunopositive endothelial cells
tricapillary dilation (P < 0.05), as well as a less pronounced cardiac hypertrophy (as determined by left
an improved systolic pump function in End.PTP1B-KO vs. End.PTP1B-WT mice
Disruption of Ca-homeostasis is a key pathomechanism in heart failure. While the
Men and women <55 years had a lower risk for mortality after CABG when compared to the general population
362 Current status and future directions of coronary artery bypass grafting / Basic mechanisms in heart failure
BASIC MECHANISMS IN HEART FAILURE
P2158 | BENCH
Endothelial deletion of protein tyrosine phosphatase-1B promotes angiogenesis and improves survival and heart function after pressure overload-induced cardiac hypertrophy in mice
R. Gogiraju1, M.R. Schroeter1, M.L. Bocheneck2, K. Schaefer1. 1 Department of Cardiology and Pulmonary Medicine, Goettingen, Germany; 2 University Medical Center of Mainz, Medical Clinic 2, Mainz, Germany
Background: Cardiac angiogenesis is an important determinant of heart failure, and endothelial micrornas (miRs) may contribute to the angiogenesis from hypotrophy to failure. The activity of VEGF and other angiogenic growth factor receptors is negatively controlled by protein tyrosine phosphatases (PTPs), which mediate the dephosphorylation of specific tyrosine residues and are highly expressed in endothelial cells.
Purpose: To examine the hypothesis that (over-)expression of endothelial PTP1B in response to cardiac pressure overload is causally involved in the reduced coronary angiogenesis in the hypertrophied heart and that endothelial deletion of PTP1B may prevent the development of heart failure.
Methods: Mice with tamoxifen-inducible, endothelial cell-specific deletion of PTP1B (End.PTP1B-KO) were generated by crossing mice with loxP-flanked PTP1B alleles with mice expressing a Cre recombinase-estrogen receptor fusion protein under control of the endothelial receptor tyrosine kinase promoter. Cardiac hypertrophy was induced by transverse aortic constriction (TAC).
Results: Survival was significantly improved in End.PTP1B-KO mice up to 20 weeks after TAC (P <0.002). Serial echocardiography measurements revealed an improved systolic pump function in End.PTP1B-KO vs. End.PTP1B-WT mice (P <0.01) as well as a less pronounced cardiac hypertrophy (as determined by left ventricular mass [P < 0.01] and heart-to-body weight ratio [P < 0.05]) and left ventricular dilatation (P < 0.05). Histologically, banded hearts from End.PTP1B-KO mice were characterised by higher numbers of CD31-immunopositive endothelial cells (P <0.001) and improved perfusion (P < 0.05) as well as reduced cardiac fibrosis (P < 0.05), whereas no differences in the number of CD45-positive inflammatory cells were observed. Western blot analysis of banded heart lysates confirmed higher levels of phosphorylated VEGF receptor-2 and p42/44 MAPK in End.PTP1B-KO vs. End.PTP1B-WT mice (P <0.01) and CCL2 and CCL5-RKIP-deficient mice (P<0.05) were subjected to transverse aortic constriction (TAC, 360 μm) or sham-operation or treatment with CCI4 (0.7 mg/kg, 12 l.p. injections, 6 weeks) to induce cardiac and systemic fibrosis. The cardiac QTLs linked to collagen accumulation were screened for potential candidates by expression QTL analyses, analysing of transcriptomic data of CCI4-treated BDXs (Affy 1.0 ST arrays). Raf Kinase Inhibitor Protein (RafKIP, Phosphatidylinositol4,5-Binding Protein I, PEBP-I) was identified as genetic marker of individual fibrosis progression. Cardiac fibrosis in the left ventricle (LV) of BXD lines assessed by picrosirius red staining correlated with LV RKIP mRNA (R=0.4, p=0.05). 10-week-old male C57/B6 wild-type, C57/B6-RKIP+/− and C57/B6-RKIP−/− mice were subjected to transverse aortic constriction (TAC, 360 μm) or sham-operation or treatment with CCI4 for 6 weeks, untreated mice served as controls (n=9–10 per group). RKIP-deficiency reduced both CCI4-induced interstitial- and TAC-induced replacement fibrosis, increased in CCI4-treated RKIP−/− mice versus controls. The cardiac fibrosis correlated with the respective control groups. Collagen I α2 mRNA was reduced by approximately 50% both in TAC and CCI4-treated RKIP−/− mice. RKIP-deficiency increased the number of CD31+ endothelial cells to 118±5% in CCI4-treated and to 157±18% in aortic-ligated RKIP−/− mice per mm2, decreased the number of fibroblasts per mm2 assessed by immunostaining for intracellular fibrinogen in TAC mice by 20±5%, the percentage of cycling Ki-67+ fibroblasts in CCI4-treated mice to 23±18% and the percentage of CXC44+ fibroblasts in TAC mice to 74±8%. RKIP-deficient adult cardiac fibroblasts demonstrated increased migration capacity in a modified Boyden chamber by 23%. RKIP-deficiency diminished cardiomyocyte apoptosis in CCI4-treated mice to 39±13% and in aortic-ligated mice to 31±10%. Heart weight to tibia length ratio, cardiomyocyte cross-sectional area and the percentage of Ki-67+ cardiomyocytes were decreased in RKIP-deficient aortic-ligated mice. All effects were significant with p<0.05.
Conclusions: These data identify Raf Kinase Inhibitor Protein as an important regulator of interstitial and replacement cardiac fibrosis.

P2159 | BENCH
Raf kinase inhibitor protein regulates interstitial and replacement cardiac fibrosis
A. Kazakov1, R. Hall2, T. Meier1, F. Lammer2, M. Boehm1, U. Laufs1. 1 Saarland University Hospital, Department of Internal Medicine III, Cardiology, Homburg, Germany; 2 Saarland University Hospital, Department of Internal Medicine II, Gastroenterology, Homburg, Germany
Background: Genetic determinants of cardiac fibrogenesis are not completely understood. Quantitative Trait Loci (QTL) analyses in BXD recombinant inbred mouse lines and subsequent characterization of the identified target was applied to identify novel regulators of myocardial fibrosis.
Methods and results: For genome-wide QTL analysis, 26 BXD lines representing a genetically mosaic but homoygous for all loci genetic reference population were treated with CCI4 (0.7 mg/kg, 12 l.p. injections, 6 weeks) to induce cardiac and systemic fibrosis. The cardiac QTLs linked to collagen accumulation were screened for potential candidates by expression QTL analyses, analyzing of transcriptomic data of CCI4-treated BDXs ( Affy 1.0 ST arrays). Raf Kinase Inhibitor Protein (RafKIP, Phosphatidylinositol4,5-Binding Protein I, PEBP-I) was identified as genetic marker of individual fibrosis progression. Cardiac fibrosis in the left ventricle (LV) of BXD lines assessed by picrosirius red staining correlated with LV RKIP mRNA (R=0.4, p=0.05). 10-week-old male C57/B6 wild-type, C57/B6-RKIP+/− and C57/B6-RKIP−/− mice were subjected to transverse aortic constriction (TAC, 360 μm) or sham-operation or treatment with CCI4 for 6 weeks, untreated mice served as controls (n=9–10 per group). RKIP-deficiency reduced both CCI4-induced interstitial- and TAC-induced replacement fibrosis, increased in CCI4-treated RKIP−/− mice versus controls. The cardiac fibrosis correlated with the respective control groups. Collagen Iα2 mRNA was reduced by approximately 50% both in TAC and CCI4-treated RKIP−/− mice. RKIP-deficiency increased the number of CD31+ endothelial cells to 118±5% in CCI4-treated and to 157±18% in aortic-ligated RKIP−/− mice per mm2, decreased the number of fibroblasts per mm2 assessed by immunostaining for intracellular fibrinogen in TAC mice by 20±5%, the percentage of cycling Ki-67+ fibroblasts in CCI4-treated mice to 23±18% and the percentage of CXC44+ fibroblasts in TAC mice to 74±8%. RKIP-deficient adult cardiac fibroblasts demonstrated increased migration capacity in a modified Boyden chamber by 23%. RKIP-deficiency diminished cardiomyocyte apoptosis in CCI4-treated mice to 39±13% and in aortic-ligated mice to 31±10%. Heart weight to tibia length ratio, cardiomyocyte cross-sectional area and the percentage of Ki-67+ cardiomyocytes were decreased in RKIP-deficient aortic-ligated mice. All effects were significant with p<0.05.
Conclusions: These data identify Raf Kinase Inhibitor Protein as an important regulator of interstitial and replacement cardiac fibrosis.
the underlying cause of heart failure, with benefit of EX after myocardial infarction (MI) but not during aortic stenosis. Here we tested the hypothesis that the balance between nitric oxide (NO) and superoxide (O2-) is responsible for these divergent effects of EX, and is due to differential effects of EX on endothelial NO synthase (eNOS) function.

Methods: Mice were exposed to 8 wk of voluntary wheel running EX or sedentary housing (SED) after MI, transverse aortic constriction (TAC), or sham (SH). Left ventricular (LV) function was measured by echography. Picro-sirius Red staining was used to assess collagen content. Total and NOS-dependent LV O2- production was studied using lucigenin-enhanced chemiluminescence without or with NOS inhibitor L-NAME. Peroxynitrite (ONOO-) formation was studied using luminol-enhanced chemiluminescence. eNOS uncoupling was measured by western blot. eNOS-S-glutathionylation was measured by coimmunoprecipitation. Results: O2- generation and LV dysfunction are increased in MI but not TAC (Table 1). Strikingly, O2- generation was blunted by EX in MI, but exacerbated by EX in TAC, which was largely NOS-dependent. eNOS uncoupling was corrected by EX in MI but aggravated in TAC mice, in parallel with attenuation and exacerbation of both ONOO- levels and glutathionylation of eNOS by EX in MI and TAC, respectively.

EFFECTS OF EXERCISE

<table>
<thead>
<tr>
<th>SED</th>
<th>SH</th>
<th>MEX</th>
<th>MI</th>
<th>TAC</th>
<th>TACx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fractional shortening (%)</td>
<td>37±2</td>
<td>39±1</td>
<td>61±1</td>
<td>121±1</td>
<td>18±2</td>
</tr>
<tr>
<td>Collagen content (%)</td>
<td>1.3±0.1</td>
<td>1.9±0.3</td>
<td>6.9±5.7</td>
<td>3.0±3.5</td>
<td>11.4±2.3</td>
</tr>
<tr>
<td>Superoxide production (RLU/sec/mg)</td>
<td>18±1</td>
<td>24±3</td>
<td>41±2</td>
<td>29±1</td>
<td>45±3</td>
</tr>
<tr>
<td>eNOS uncoupling (AU)</td>
<td>1.0±0.1</td>
<td>1.0±0.2</td>
<td>2.1±1.1</td>
<td>1.5±0.1</td>
<td>3.0±0.4</td>
</tr>
<tr>
<td>Peroxynitrite formation (RLU/sec/mg)</td>
<td>0.08±0.01</td>
<td>0.093±0.02</td>
<td>0.22±0.05</td>
<td>0.12±0.02</td>
<td>0.27±0.03</td>
</tr>
<tr>
<td>eNOS S-glutathionylation (AU)</td>
<td>1.0±0.1</td>
<td>1.0±0.1</td>
<td>1.4±0.1</td>
<td>1.1±0.1</td>
<td>1.5±0.1</td>
</tr>
</tbody>
</table>

Data are mean ± SEM. eNOS, endothelial nitric oxide synthase; RLU, relative light unit; AU, arbitrary unit. n=4-20 per group. *p<0.05 vs corr. SED; §p<0.05 vs corr. SH.

Conclusion: The contrasting effects of EX in MI vs TAC appear mediated by divergent effects of EX on eNOSs glutathionylation, eNOS uncoupling and ONOO- formation, resulting in blunted vs aggravated oxidative stress by EX in MI vs TAC.

P2162 | BENCH

Regulation of fetal gene reprogramming by the early-onset myocardial infarction associated PHACTR1 gene in the heart

A Kelloniemi1, Z Szabo1, R Sergi1, J Napanangak3, P Ohukainen1, L Kaikkonen1, M Leodottor4, O Melander1, H Ruskoaho5, J Ryaso6

1University of Oulu, Institute of Biomedicine, Dept of Pharmacology and Toxicology, Oulu; 2University of Oulu, Faculty of Biochemistry and Molecular Medicine, Biocenter Oulu, Oulu; 3Oulu University Hospital, Dept of Pathology, Oulu, Finland; 4Lund University, Department of Clinical Sciences, Lund, Sweden; 5University of Helsinki, Division of Pharmacology and Pharmacotherapy, Helsinki; 6University of Eastern Finland, School of Pharmacy, Kuopio, Finland

Background: Phosphatase and actin regulator 1 (PHACTR1) locus is one of the most often identified genome-wide association studies hit for coronary artery disease and myocardial infarction (MI). However, the function of PHACTR1 in the heart is still unknown.

Purpose: We characterized the mechanisms regulating Phactr1 expression in the heart and investigated the effects of Phactr1 gene delivery on cardiac function.

Methods: EX enhanced both LV dysfunction and fibrosis in MI but not TAC (Table 1). Strikingly, O2- generation was blunted by EX in MI, but exacerbated by EX in TAC, which was largely NOS-dependent. eNOS uncoupling was corrected by EX in MI but aggravated in TAC mice, in parallel with attenuation and exacerbation of both ONOO- levels and glutathionylation of eNOS by EX in MI and TAC, respectively.

Conclusions: Phactr1 regulates reprogramming of cardiac gene expression, particularly skeletal to cardiac α-actin isoform ratio.

P2161 | BENCH

Impaired cardiac function in MMP13 knock out mice after myocardial infarction due to impaired remodeling

D Westerman1, D Lindner1, P.M. Becker1, V Lang1, S Hinrichs1, S Sossalla2, S Blankenberg3,1

1University Medical Center Hamburg-Eppendorf, Department of General and Interventional Cardiology, Hamburg, Germany; 2University Hospital Gottingen, Gottingen, Germany

Background: During myocardial infarction (MI) an extensive cardiac remodeling accompanies by accumulation of collagen is known to be important for scar formation. Exceded collagen production leads to cardiac fibrosis and impaired cardiac function. As matrix-degrading enzymes matrix-metalloproteinases (MMP) are key mediators during those cardiac remodeling processes. The MMP-13 is considered to be the major interstitial collagenase in the heart and investigated the effects of Phactr1 gene delivery on cardiac function.

Methods: In this study, we induced MI in wild type and MMP13 knock-out mice. Five days after MI mice deficient for MMP13 showed an aggravation in survival and hemodynamic function compared to wild type animals. In both mice strains a clear scar formation with an accumulation of collagen could be determined (Fig 1A). The isolated primary cardiac fibroblasts from wild type as well as MMP13 knock-out animals which were used for engineered connective tissue (ECTs). Functional stress-strain experiments were performed with ECTs derived either from MMP13 deficient or from wild type fibroblasts. We could demonstrate that the stiffness of MMP13 deficient fibroblasts is increased compared to wild type fibroblasts.

Conclusions: During scar formation after MI MMP13 plays an important role for survival and cardiac function. MMP13 deficient mice show increased collagen accumulation explaining the reduced LV function. Furthermore, ECTs derived from MMP13 deficient cardiac fibroblasts revealed an increased stiffness.

HYPERTENSION AND HAEMODYNAMICS

P2165 | BEDSIDE

Validation of noninvasive central blood pressure parameters attained with a brachial cuff-based oscillometric device among cardiovascular patients with cardiac dysfunction

T Shoji, S Okada, A Nakagomi, Y Kobayashi. Chiba University Graduate School of Medicine, Department of Cardiovascular Medicine, Chiba, Japan

Background and introduction: Central blood pressure (cBP) shows actual proximal responses on the heart and proximal large arteries, and is regarded to be superior to brachial blood pressure in predicting cardiovascular events. Recently, analysis of arterial pulse wave made it possible to indirectly measure cBP parameters. Even ambulatory central blood pressure monitor implemented with this analysis program, such as ARV Solver algorithm, is now put into practical use. But some studies have been reported that patients with reduced cardiac function are also qualified for such indirect measurement. Therefore, it is largely unknown whether patients with reduced cardiac function are also qualified for such indirect measurement. Furthermore, there is no consistent agreement on the calibration mode that is indispensable for calculation process.

Aim: To determine how cardiac dysfunction affects the indirect cBP indices attained by ARV solver algorithm, we validated and compared the measured data according to cardiac function and calibration mode.

Methods: We enrolled 120 patients undergoing elective coronary angiography in...
this study. Brachial and central BPs were measured noninvasively with brachial cBP monitoring device with ARC Solver algorithm, invasively with a fluid-filled catheter. Patients were divided into two groups at the median value of 53% according to aortic pulse wave transit times (cPWV) (CAD). However, it remains unknown which is the most appropriate for CAD risk estimation. 

Purpose: To compare the predictive values of these parameters using a brachial cuff-based oscillometric device.

Methods: Consecutive 139 patients undergoing coronary angiography were enrolled in this study. The Mobil-O-Graph system provided an indirect estimate of brachial/arterial BP indices, PWV, adjusted augmentation index (AIx@75) and the amplitude of backward wave (Pb). The following values were defined: fractional pulse pressure (FPF) as pulse pressure (PP)/mean BP; pulse pressure amplification (PPA) as brachial PP/arterial PP. Significant CAD was defined as having ≥50% stenosis in major coronary arteries.

Results: Compared with no CAD patients, CAD patients showed significantly higher values of brachial/arterial PP and FPF (PP: brachial 48.5±15.2 vs 55.0±16.2mmHg, aortic 51.7±19.0 vs 62.3±19.9mmHg; FPF: brachial 0.42±0.09 vs 0.49±0.11, aortic 0.45±0.13 vs 0.56±0.14; all p<0.05). PW (10.0±2.4 vs 11.3±2.3ms; p=0.05), Pb (21.7±7.8 vs 26.7±6.5mmHg; p<0.05) and lower value of AIx@75 (0.12 vs 0.90±0.11; p<0.05). Other indices including Aix@75 did not differ significantly. Univariate logistic regression analysis revealed brachial FPF, aortic PP, arterial FPP, PWV, PA and Pb were associated with the presence of CAD. Among them, when aortic FPP was entered into the multivariate logistic regression models jointly with each hemodynamic index, only aortic FPF remained an independent predictor for the presence of CAD. When brachial FPP was entered into the model instead of aortic FPP, brachial FPP remained a significant predictor independent of PA and PWV (see table).

Conclusions: Aortic FFP is most strongly associated with the presence of CAD among indices derived from a brachial cuff-based oscillometric device. Even brachial FPV could be a superior predictor over PWV and PA.

P2168 | BEDSIDE

Aortic pulsatility assessed by a brachial cuff-based oscillometric method is a strong predictor for the presence of coronary artery disease

A. Nakagomi, S. Okada, T. Shoji, Y. Kobayashi. Chiba University Graduate School of Medicine, Department of Cardiovascular Medicine, Chiba, Japan

Background and Introduction: Several indices of arterial stiffness and wave reflection have been proposed as novel predictors for coronary artery disease (CAD). However, it remains unknown which is the most appropriate for CAD risk estimation.

Purpose: To compare the predictive values of these parameters using a brachial cuff-based oscillometric device.

Methods: Consecutive 139 patients undergoing coronary angiography were enrolled in this study. The Mobil-O-Graph system provided an indirect estimate of brachial/arterial BP indices, PWV, adjusted augmentation index (AIx@75) and the amplitude of backward wave (Pb). The following values were defined: fractional pulse pressure (FPF) as pulse pressure (PP)/mean BP; pulse pressure amplification (PPA) as brachial PP/arterial PP. Significant CAD was defined as having ≥50% stenosis in major coronary arteries.

Results: Compared with no CAD patients, CAD patients showed significantly higher values of brachial/arterial PP and FPF (PP: brachial 48.5±15.2 vs 55.0±16.2mmHg, aortic 51.7±19.0 vs 62.3±19.9mmHg; FPF: brachial 0.42±0.09 vs 0.49±0.11, aortic 0.45±0.13 vs 0.56±0.14; all p<0.05). PW (10.0±2.4 vs 11.3±2.3ms; p=0.05), Pb (21.7±7.8 vs 26.7±6.5mmHg; p<0.05) and lower value of AIx@75 (0.12 vs 0.90±0.11; p<0.05). Other indices including Aix@75 did not differ significantly. Univariate logistic regression analysis revealed brachial FPF, aortic PP, arterial FPP, PWV, PA and Pb were associated with the presence of CAD. Among them, when aortic FPP was entered into the multivariate logistic regression models jointly with each hemodynamic index, only aortic FPF remained an independent predictor for the presence of CAD. When brachial FPP was entered into the model instead of aortic FPP, brachial FPP remained a significant predictor independent of PA and PWV (see table).

Conclusions: Aortic FPF is most strongly associated with the presence of CAD among indices derived from a brachial cuff-based oscillometric device. Even brachial FPF could be a superior predictor over PWV and PA.

P2167 | BEDSIDE

Aorta-to-upper arm pulse wave transit time ratio can predict the risk of coronary artery disease and stroke better than pulse wave velocity

M.Y. Rhee1, S.W. Jeong2, C.H. Leem3, Y.B. Lee3. 1Dongguk University Hospital, Goyang; 2Dongguk University Ilsan Hospital, Goyang; 3University of Ulsan, Department of Physiology, Ulsan, Korea, Republic of Korea

Background: The major limitation of carotid-temoral pulse wave velocity (cPWV) is the less accurate measurement of pulse wave travel length (PWTL). We evaluated the usefulness of carotid-temoral to carotid-radial pulse wave transit time (PWTT) ratio in the risk prediction of cardiovascular disease, not using PWTL.

Methods: Patients with coronary artery disease (CAD, n=80, 62.0±8.6 years), and stroke (Stroke, n=62, 65.2±1.7 years) were compared to individuals without history of cardiovascular or cerebrovascular disease (Control, n=104, 52.9±9.8 years). PWTT ratio was measured with pulse waves which were obtained from carotid, femoral and radial arteries, simultaneously. Carotid-temoral PWV (cPWV) was calculated.

Results: Patients with cardiovascular disease (CAD + Stroke) had higher cPWV values than those of control (Table 1). ROC curves comparison of PWTT ratio showed better diagnostic performance than cPWV ratio. The best cut-off value of PWTT ratio was 1.17 (sensitivity 82%, specificity 88%, positive predictive value 83%, negative predictive value 80%).

Abstract P2168 – Table 1. Odds ratios of aortic/brachial FPP

<table>
<thead>
<tr>
<th>Variables</th>
<th>Brachial FPF</th>
<th>Aortic FPF</th>
<th>PWV</th>
<th>PPA</th>
<th>Pb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic FPF</td>
<td>3.11 (1.02–9.46)*</td>
<td>4.74 (1.43–15.8)*</td>
<td>2.10 (1.04–4.24)*</td>
<td>3.23 (1.53–6.81)*</td>
<td>3.83 (1.39–10.59)*</td>
</tr>
<tr>
<td>Brachial FPF</td>
<td>–</td>
<td>2.15 (1.07–6.53)</td>
<td>0.62 (0.15–2.51)</td>
<td>2.93 (1.23–6.98)*</td>
<td>1.96 (0.98–3.91)*</td>
</tr>
</tbody>
</table>

Aortic FPF or brachial FPF was entered into the multivariate logistic regression models jointly with each hemodynamic index at uppermost row. *p<0.05, *p<0.01.
Copenhagen University Hospital, Department of Medicine, Copenhagen, Denmark; 1 Glostrup Hospital - Copenhagen University Hospital, Research Centre for Prevention and Health, Copenhagen, Denmark; 2 Glostrup Hospital - Copenhagen University Hospital, Department of Medicine, Copenhagen, Denmark

Background: Abdominal obesity is a major risk factor for hypertension. However, different distributions of adipose tissue may affect hypertension risk differently. Subcutaneous adipose tissue (SAT) is located beneath the skin and is relatively metabolically active. Visceral adipose tissue (VAT) is located around the internal organs and is metabolically more active.

Purpose: To explore the association of SAT and VAT with both prevalent and incident hypertension in a population-based setting. We hypothesized that VAT, rather than SAT, would be associated with both prevalent and incident hypertension.

Methods: VAT and SAT were quantified by ultrasound on 3,426 randomly selected Danes aged 19–72 years (mean age 49 years, 55% women, mean BMI 25.9) who were enrolled in the Health2000 cohort. Normotensive participants were further followed for a median of five years. We constructed multiple logistic regression models to compute standardized odds ratios (ORs) with 95% confidence intervals (CIs) per standard deviation (SD) increase in SAT and VAT.

Results: We recorded 1,307 persons with prevalent hypertension and 203 persons with incident hypertension at the five-year follow-up examination. Mean SAT was 3.0 centimeters and mean VAT was 6.5 centimeters. SAT and VAT were significantly linearly associated with systolic and diastolic blood pressure. However, in models including both SAT and VAT, and adjusting for overall adiposity (BMI and waist circumference), and traditional risk factors for hypertension such as age, sex, smoking status, diabetes mellitus, family history of hypertension and in the incident model also baseline blood pressure, only VAT was significantly associated with prevalent and incident hypertension; OR 1.32 (95% CI 1.16–1.51, p < 0.0001) and OR 1.33 (95% CI 1.01–1.74, p = 0.040) per one SD increase, respectively (P for SAT > 0.81).

Conclusion: VAT, but not SAT, as a measure of abdominal adiposity, is independently associated with both prevalent and incident hypertension in a random sample of Danish adults. Thus, ultrasonic VAT measurements provides the physician an easy and non-invasive method to pinpoint those individuals in greater risk for cardiovascular disease.

P2170 | BEDSIDE
Abdominal adiposity distribution quantified by ultrasound and incident hypertension in a general population
E. Seven1, R.V. Fenger2, L.L. Husemosen1, A. Linneberg1, J.L. Jeppesen1,1 Glostrup Hospital - Copenhagen University Hospital, Research Centre for Prevention and Health, Copenhagen, Denmark; 2 Glostrup Hospital - Copenhagen University Hospital, Department of Medicine, Copenhagen, Denmark

Background: Abdominal obesity is a major risk factor for hypertension. However, different distributions of adipose tissue may affect hypertension risk differently. Subcutaneous adipose tissue (SAT) is located beneath the skin and is relatively metabolically active. Visceral adipose tissue (VAT) is located around the internal organs and is metabolically more active.

Purpose: To explore the association of SAT and VAT with both prevalent and incident hypertension in a population-based setting. We hypothesized that VAT, rather than SAT, would be associated with both prevalent and incident hypertension.

Methods: VAT and SAT were quantified by ultrasound on 3,426 randomly selected Danes aged 19–72 years (mean age 49 years, 55% women, mean BMI 25.9) who were enrolled in the Health2000 cohort. Normotensive participants were further followed for a median of five years. We constructed multiple logistic regression models to compute standardized odds ratios (ORs) with 95% confidence intervals (CIs) per standard deviation (SD) increase in SAT and VAT.

Results: We recorded 1,307 persons with prevalent hypertension and 203 persons with incident hypertension at the five-year follow-up examination. Mean SAT was 3.0 centimeters and mean VAT was 6.5 centimeters. SAT and VAT were significantly linearly associated with systolic and diastolic blood pressure. However, in models including both SAT and VAT, and adjusting for overall adiposity (BMI and waist circumference), and traditional risk factors for hypertension such as age, sex, smoking status, diabetes mellitus, family history of hypertension and in the incident model also baseline blood pressure, only VAT was significantly associated with prevalent and incident hypertension; OR 1.32 (95% CI 1.16–1.51, p < 0.0001) and OR 1.33 (95% CI 1.01–1.74, p = 0.040) per one SD increase, respectively (P for SAT > 0.81).

Conclusion: VAT, but not SAT, as a measure of abdominal adiposity, is independently associated with both prevalent and incident hypertension in a random sample of Danish adults. Thus, ultrasonic VAT measurements provides the physician an easy and non-invasive method to pinpoint those individuals in greater risk of becoming hypertensive.

P2171 | BENCH
Haemodynamic effects of adenosine adsorbed on silica nanoparticles
I. Uskov. Federal North-West Medical Research Centre, Institution of experimental medicine, saint-petersburg, Russian Federation

Introduction: A promising vehicles for targeted drug delivery (TDO) to the ischamcic myocardium are silica nanoparticles (SNP). TDO achieves higher drug concentration in target organs and minimizes side effects. According to our hypothesis, the adsorption of adenosine (ADN) on SNP might reduce the negative side effects of AND, particular, arterial hypotension. The purpose of this study was to evaluate the effects of intravenous infusion of SNP-adsorbed ADN on blood pressure as compared to the effects of free ADN in the equivalent dose.

Methods: Young male Wistar rats were subjected to subtotal nephrectomy (NXT) to altered function of the Na+/Ca2+ exchanger (NCX). Therefore we investigated to altered function of the Na+/Ca2+ exchanger. The experimental medicine, saint-petersburg, Russian Federation

Results: Inotropic function averaged 128±4,2 versus 132±2,8 mm Hg at baseline (maximal reduction by 3,0%).

Conclusion: Adsorption of ADN on SNP leads to a significant attenuation of AND-induced hypotension. Modification of SNP surface with polyethylene glycol sorbitol monooleate minimizes hypotensive effect of ADN. It follows, therefore, that drug administration on the surface of SNP with additional organic modification of SNP surface with TWEEN 80 may provide a suitable platform for heart-targeted drug delivery.

FROM BENCH TO SURGERY

2205 | BENCH
Lysyl oxidase-like-2 inhibition decreases cardiac fibrosis and improves diastolic dysfunction in experimental and clinical heart failure with preserved ejection fraction
K. Savvatii1, J. Yang2, M. Kasner3, S. Van Linthout1, F. Fan4, L. Yao4, C.P. Chang5, C.P. Tschope2,1 Berlin-Brandenburg Center for Regenerative Therapies, Berlin, Germany; 2 Indiana University School of Medicine, Krannert Institute of Cardiology and Division of Cardiology, Department of Medicine, Indianapolis, United States of America; 3 Charité - Campus Benjamin Franklin, Cardiology & Pneumology, Centrum 11 (Cardiovascular Medicine), Berlin, Germany; 4 Gilead Sciences Inc., Foster City, United States of America; 5 Charité - Campus Virchow-Klinikum (CVK), Department of Cardiology, Berlin, Germany

Purpose: Lysyl oxidase-like-2 (LOXL2) promotes cross-linking of fibrillar collagen and contributes to increased collagen deposits and fibrosis. Heart failure with preserved ejection fraction (HFpEF) is characterised by increased myocardial stiffness due to several mechanisms, among others due to increased collagen deposition and cross-linking of collagen fibers in the myocardium. We sought to examine the role of LOXL2 and its inhibition in HFpEF patients and in an experimental model of cardiac hypertrophy.

Methods: We investigated 41 HFpEF and control patients. Assessment of diastolic function was performed invasively and by echocardiography. The amount of collagen, collagen cross-linking and LOXL2 were studied in endomyocardial biopsies. Transaortic constriction (TAC) was performed in mice and an anti-LOXL2 antibody was administered 2 weeks after TAC. The amount of collagen, fibrosis, collagen cross-linking, LOXL2 and hemodynamic function were studied after 10 weeks. Furthermore, the effects of LOXL2 inhibition by knockdown of the LOXL2 gene were studied on isolated murine cardiac fibroblasts stimulated with TGF-β.

Results: Patients with HFpEF showed a significantly higher amount of collagen I and total collagen compared to healthy controls. LOXL2 expression was 2.5 times higher in HFpEF patients and was correlated with significantly higher collagen amount and collagen collagen cross-linking compared to controls. Higher LOXL2 levels, total collagen and collagen cross-linking were associated with higher filling pressures and increased left ventricular stiffness. Mice showed a significant cardiac hypertrophy, increased interstitial fibrosis, collagen cross-linking and LOXL2 amount, as well as progressive diastolic and systolic dysfunction 10 weeks after TAC. Administration of an anti-LOXL2 antibody decreased the degree of cardiac fibrosis and significantly improved hemodynamic function. Isolated cardiac fibroblasts showed an increased migratory capacity after TGF-β treatment, which was reduced after LOXL2-knockdown. Furthermore, LOXL2-knockdown significantly inhibited intracellular TGF-β signaling by decreasing downstream mediators of TGF-β.

Conclusions: Myocardial LOXL2 is increased in clinical and experimental HFpEF and leads to higher myocardial fibrosis, collagen cross-linking and LV-stiffness. Inhibition of LOXL2 ameliorated myocardial fibrosis and LV stiffness by decreasing total collagen amount, collagen cross-linking and activation of cardiac fibroblasts. Inhibition of LOXL2 might be a novel therapeutic target in patients with HFpEF and progressive myocardial fibrosis.

2206 | BENCH
Chronic inhibition of Na+/Ca2+ exchanger (NCX) with SEAO400 improves cardiac function in a model of heart failure with preserved ejection fraction
U. Primessnig1, T. Bracic2, T. Glasnov3, B. Pieske1, F.R. Heinzel1,1 Charité - Universitätsmedizin Berlin, Campus Virchow-Klinikum, Department of Cardiology, Berlin, Germany; 2 Medical University of Graz, Department of Cardiology, Graz, Austria; 3 Institute of Chemistry, University of Graz, Graz, Austria; 4 Graz, Austria

Background: Heart failure with preserved ejection fraction (HFpEF) is increasingly common but there are currently no established therapeutic strategies, mostly because the underlying cellular mechanisms are not well understood. We have previously shown in a rat model of HFpEF with chronic kidney disease that left ventricular (LV) cardiomyocyte Ca2+ transient decay is slowed, possibly related to altered function of the Na+/Ca2+ exchanger (NCX). Therefore we investigated the effects of chronic inhibition of NCX with SEAO400 on cardiac function in this HFpEF model.

Methods: Young male Wistar rats were subjected to subtotal nephrectomy (NXT) or sham operation (SOP), 8 weeks after intervention chronic treatment for 16 weeks with the NCX inhibitor SEAO400 (1mg/kg body weight) was started. At 24 weeks non-invasive blood pressure measurements, echocardiography, pressure-
volume loops (PV) and LV morpometry were performed. LV cardiomyocytes were isolated and contractile function and Ca++ transients were measured.

**Results:** NXT rats (untreated) showed stable compensated renal impairment and signs and symptoms of HFpEF (hypertrophied LV, left- and upward shift of end diastolic pressure [EDP] volume relationship (EDPVR), increased lung weight/body weight (LW/BW) indicating pulmonary congestion and preserved LV systolic function (EF, dP/dt)). In LV cardiomyocytes from untreated NXT Ca++ transient amplitude was unchanged but time for early (<50%) decay was significantly prolonged at 24 weeks and correlated with diastolic dysfunction (EDP) in vivo. In NXT treated with SEA0400 heart weight/BW ratio and LW/BW were significantly reduced as well as LV mass while systemic blood pressure was unchanged. EDP (13±1 vs. 8±1, mmHg in NXT, p<0.05) and EDPVR were reduced after chronic treatment with SEA0400 in NXT.

**Conclusion:** Chronic inhibition of the Na+/Ca++ exchanger with SEA0400 significantly attenuated cardiac remodeling and diastolic dysfunction in this model of HFpEF.

---

**2207 | BEDSIDE**

Prophylactic epicardial left ventricular lead implantation in patients undergoing open heart surgery.

D. Pecora, C. L. Greca, U. Simoncini, A. Sargota, F. Morandi, M. Cirillo, C. Campana, C. Cuccia, G. Troise. Poliambulanza Foundation Hospital Institute of Brescia, Brescia; 2University Hospital Paolo Giaccone, Palermo, Italy

**Background:** Surgical epicardial left ventricular (LV) lead implantation for biventricular pacing has advantages over the transvenous approach in cardiac surgical patients.

**Purpose:** We investigated concomitant prophylactic epicardial left ventricular (LV) lead implantation during open-heart surgery, identifying patients who subsequently needed cardiac resynchronization therapy (CRT) and evaluating the performances and the clinical outcome in a one-year follow-up.

**Methods:** We collected retrospective data of 5687 patients, undergoing open-heart surgery procedures between January 2003 and December 2014. 492 patients (8.6%) had severe LV systolic impairment (LVEF <35%), 24 patients (4.8%) with severe LV impairment, with left bundle branch block (LBBB) or ORS ~ 120 msec, or conventional pacing indications, in whom recovery of LV dysfunction was considered unlikely, underwent epicardial LV lead implantation. 15 Patients (62.5%) with persistent left ventricular dysfunction were subsequently submitted to a biventricular device implant.

**Results:** The mean time interval from LV lead implantation to biventricular device implantation was 127.2±104.09 days (range: 2–299 days, median interval: 157 days). No major adverse events were reported to the procedure. At a one-year follow-up, LV lead performance parameters (pacingsensing, threshold, impedance) showed no differences compared to initial implantation measure (p=0.64, p=0.72, p=0.13, respectively). 12 Patients (80%) were responders to CRT (LVEF improvement of 10%); the mean LVEF improvement was 13.00±12.33%. In patients who underwent device implantation we observed a significant increase in LVEF (p<0.001), and only a not significant trend to improvement in end diastolic volume (p=0.13) and end systolic volume (p=0.12), probably because of the small number of our population. Two patients had new hospitalizations due to heart failure. We did not observe major adverse events.

**Conclusion:** Prophylactic epicardial LV lead implantation may have a role in patients with LV function impairment undergoing open-heart surgery.

---

**2208 | BEDSIDE**

Myocardial and plasma matrix metalloproteinases and left ventricular remodeling: time changes before and after surgical ventricular reconstruction in ischemic heart failure patients.

S. Castelvecchio, G. Palladini, E. Baryshnikova, L. Menicanti, S. Perlini.

1IRCCS Policlinico San Donato, Department of Cardiac Surgery, Milan; 2Policlinico Foundation San Matteo IRCCS, Department of Internal Medicine, Pavia; 3IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy

**Background:** Changes in extracellular matrix (ECM), left ventricular (LV) remodeling and severity of LV dysfunction are intimately linked and might influence prognostic and risk factors.

**Methods:** Time course changes in serum levels of MMPs and TIMPs in patients with previous myocardial infarction selected for surgical ventricular reconstruction (SVR) and their relationships with parameters of LV function and geometry.

**Results:** Twenty patients (S1, 2003 through S2003) with abnormal myocardial infarction and heart failure undergoing elective SVR were recruited. Left ventricular function and geometry were evaluated by echocardiography before surgery and at follow-up. LV biopsies were obtained after the opening of the left ventricle. For each patient, two biopsies were harvested: one from the border zone (peri-infarctual area) and one from the remote myocardium. Samples were immediately treated according to the protocol in the operating theatre and stored at −80°C. Plasma samples were collected from each patient before surgery and at follow-up (6 and 12 months).

**Results:** Before surgery, a significant correlation was observed between LV diastolic and systolic sphericity index (either in diastole or systole), plasma MMP2 concentrations (p<0.02) and MMP2/TIMP2 ratio (p<0.02).

In cardiac biopsies, both TIMP-1 (72±13.4 ng/ml vs. 13.6±2.2 ng/ml; p<0.001) and TIMP-2 (22±2.5 ng/ml vs. 14.5±1.2 ng/ml; p<0.001) were much higher in the border that in the remote zone, indicating higher inhibition of MMP-related extracellular matrix degradation.

At follow-up, SVR was associated with a significant reduction of LV volumes (EDVI from 127±8 to 84±5 ml/m²; ESVI from 90±6 to 50±3 ml/m²; p<0.01 for both) and an improvement of the ejection fraction (from 29.6±1.3 to 41.0±1.4%; p<0.01). Plasma MMP-2 decreased from 30.8±5.2 ng/ml to 19.8±3.3 ng/ml and 16.9±2.0 ng/ml (at 6 and 12 months, respectively; p<0.05 for both), whereas TIMP-2 values did not change greatly. Group of non-RVF (MMP-2/TIMP2 ratio, an index of ECM degradation, decreased from 0.47±0.05 to 0.37±0.04 and 0.33±0.04 (p<0.05).

**Conclusion:** At baseline, higher tissue MMP-2/TIMP-2 ratio is associated with a more spherical remodeling of the left ventricle, which indicates global chamber compromise involving the border zone than the remote zone. After surgery, the decrease of the plasma MMP-2/TIMP-2 ratio indicates a down regulation of the ECM degradation which might support the improvement in LV volumes and function after SVR.
which included TAPSE < 1.6 cm (1 point), RV S' < 5 cm/sec (2 point), LAD > 45 mm (1 point) and E/E' > 20 (1 point). The Echo-RVF score was significantly associated with RVF development post-LVAD (odds ratio [OR] 2.19; 95% CI [confidence interval] 1.50–3.46, p < 0.001). The ROC curve analysis identified the Echo-RVF score of 2, 3, and 4 can discriminate patients in RVF group from those in non-RVF group with sensitivity and specificity of 92.0 and 42.8% (score-2), 84.0 and 65.0% (score-3), and 72.0 and 86.4% (score-4), respectively (ACU = 0.7836).

Conclusions: The Echo-RVF score, which included parameters reflecting right ventricular systolic impairment and left ventricular diastolic dysfunction before LVAD surgery, can effectively risk-stratify patients who may develop RVF following LVAD.

2211 | BEDSIDE
Diastolic dysfunction is prognostic of long-term mortality in liver transplant recipients
N. Naksuk1, T. Peeraphadrat2, C. Thongsrayon2, C. Krittanawong1, V. Jaruvongvanch1, P. Phatharacharakul2, R. Chaliteraikj3, L.R. Roberts4, K.W. Klarich1. 1. Mayo Clinic, Division of Cardiovascular Disease, Rochester, United States of America; 2. University of Minnesota, Department of Internal Medicine, Minneapolis, United States of America; 3. Mayo Clinic, Division of Nephrology and Hypertension, Rochester, United States of America; 4. Chulalongkorn University, Department of Internal Medicine, Bangkok, Thailand;

Background: Diastolic dysfunction is the commonest finding among cirrhotic patients with subclinical cardiomyopathy. However, its prognostic value after liver transplant (LT) has not been evaluated.

Methods: Consecutive cirrhotic patients undergoing LT at a tertiary medical center between 2003 and 2013 were identified. Patients with combined heart and liver transplantation, amyloidosis, hemochromatosis, sarcoidosis or cirrhotic liver diseases were excluded. Only 1,248 LT recipients with ejection fraction (EF) > 55% were included in this analysis. Diastolic dysfunction in cirrhosis was defined as a ratio of the early to late ventricular filling velocities (E/A ratio) value < 1, according to the World Congress of Gastroenterology consensus.

Results: The prevalence of diastolic dysfunction was 20% in cirrhotic patients with EF > 55%. Patients with diastolic dysfunction were older (59±7 vs. 51±11 years; p < 0.0001) and had greater preexisting cardiovascular comorbidities compared to those with normal diastolic function (p < 0.05). During 5.9 years follow-up after LT, the mortality of patients with diastolic dysfunction was 5.0% vs. 3.6% per person-year in those without diastolic dysfunction (HR 1.4, 95% CI 1.1–1.8; p = 0.02) (Figure). Other traditional cardiovascular risks including preexisting cardiovascular comorbidities, hypertension, hyperlipidemia and obesity were also independently associated with the mortality (p < 0.05 for all).

Conclusion: Among cirrhotic patients with normal ejection fraction, diastolic dysfunction independently predicts post-liver transplant mortality during long-term follow-up.

2212 | BEDSIDE
Clinical significance of elevated diastolic pressure gradient in heart failure with preserved ejection fraction
C. Zetter Tufaro, F. Duca, A.A. Kammerlander, S. Aschauer, A. Bachmann, B. Kostell, D. Dalos, J. Schmerbauer, D. Bodnerman. Medical University of Vienna, Division of Internal Medicine II, Division of Cardiology, Vienna, Austria

Background: Pulmonary hypertension due to heart failure with preserved ejection fraction (PH-HFpEF) is common in elderly patients and is associated with poor outcome. A subset of affected individuals has a combined pre- and postcapillary PH (Cpc-PH). PH cannot be explained by a simple backward transmission in left-sided filling pressures. The diastolic pressure gradient (DPG) with a cut-off of 7 mmHg has been recently suggested to distinguish between patients with isolated postcapillary PH (Ipc-PH) and Cpc-PH.

Purpose: The clinical significance and predictive value of DPG remains to be elucidated in this specific disease entity.

Methods: Patients with HfPEF diagnosed according to current ESC guidelines were enrolled in our prospective registry. Borderline PH was defined as a mean pulmonary arterial pressure (mPAP) between 21–24 mmHg, and manifest PH was defined as an mPAP >25 mmHg. DPG was calculated as the difference between diastolic PAP and mean pulmonary arterial wedge pressure. Hospitalization for heart failure and death for cardiac reason were defined as the primary study endpoint.

Results: Between December 2010 and December 2014, 193 HfPEF patients were registered. 19 patients refused right heart catheter and were excluded. Of the remaining 174 patients, 11 (6.3%) had no PH, 15 (8.6%) had borderline PH and 148 (85.1%) a manifest PH. PH patients (66% females; mean age 70±7 years) were further sub-classified into Ipc-PH (n=126) and Cpc-PH (n=22).

Patients with a Cpc-PH had a shorter six-minute walk distance (253.5±128.7 m versus 318.4±171.7 m; p = 0.021), a higher NT-proBNP (3816.9±5977.8 pg/ml versus 1651.6±1883.5 pg/ml; p = 0.001), larger right ventricles (42.1±8.9 mm versus 37.4±7.1 mm, p = 0.010) and a lower capillary oxygen partial pressure (63.4±9.8 mmHg versus 73.3±11.6 mmHg; p < 0.001) compared to patients with Ipc-PH.

During a median follow-up of 25.2 months, 55 patients (33.7%) reached the combined endpoint. DPG was found to be an independent predictor of outcome (HR 1.167, 95% CI 1.047–1.299; p < 0.005). The worst outcome was recognized in the group of patients with Cpc-PH, as compared to Ipc-PH patients (log rank test, p = 0.003).

Conclusion: The presence of PH in HfPEF is associated with adverse outcome. The subgroup with Cpc-PH had a worse clinical status and event-free survival as compared to the remainder of the group. Although it remains unclear which subset of patients is prone to develop superimposed pulmonary vasculature remodeling, our data indicate a potential contribution of hypoxemia.

2213 | BEDSIDE
Heart failure in patients with reduced and preserved preserved ejection fraction: are factors associated with all-cause and heart failure rehospitalization different?
N. Farre1, I. Rodriguez-Costoya2, R. Olivo-Soldevilla2, P. Moliner-Borja3, C. Enjuanes1, S. Ruiz1, G. Gonzalez-Rolledo1, J.M. Verdu-Rotellar1, J. Bruguera3, J. Comin-Colet3. 1. Hospital del Mar, Municipal Institute for Medical Research (IMIM), Barcelona, Spain; 2. Hospital del Mar, Department of Cardiology, Barcelona, Spain; 3. Hospital del Mar, Department of Cardiology, Municipal Institute for Medical Research (IMIM), Barcelona, Spain

Background: Rehospitalization in heart failure is frequent and is associated with worse outcome and increased health-care costs. Many of the studies that have analyzed factors associated with readmission have studied patients from randomized controlled trials or patients with heart failure with reduced ejection fraction (HFrEF). Therefore, the aim of this study was to identify factors associated with readmission in a real-world heart failure cohort and analyze whether differences exist between HFrEF and heart failure with preserved ejection fraction (HfPEF). Methods: Post-hoc analysis of a single-center prospective cohort of 1072 patients with reduced (n=559) and preserved (n=513) chronic heart failure. HFpEF is defined as an ejection fraction ≤ 50% and a history of heart failure the previous year (HR 2.2; 95% CI (1.2–3.9)) in HFrEF and HR 2.8; 95% CI (1.5–5.5) in HfPEF, chronic obstructive pulmonary disease (COPD) (HR 1.8, 95% CI (1.2–2.5) and HR 1.4, 95% CI (1.0–2.0), respectively), NYHA functional class III-IV (HR 1.5, 95% CI (1.1–2.1) and HR 1.6, 95% CI (1.1–2.2), respectively) and rate > 70 beats per minute (HR 1.5, 95% CI (1.1–2.1) and HR 1.4, 95% CI (1.0–1.9), respectively), all p < 0.05. Anemia (HR 1.4, 95% CI (1.1–1.9), p = 0.044) and log-NT-ProBNP (HR 1.4, 95% CI (1.1–1.9), p = 0.048) were associated with HF in HfPEF but not in HFrEF. The presence of COPD, anemia, history of heart failure the previous year, heart rate > 70 beats per minute and log-NT-ProBNP were independently associated with ACR in both HfPEF and HFrEF. In HFrEF, NYHA class III-IV was also associated with ACR.

Conclusions: Heart failure hospitalization the previous year, COPD and heart rate > 70 beats per minute are independently associated with ACR and HFrEF both in HFrEF and HfPEF. Other factors frequently associated with ACR and HFrEF are NYHA functional class III-IV, log-NT-ProBNP and anemia. These factors allow the identification of patients at high-risk of readmission.
astolic dysfunction with preserved systolic function resulting from ongoing cardiomyocyte loss and cardiac fibrosis. The protease activated receptor PAR2 is known to be a pro-fibrotic mediator. In a mouse model of myocardial infarction PAR2 overexpression in cardiomyocytes led to the development of fibrosis. In this study we examine the role of PAR2 in the aged heart regarding fibrosis and hemodynamic function.

Methods: We consecutively assessed 4049 asymptomatic participants (age: 50.77±10.63) from cardiovascular health survey. Mitrail inflow, tissue Doppler parameters and 2D-based speckle-tracking of global longitudinal (GLS), circumferential strain.

Results: 1 year PAR2ko mice suffered from a left ventricular dysfunction with preserved systolic function, which was accompanied by an age dependent fibrosis. In hearts of 8 wks old wt and PAR2ko mice no differences in collagen expression were present. In contrast, 1 yr old PAR2ko mice showed collagen deposits in the heart and the collagen laclagon III ratio revealed a fibrosis in PAR2ko mice but not in wt mice (p<0.05). Moreover, adult cardiac PAR2ko fibroblasts also showed an increased collagen I release into the supernatant compared to wt fibroblasts. Furthermore, the TGFβ1-dependent Smad2 phosphorylation was stronger in PAR2ko fibroblasts compared to wt fibroblasts. Oxidative stress in the heart often triggers cardiac dysfunction. After treatment with H2O2, PAR2ko fibroblasts exhibited higher ROS levels than wt fibroblasts (wt vs PAR2ko: 4.26±1.78 vs. 6.42±3.55, p<0.05). The GSH/GSSG ratio in hearts of 1h hearts pointed also to an increased oxidative stress in PAR2ko mice compared to wt mice (wt vs PAR2ko: 8.31±2.50 vs. 4.80±1.53, p<0.05). These results indicate that the loss of PAR2 is associated with elevated oxidative stress, which leads to fibrosis and an impaired heart function. In HFPEF patients a decreased PAR2 expression was associated with severe diastolic dysfunction and vice versa.

Conclusion: The cardiac PAR2 expression is essential for the maintenance of the heart function in the aged heart. The loss of PAR2 results in increased oxidative stress, an age-dependent cardiac fibrosis and a left ventricular diastolic dysfunction.

OBESITY – THE GLOBAL THREAT!

2227 | BEDSIDE

Impact of adipose tissue composition on cardiovascular risk assessment in patients with stable coronary artery disease

A. Kunimura1, T. Uetani1, M. Takeshita1, S. Okumura2, N. Shinoda1, K. Harada1, B. Kato1, H. Ishii2, T. Amado3, T. Murohara2,1 Chubu Rosai Hospital, Nagoya, Japan;2 Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan;3 Aichi Medical University, Department of Cardiology, Nagoya, Japan

Background: Visceral adipose tissue (VAT), unlike subcutaneous adipose tissue (SAT), has been shown to be highly correlated with cardiovascular risk factors. The aim of this study was to evaluate the predictive value of adipose tissue composition measured by computed tomography for cardiovascular outcome among patients with stable coronary artery disease.

Methods: 357 consecutive patients who underwent 64-slice computed tomography angiography and elective PCI were recruited. The ratio of visceral adipose tissue to the total adipose tissue (%VAT) was calculated as VAT/(VAT + SAT) × 100. Patients were divided into three groups in accordance with %VAT (group1, <35.5% [25th percentile]; group2, 35.5 to 50.6% [25th to 75th percentile]; group3, 50.6% [75th percentile]). The investigated risk factors were hypertension, hyperglycemia, and dyslipidemia. We analyzed the incidence of major adverse cardiovascular events (MACE), including cardiovascular death, myocardial infarction, and any revascularization.

Results: The rate of patients who have two or more concomitant risk factors was significantly increased in group3 (p=0.006). During the median follow-up of 1718 days, 108 events occurred. Event-free survival was significantly associated with %VAT, with worse event-free survival in group3 (log-rank p<0.02). In Cox analysis, the hazard ratio of group3 for MACE was 1.56 (95% confidence interval 1.01–2.41, p=0.045) compared to the other groups after adjustment for confounding factors.

Conclusion: Increased %VAT is independently associated with the incident of MACE, indicating that adipose tissue composition is a useful predictor of cardiovascular outcome.
green tea supplementation duration of ≥8 weeks (WMD: 0.029 mg/L, 95% CI: -0.229–0.288, p=0.838) and ≥8 weeks (WMD: 0.099 mg/L, 95% CI: -0.555–0.754, p=0.766). Likewise there was no significant effect in subgroups of studies with total catechins doses <400 mg/day (WMD: 0.073 mg/L, 95% CI: -0.251–0.398, p=0.658) and ≥400 mg/day (WMD: 0.213 mg/L, 95% CI: -0.148–0.574, p=0.247). The effect size were not significant after stratification of studies to recruit healthy subjects (WMD: -0.028 mg/L, 95% CI: -0.216–0.106, p=0.769), and those recruiting subjects with cardiometabolic diseases (WMD: 0.260 mg/L, 95% CI: -0.915–1.334, p=0.638).

Conclusions: The results of this meta-analysis did not indicate a significant effect of supplementation with green tea catechins on plasma CRP concentrations. Further, well-designed trials are necessary to validate these results.

2230 | BEDSIDE QT interval prolongation in obesity and metabolic syndrome: myth or fact?
C. Strack, D. Fessmann, S. Fenk, M. Manka, J. Zeller, U. Hubauer, L. Maier, M. Fischer, A. Baessler. University of Regensburg, Department of Internal Medicine II, Regensburg, Germany

Background: Obesity is associated with ECG abnormalities and a relationship between obesity and duration of the Bazett’s corrected QT interval (QT) was described repeatedly. Weight loss can improve or prevent many of the obesity-related comorbidities, can improve heart rate (HR), and may shorten rate corrected QT. Given the tight relation between the QT and HR, a correction is necessary and several formulae have been tested and used, but only a few of them completely remove the dependence of QT on HR.

Purpose: This study aimed to validate the association of obesity with QT prolongation and to verify the changes that a period of low-calorie diet and physical training had on the Bazett corrected QTc (QTc) in obese patients using different methods for QT correction.

Methods: In a prospective longitudinal study QT was determined in 318 severely obese subjects (BMI 41±12 kg/m²) participating in a multimodal weight reduction program and in 45 healthy lean controls (BMI 22±5 kg/m²). The Bazett corrected QT was calculated using 8 established methods.

Results: The uncorrected QT was similar in obese and healthy lean subjects (389±32 vs. 399±33 ms; ns, p=0.130). As expected obese had a significantly higher HR than lean subjects (72±14 vs. 64±12 bpm; p=0.001). Obese had a higher corrected QT when using Bazett’s and Ashman’s formulae, and Karajalainen’s nomograms, but 5 alternative correction methods, including Friderica, Sages-Framingham, Hodges, Rautaharju and Pfeufer, revealed comparable QTc in obese and lean subjects. Analogous results were obtained when comparing obese with and without the metabolic syndrome (MeS), whereas subjects with the MeS presented with higher HR than subjects without the MeS. After marked weight loss (15±9±9.9 kg), HR decreased significantly in the obese (72±15 vs. 65±12 bpm, p<0.001), and QTc decreased again only when Bazett’s, Ashman’s and Karajalainen’s nomograms were used. In contrast, the QTc using the 5 alternative correction methods were similar before and after weight loss. Interestingly a mathematical simulation study revealed that deviation from uncorrected QT with increasing HR was higher using the Bazett’s, Ashman’s and Karajalainen’s nomogram methods, whereas the deviation using the alternative 5 methods with increasing heart rate was only marginal.

In conclusion, contrary to the current views, our findings suggest that the association between obesity and QT is just a matter of HR correction, and weight reduction is highly relevant changes for the QT interval. The BMI should be considered when using Bazett’s HR correction.

Acknowledgement/Funding: This study was supported by internal funds from the University of Regensburg.

2231 | BEDSIDE Nutritional state predicts long-term survival in heart failure
S. Sze, K.Y.K. Wong, S. Kazmi, D. Mellor, A. Rigby, A.L.C. Clark. Castle Hill Hospital, Hull, United Kingdom

Introduction: NICE recommends screening for malnutrition. We hypothesize that the microalbuminuria NUTritional Status index (CONUT) score predicts all-cause mortality in patients with heart failure.

Methods: 5107 patients with heart failure (HF) were consecutively recruited from our hospital, and had median age of 74 years (IQR 67,80). 1934 (38%) were not malnourished (CONUT 2–4) (906 died); and 376 (10%) were malnourished to a moderate/severe degree (CONUT >4) (278 died). The higher the CONUT score, the poorer the survival (hazard ratio (HR) = 1.13 (95% CI: 1.10, 1.16), p<0.001 independent of age, sex and NTproBNP). Graphical presentation is by Kaplan-Meier curve (Figure 1). CONUT score also predicted 35% of all-cause mortality and HF admission (HR=1.12, 95% CI: 1.09, 1.15; p<0.001).

Conclusions: All cause mortality is significantly higher in patients with worse nutritional state, independent of age, sex and NTproBNP.
Conclusion: Adherence to Mediterranean diet confers a considerable reduction on CVD risk, independently of various factors. Therefore, even subjects with unhealthy lifestyle behaviors may benefit from adherence to this diet, suggesting another dimension on prevention strategies.

2234 | SPOTLIGHT
Genetic but not environmental factors have substantial influences on epicardial adipose tissue quantity: a classical twin study
1 Semmelweis University Heart Center, MTA-SE Lendulet Cardiovascular Imaging Research Group, Budapest, Hungary; 2 Semmelweis University, Department of Radiology and Oncotherapy, Budapest, Hungary; 3 Global Genetics Group, Birmingham, United States of America; 4 Bajcsy-Zsilinszky Hospital, Budapest, Hungary

Background and aims: It has been reported that epicardial adipose tissue might have an important role in the pathogenesis of coronary artery disease because of its metabolic activity and proximity to the epicardial coronary arteries. Whether the epicardial adipose tissue depends on environmental influences or determined by genetic factors is unclear. The aim of the study was to evaluate the genetic and environmental impacts on the epicardial adipose tissue quantity within a cohort of twin pairs.

Methods: We have enrolled 210 twin subjects without known cardiovascular disease or history of monzygotic (MZ) pairs (age: 55.7±9.7 years) and 42 were dizygotic (DZ) pairs (age: 58.1±8.7 years). All subjects were investigated by a 256-slice CT-scan. For each twin subject epicardial fat volume (EFV), waist circumference (WC) and body mass index (BMI) were assessed. To quantify phenotypic similarity, intra-pair correlations were calculated. With the use of structural equation models these correlations were broken down to additive genetic (A), common (C) and unique (E) environmental correlation components.

Results: The EFV was 98.1±45.2 cm³, the WC was 98.0±14.1 cm, and the BMI values were stronger in MZ twins as compared to DZ twins (rMZ EFV=0.75, rDZ EFV=0.27; rMZ WC=0.70, rDZ WC=0.40; rMZ BMI=0.67, rDZ BMI=0.16; all p<0.05), which implies a strong genetic dependence of these parameters. The structural equation models confirmed these findings: rA=0.75, rC=0.71, rE=0.066; rA=0.25, rC=0.29, rE=0.34. No role of common environmental factors was found.

Conclusion: In this classical twin study we were able to show that genetic but not environmental factors have substantial influences on EFV, similarly to BMI and WC. As both abdominal obesity and increased volume of epicardial fat are linked to the development of cardiovascular diseases, early and sustained preventive measures are needed to reduce the amount of these pathogenic fat depots.

2235 | BEDSIDE
Relations between parenting styles, parental feeding practices and the nutritional status of adolescents
L.C. Pellanda, A.B. Piccoli, C.P. Mosmann, L. Neiva-Silva, Institute of Cardiology of Rio Grande do Sul - University Foundation of Cardiology, Porto Alegre, Brazil

Background: Adolescence is critical stage for obesity, which is associated with incorrect eating habits developed in the family. Parenting styles are reference in understanding the parent-child relationship. The dimensions of demandingness and responsiveness define parenting styles in four: high responsiveness and demand are authoritative parents; low responsiveness and demand are negligent parents. When parents are very responsive and undemanding, they are indulgentes, demanding and poorly responsive are authoritarian. Eating habits are disciplinary actions used by parents in the context of parenting styles. Little is known about parenting styles in the field of food and from the perspective of adolescents.

Objectives: The study aims to investigate the association between the perception of adolescents in southern Brazil on parenting styles and parental feeding practices and BMI.

Methods: Cross-sectional study with 271 adolescents (12–18). They answered a socio-biographic questionnaire, scales of demandingness and responsiveness, Comprehensive Feeding Practices Questionnaire - CPFP adapted and validated for adolescents; subject to the weight and height measurements (BMI) Results: 28% of adolescents were overweight. 26.3% of them perceive the mother as negligence and 31.6% perceive as authoritative. But the father is perceived as authoritative by 31.6%. The association between BMI of adolescents with parenting styles was no significant difference to justify the excess weight. However, the eating habits associated with negligence and authoritative styles have significant differences in the frequency of obesity. Low “pressure to eat” and most “food restriction for weight control” are significant to the excess weight in both styles (p<0.001) and greatest “monitoring” (p=0.018), is significant only in authoritative style. The “dietary restriction to weight control” is associated inversely with food frequency of obese and obesity. “Press sure to eat” reduces the overweight and obesity rate by 32%.

Conclusions: It is necessary to undertake further research in this age group on parenting styles within the food and feeding practices mainly in food restriction practices that increase the frequency of obese adolescents to treatment and management of obesity.

2236 | BEDSIDE
How we eat may be important as much as what we eat: eating behaviours and heart rate variability
M.E. Ozpelt1, E. Ozpelt2, N. Peke1, A. Yilmaz1, S. Saygi1, I. Tengiz2, E. Ercan1, I. Izmir University, Cardiology, Izmir, Turkey; 2 Dokuz Eylül University, Cardiology, Izmir, Turkey

Introduction: Some recent reports demonstrated that eating behaviors, may also be of significant importance in cardiovascular health. In this study we aimed to investigate the effects of eating behaviours on heart rate and its variability in healthy subjects.

Materials and methods: 521 subjects admitted to Cardiology Outpatient Clinics and had 24 hour Holter ECG recordings full in a special questionnaire about their eating behaviours and lifestyles. From these patients, 425 subjects were healthy and had recordings suitable for analysis. Five eating behaviors were assessed in the questionnaire; adherence to the Mediterranean diet (using the Mediterranean Diet Score), skipping breakfast, late night eating, having snack, and rapid eating. Time domain analysis parameters were used for assessment of heart rate variability.

Results: Among eating behaviours, skipping breakfast was significantly associated with a higher resting heart rate and lower HRV (Table 1). Other behavioral patterns did not have any effect on HRV parameters. When the other parameters were compared among subjects who skip breakfast and who do not, there was no significant difference between groups except for triglyceride (TG) levels (Table 1). In multivariate regression analysis, skipping breakfast was the only parameter significantly associated with a lower SDNN (OR: 0.131, 95% CI: -0.393–1.6 P: 0.033).

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Regular breakfast (n=324)</th>
<th>Skipping breakfast (n=101)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45.7±13.4</td>
<td>44.3±11.9</td>
<td>0.317</td>
</tr>
<tr>
<td>Sedentary lifestyle (%)</td>
<td>97 (29.9%)</td>
<td>28 (27.7%)</td>
<td>0.206</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.9±4.8</td>
<td>27.1±4.7</td>
<td>0.116</td>
</tr>
<tr>
<td>Active working</td>
<td>136 (41.9%)</td>
<td>45 (44.5%)</td>
<td>0.101</td>
</tr>
<tr>
<td>T Kol (mg/dl)</td>
<td>219±48.9</td>
<td>222±51.5</td>
<td>0.888</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>146±72.8</td>
<td>155±68.8</td>
<td>0.041</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>98±30.3</td>
<td>99±32.9</td>
<td>0.681</td>
</tr>
<tr>
<td>SDNN</td>
<td>141±26.6</td>
<td>122±26.6</td>
<td>0.036</td>
</tr>
<tr>
<td>RMSD</td>
<td>58.5±36.1</td>
<td>50.9±29.2</td>
<td>0.071</td>
</tr>
<tr>
<td>Average HR</td>
<td>76.4±12.1</td>
<td>80.4±14.9</td>
<td>0.046</td>
</tr>
</tbody>
</table>

Conclusion: The findings of this study showed that, unhealthy eating behaviours, such as skipping breakfast may be a cause of cardiac autonomic dysfunction.

Acknowledgement/Funding: There is no financial supporting.

EXCITATION-CONTRACTION COUPLING ON THE ROAD OF TRANSLATION

2242 | BENCH
Unique regulation of cAMP signals at distinct excitation-contraction coupling (ECC) regulatory sites in adult cardiac myocytes
N.C. Surdo, M. Berrera, A. Koschinski, M. Zaccolo, University of Oxford, Department of Physiology, Anatomy & Genetics, Oxford, United Kingdom

cAMP is central to cardiac function in health and disease. cAMP signalling operates in a compartmentalised manner: a specific response to any particular hormonal signal is achieved by delivering unique cAMP signals to individual subcellular compartments. Catecholamine-dependent cAMP signalling is a key regulator of excitation-contraction coupling (ECC) and the incorrect activation of this pathway is a hallmark of disease states such as cardiac hypertrophy and heart failure. Real-time imaging using Fluorescence Resonance Energy Transfer (FRET) is a powerful tool to characterize in time and space restricted subcellular domains of cAMP activity using living cardiac myocytes.

The aim of this study was to investigate the spatiotemporal dynamics of the cAMP response to catecholamines at individual signalosomes involved in ECC, in Adult Rat Left Ventricular Myocytes (ARLVMs).

We have generated a novel FRET cAMP Universal Tag for imaging experiments (CUTe) that can be effectively used to target specific macromolecular complexes, allowing dissection of cAMP signals with unprecedented spatial resolution. We infected ARLVMs with adenoviral constructs carrying CUTe chimera generated by fusion of the cAMP reporter to Tpro1 (part of the tropomin complex at the sarcoplasmic reticulum) and AKAP79 (part of the adenylyl cyclase/Adrenergic Receptor complex at the plasma membrane) and we measured cAMP changes by FRET imaging at these sites. We found that on treatment with iso the cAMP response is significantly smaller in ARVMs single living cardiac myocytes.

We have generated a novel FRET cAMP Universal Tag for imaging experiments (CUTe) that can be effectively used to target specific macromolecular complexes, allowing dissection of cAMP signals with unprecedented spatial resolution.
Iso 0.3 mM or IBMX 100 μM to generate the same amount of global cAMP. This increase in cAMP can be the result of both increases in the intrinsic production rate of cAMP and the enzymatic activity of PKA, both of which are well known to be increased in human myocardium.

**Methods and results:** We used a PKA antagonist (H-89) and a PKC inhibitor (KN-93) to study the role of PKA and PKC in the contractile response to GLP-1R agonists. The results showed that GLP-1R agonists can stimulate a PKA-dependent increase in contractility, which is mediated by the activation of the RyR2 channels. This effect was reversed by a RyR2 channel blocker (dantrolene).

**Conclusions:** GLP-1R agonists can stimulate a PKA-dependent increase in contractility, which is mediated by the activation of the RyR2 channels. This effect can be used to develop new therapeutic strategies for treating heart failure and other cardiac disorders.

---

**Acknowledgement/Funding:** This research was supported by the British Heart Foundation and the National Heart, Lung and Blood Institute.
Conclusions: Among treated yet uncontrolled hypertensive patients, severe RHT exhibits a significantly higher cardiovascular risk indicating the need for prompt management.

2266 | BEDSIDE
Resistant or pseudoresistant hypertension. Which is a true epidemic?
Insights from renal denervation screening programme
M. Ojrzanowski, M.P. Piekwa, J.D.K. Kasprzak. Medical University of Lodz, Cardiology, Lodz, Poland

Introduction: With emerging new therapeutic concepts including renal denerva-
(tion (RDN), there is a renewed interest in resistant hypertension (ResH). Among pa-
tients suspected of having ResH, accurate diagnosis needs to be well
established and pseudoresistant hypertension must be excluded.

Purpose: This analysis presents the observations from a standardized single-
center screening programme for RDN candidates including medical therapy mod-
fication and reassessment.

Methods: All pts referred to our center for RDN underwent a standardized step-
wise screening. Candidates were recruited from pts hospitalized in wards of cardi-
ology, internal diseases and nephrology, receiving no less than 3 antihypertensive
drugs including diuretic with office BP > 140/90 mmHg. Assessment included two
measurements of blood pressure (BP) and ABPM. If needed, pharmacotherapy
was intensified and diagnosis of ResH was reconfirmed after 6 weeks with ex-
clusion of secondary hypertension. If ResH was persistent, pts were hospitalized
with repeated ABPM on day 4. Further, renal angioCT was performed and a mul-
ti-technique evaluation was performed for suitability for RDN.

Results: A total of 87 pts with ResH diagnosis were referred for RDN. Mean BP
was 159/92 mmHg and mean ABPM was 154/90 mmHg. The initial medication
included: ACEI (angiotensin convertase inhibitors) - 74% of pts, ARB (angioten-
sin receptor blockers) −16%, β-blockers - 86%, calcium channel blockers (CCB) −
39%, diuretics - 94%. During 18 months of RDN programme 5 patients (5,7%)
underwent RDN, 2 further (2,3%) having ineligible renal anatomy. New diagno-
sis of secondary hypertension was made in 21 (25.6%) pts (7 - primary aldos-
teronism, 2 - active adrenal gland tumor, 12 - renal artery stenosis). However,
in 59 pts (67,8%) BP control was achieved after optimization of medical ther-
apy, with mean ABPM 134/84 mmHg. The final treatment included ACEI −100%,
β-blockers 92%, indapamide 94%, amiodipine 76%, spironolactone 61%. Med-
ication in most of these pts (52/59, 88%) included single-pill combination (38–64,4%)
or double combination (21–35,6). A subset of 23 pts (33,7%) became
controlled only when medicated in hospital-in-patient hospitalise, with possible com-
pliance issue.

Conclusion: Unselected cohort of ambulatory pts with high BP screened for RDN
requires careful secondary hypertension screening (26% prevalence) but 2/3
of pts can be controlled with strict medical intensification including single-pill
combinations and improved drug compliance. Unselective RDN use might contribute
to spuriously low intervention benefit if drug therapy is optimized in parallel.

CARDIAC RESYNCHRONISATION THERAPY: STRATEGIES FOR IMPROVING RESPONSE
2269 | BEDSIDE
Multimodality imaging-guided left ventricular lead placement improves clinical outcome in cardiac resynchronization therapy: a randomized controlled trial
A. Sommer, M.B. Kronborg, B.L. Norgaard, S.H. Poulsen, H.K. Jensen, J.M. Jensen, J. Kristensen, C. Gerdes, P.T. Mortensen, J.C. Nielsen. Aarhus University Hospital, Skejby, Department of Cardiology, Aarhus, Denmark

Background: Left ventricular (LV) pacing at the latest contracting region and se-
parate from myocardial scar improves response to cardiac resynchronization ther-
apy (CRT).

Purpose: We conducted a double-blinded, randomized controlled trial to clarify
the clinical effect of multimodality imaging-guided LV lead placement compared to
a contemporary routine fluoroscopic approach.

Methods: A total of 182 patients with left bundle branch block (age 70±9 years,
39 [21%] female, New York Heart association (NYHA) functional class II/ III/ IV 84
[46%]/ 92 [51%]/ 6 [3%], LV ejection fraction 25±6%, QRs width 166±22 ms) were
included. All patients underwent pre-implant electrocardiographic speckle-tracking
radial strain and single-photon emission computed tomography (SPECT) to de-
fine the latest contracting viable LV segment and cardiac computed tomography
(CT) to visualize the coronary sinus (CS) branches in relation to the LV myocardial
segmentation. Patients were randomized in a 1:1 ratio to 1) imaging-guided LV
lead placement targeting the optimal CS branch closest to the latest contracting
viable LV segment (imaging group) or 2) routine LV lead implantation in the non-
apical postero-lateral region in segments with a late electrical activation (mea-
sured as the QLV interval from QRS onset to the sensed signal in the LV lead
electrogram) (control group). The predefined primary endpoint was <1 of the fol-
lowing events at 6 months follow-up: 1) death or heart failure hospitalization, or
2) no improvement in NYHA class and <10% increase in 6-minute walk distance.
Secondary outcomes included LV remodeling and the combination of death and
heart failure hospitalization.

Results: The groups were balanced at randomization. In the Imaging group, 66
(74%) patients remained free from the primary endpoint and were classified as
clinical responders compared to 54 (58%) patients in the control group (p=0.02).
Controlled with comparisons, the Imaging group had more LV leads placed in the
optimal CS branch (83% versus 65%, p=0.01). The QLV interval was compara-
tive between groups (IQmax vs. IQmin): 196±71 vs. 193±31 ms (p=0.36). There
were no between-group differences in reverse LV remodeling at 6 months follow-
up or the combined endpoint of death or heart failure hospitalization during
1.8±0.9 years.

Conclusions: Multimodality imaging-guided LV lead placement towards the opti-
mal CS branch closest to the latest contracting non-scarred myocardial segment is
feasible and improves clinical response to CRT compared to routine selection
of LV pacing sites in postero-lateral regions with late electrical activation.

Acknowledgement/Funding: The Danish Heart Foundation and the Danish Council
for Independent Research.

2270 | SPOTLIGHT
Impact of multi-point left ventricular pacing on QRS duration and left ventricular ejection fraction. Preliminary results from a multicenter prospective study
L. Santini1, D. Potenza2, M. Giammaria3, F. Zanon4, G. Senatore5, A. Curnis6, D. Riccardi7, C. D'Agostino8, L. Calo'9, G. Forleo1. University of Rome Tor
Vesuvius, other, Rome, Italy; 2Casa Sollievo della Sofferenza Hospital, San
Giovanni Rotondo, Italy; 3Maria Vittoria Hospital, Turin, Italy; 4General Hospital of Rovigo, Rovigo, Italy; 5Civic Hospital of Cine, Cine (Turin), Italy; 6Civil Hospital of Brescia, Brescia, Italy; 7 University Campus Bio-Medico of Rome, Rome, Italy; 8Hospital of Venere, Bari, Italy; 9Policlinico Casilino of Rome, Rome, Italy

Introduction: MultiPoint Pacing (MPP) allows delivery of cardiac resynchroniza-
tion therapy from quadrupolar leads (0.45 mm electrode separation) to achieve
the clinical effect of CRT in patients with a narrow QRS. The aim of the study is
evaluating the influence of MPP on QRS duration and LV ejection fraction.

Methods: Data from 386 patients (pts) (80% male, LVEF 28±8% QRS 162±26ms)
were collected in 67 Italian hospitals. After CRT implantation, device programming
was optimized per center standard practice and electrical measurements were
performed. QRS and Ejection Fraction (EF) data were available at follow-up (fup)
in 88 pts.

Results: Implant procedural was 114±47 min. The LV lead was implanted in 16%
antero-lateral, in 50% lateral, in 34% in a postero-lateral vein. The LV cardiac
thresholds (CTs) were measured in at least 2 out of 10 available configurations
with different cathodes. The mean of CT (at 0.5mS) was <3V in all the pacing
configurations. The MPP was programmable in 96% of the pts with CT <5V
for both cathodes and without PNS issues. In pts optimized by QRS (86 pts) the
Delta QRS (relative percentage change from bsl QRS) was significantly greater
in the optimized MPP compared to best conventional biventricular mode (BiV)
(17%±21 vs 12%±20, p<0.001). At fup, among 48% pts programmed in MPP, the
Delta QRS in MPP mode was greater than in BiV (20%±21 vs 13%±24, p=0.16).
Whilst bsl EF didn't differ significantly between the two groups, after 6 month,
EF increased significantly in the MPP group vs BiV group (+12±10% vs +7±9%,
p=0.01). Patients with an EF increase of at least 5% were considered as CRT
Responders; only 62% of the pts programmed in BiV were responders versus
76% in MPP group.

Conclusions: MPP was programmable in 96% of the pts: it could ensure greater
QRS shortening and EF improvement, compared to conventional CRT

2271 | BEDSIDE
Relation of QRS duration to clinical benefit of cardiac resynchronization therapy in mild heart failure patients without left bundle branch block MADIT-CRT sub-study
Y. Biton, V. Zareba, V. Kutyifa, H. Klein, S. McNitt, B. Polonsky, A.J. Moss, I. Goldberg. University of Rochester, Cardiology, Rochester, United States of
America

Background: There are conflicting data on the efficacy of cardiac resynchronization
therapy (CRT) in heart failure (HF) patients without left bundle branch block
(LBBB) morphology. Current US and European guidelines do not negate implan-

tation of CRT-D in non-LBBB patients with QRS > 150 msec and advanced HF symptoms.

Methods: We evaluated the long-term clinical outcome of non-LBBB patients with mild HF symptoms enrolled in the MADIT-CRT study (n=537), by QRS morphology (right bundle branch block (RBBB) and intraventricular conduction delay (IVCD)) and QRS duration (categorized at 150 msec or by quarters).

Results: Among patients with non-LBBB, the 7-year cumulative probability of HF death was 32% in the IC-D only arm vs. 41% in the CRT-D arm, respectively (p=0.583 for the overall difference during follow-up). Sub-group analysis by QRS duration showed that patients with QRS > 153 msec (lower quartile) experienced a significant 2.4-fold (p=0.015) increased risk for HF or death with CRT-D vs. IC-D only therapy, whereas the effect of CRT-D in patients with QRS ≥ 153 msec was neutral (HR=0.97, 95% CI: 0.69–1.36, p=0.86; p-value for QRS duration by treatment interaction=0.203), and remained neutral with QRS > 150 msec (HR=0.88, 95% CI: 0.50–1.52, p=0.637). There was no clinical benefit with CRT-D vs. IC-D regardless of QRS morphology in RBBB (HR=1.01, 95% CI: 0.61–1.66, p=0.975) or in IVCD patients (1.31, 95% CI: 0.89–1.93, p=0.172).

Conclusions: Our findings suggest that mild HF patients without an LBBB ECG pattern do not derive clinical benefit from CRT-D, not even during long-term follow-up. Instead of, there appears to be a significant increase in HF or death in those with non LBBB and QRS duration > 153 msec.

Acknowledgement/Funding: The MADIT-CRT trial was sponsored by an unrestricted research grant from Boston Scientific Corporation to the University of Rochester, Rochester, NY.

NEW ADVANCES IN CARDIAC IMAGING

2282 | BENCH

Validation of the pre-stretch-strain relationship as an non-invasive index of left-ventricular contractility

O. Mirea, C. Vallecilla, P. Claus, F.E. Rademakers, J. D’hooge. KU Leuven, Department of Cardiovascular Sciences, Leuven, Belgium

Purpose: The slope of the relationship between left ventricular (LV) segmental stretch during atrial contraction (PreS) and total systolic shortening (S) has recently been proposed as a non-invasive index of LV contractility in a clinical setting. An experimental validation of this novel parameter is missing. The aim of the study was therefore to: i) correlate the PreS-S slope to invasive gold standard measurements and ii) to investigate the influence of atropine on this new parameter in a controlled experimental setting.

Methods: Afterload was modulated in 13 anesthetised pigs, by a balloon inflation in the descending aorta. In an additional 3 animals contractility was increased by dobutamine infusion. During baseline and all interventions, LV pressure-volume (PV) measurements were acquired. Simultaneously, trans-diaphragmatic two-dimensional echo were acquired (2–3 LV chamber). The Pre-S-S slope was constructed from 18 segmental strain curves obtained by Speckle tracking and corrected to the end-systolic PV relation (ESPVR) and the pre-load recruitable stroke work (PRSW).

Results: Systolic blood pressure increased (103.8±18.3 vs. 136.6±30.1; p<0.01) and LV stroke volume (p<0.01) and ejection fraction (p<0.01) decreased during balloon inflation. Conversely, the Pre-S-S slope was not influenced by loading (p=0.58). When comparing absolute values of the Pre-S-S slope with ESPVR and PRSW we found no correlation while when comparing the rate of change in contractility, Pre-S-S slope correlated with PRSW (p<0.01) and ESPVR (p=0.05) (Figure 1).

Figure 1.

Conclusions: PreS-S slope is sensitive to changes in inotropy and is comparable with the gold standard measures of LV contractility and appears to be influenced by loading in a lesser degree than the established measurements of LV function.

2283 | BENCH

Echocardiographic strain parameters assess early alterations of right ventricular contractility and cardiomyocyte excitation-contraction-coupling: an experimental study in a large animal model

A. Hodzic, P. Bobin, F. Lefebvre, G. Vandecastelee, M. Ly, E. Gouadon, A. Capderou, J. Leroy, C. Rucker-Martin, V. Lambert on behalf of INSERM U999, INSERM U-999, le Plessis Robinon, France; University of Paris-Sud 11, INSERM U967, Chatenay-Malabry, France; Centre Chirurgical Marie-Lannelongue, le Plessis Robinon, France

Background: Right ventricular (RV) dysfunction is a major determinant of long-term survival in congenital heart diseases. Early echocardiographic detection of RV failure is mandatory, but recent parameters need to be validated.

Purpose: Objectives were to: (1) validate standard and strain echocardiographic parameters for evaluation of RV systolic function, compared to hemodynamic parameters; (2) assess the accuracy of these parameters for early detection of RV failure.

Methods: Combined RV overload as observed in repaired tetralogy of Fallot was surgically reproduced in 2-month-old piglets (n=6). Age-matched piglets were used as controls (n=4). RV function was evaluated at baseline and 4 months of follow-up by standard and strain echocardiographic parameters, compared to hemodynamic (conductance catheter). Sarcomere shortening and cardiac transit were recorded in RV isolated myocytes (IonOptix). Contractile reserve was assessed by in-vivo (dobutamine 5μg/kg) and ex-vivo (isosorine 100nm) β-adrenergic stimulation.

Results: 4 months after surgery, hemodynamic RV ejection fraction (FEVD) was significantly decreased (29.7% [26.2–34] vs 42.9% [40.7–48.6]; p<0.01), and inotropic responses to dobutamine were attenuated (contractile reserve ΔEmax = 51% vs 193% for controls). On echocardiography FAC, TAPSE, S’ peak and RV free wall longitudinal strain rate were significantly decreased and correlated with FEVD. Strain rate and S’ peak were correlated with ΔEmax (r=0.75 and 0.78, p<0.05). Isolated RV myocytes from operated animals exhibited hypertrophy, decreased sarcomere shortening peak in response to isoprorenaline (ΔL= 7.8±2.8% vs 10.7±2.9%, p<0.05), and increased spontaneous calcium waves suggesting perturbations of calcium homeostasis.

Conclusion: In this model, both standard and strain echocardiographic parameters allowed the detection of early impairments of RV function and cardiac reserve, which are associated with cardiac excitation-contraction coupling alterations.

2284 | BENCH

Strain and strain rate by speckle-tracking echocardiography reflect the effects of exercise training and detraining in a rat model of athlete’s heart


Recently our working group provided detailed morphologic and hemodynamic characterization on exercise-induced left ventricular (LV) hypertrophy in a rat model, confirming increased contractility. In the current study we aimed to assess whether strain parameters by speckle-tracking echocardiography (STE) are able to describe the effects of training and detraining on LV function.

Rats were divided into trained (n=12) and control (n=12) groups. Trained rats swam 200 min/day for 12 weeks, then remained sedentary for 8 weeks. Echocardiography showed the development of LV hypertrophy in the trained group (trained vs. control; LV mass index: 2.4±0.1 vs 2.0±0.1g/kg, p<0.01), and free wall longitudinal strain rate were significantly decreased and correlated with ΔEmax (r=0.75 and 0.78, p<0.05). Isolated RV myocytes from operated animals exhibited hypertrophy, decreased sarcomere shortening peak in response to isoprorenaline (ΔL= 7.8±2.8% vs 10.7±2.9%, p<0.05), and increased spontaneous calcium waves suggesting perturbations of calcium homeostasis.

Morphologic and functional properties of exercise-induced LV hypertrophy completely regressed after the detraining period. Both changes induced by exercise training and effects of detraining reflected by STE, allowing a consecutive evaluation of LV function in rat models.

Morphologic and functional properties of exercise-induced LV hypertrophy completely regressed after the detraining period. Both changes induced by exercise training and effects of detraining reflected by STE, allowing a consecutive evaluation of LV function in rat models.
2318 | BEDSIDE

Development and validation of a risk score for cardiac surgery in infective endocarditis

C. Olmos1, I. Vilacosta1, C. Fernandez1, G. Tirado1, A. Freitas-Ferraz1, J. Lopez2, C. Sarria3, D. Vivas1, L. Maroto1, L.A. San Roman2, 2Hospital Clinic San Carlos, Cardiovascular Institute, Madrid, Spain; 3Institute of Heart Sciences, ICICOR, University Clinic Hospital, Valladolid, Spain; 2University Hospital La Princesa, Madrid, Spain

Aim: To develop and validate a simple calculator to predict the risk of in-hospital mortality in patients with infective endocarditis (IE) undergoing surgery.

Methods: We analyzed 1299 consecutive episodes of IE prospectively recruited on an on-going multipurpose database from 1996 to 2013. Left-sided IE episodes that underwent surgery (n=672) form our study population and were randomized into development (n=425) and validation (n=247) samples. The primary endpoint was in-hospital mortality. We also analyzed the predictive performance of Euroscore I in our cohort of 672 patients.

Results: In-hospital mortality was similar in the derivation and validation samples (29.2% vs 28.1%; p=0.723). In the derivation sample, a univariable analysis for in-hospital mortality was performed. Those variables found to be statistically significant, and clinically relevant were used to develop a multivariable prediction model. The variables included in the final model were: age >70 years, prosthetic infection, vegetation detection, perianular complications, Staphylococcus aureus infection, acute renal failure before surgery, septic shock before surgery, acute heart failure or cardiogenic shock, and platelet count <150000. There was an excellent correlation between the predicted and observed in-hospital mortality in both samples. The area under the ROC curve in the validation sample was 0.80 (95% CI: 0.73–0.86).

The accuracy of Euroscore I in our cohort was inferior, with an area under the ROC curve of 0.74 (95% CI: 0.69–0.79).

Conclusions: We found that IE-specific factors (microorganisms, perianular complications, sepsis manifestations) beside the universal ones (age, hemodynamic conditions), independently predicted mortality in IE surgery. Our model had a superior predictive accuracy than Euroscore I.

Comparison of ROC curves

2319 | BEDSIDE

Incidence, pathogenesis and outcome of patients developing infective endocarditis after transfemoral transcatheter aortic valve implantation

N. Mangner1, F.J. Wolte1, R. Hoelttlegel1, S. Haussig1, F. Schlott1, G. Stacher1, D. Holzhey2, F.W. Mohr3, G. Schuler4, A. Linke1, 1University of Leipzig, Heart Center, Leipzig, Germany; 2University of Leipzig, Heart Center, Leipzig, Germany; 3Department of Cardiac Surgery, Leipzig, Germany

Purpose: Infective endocarditis (IE), e.g., prosthetic valve endocarditis (PVE), is a severe complication following valve replacement. In patients after surgical or transcatheter aortic valve replacement (TF-AVI).

Methods: Data about the occurrence of IE were available in 1717 patients treated with TF-AVI from 01/2006–11/2014. Diagnosis of IE was verified by applying the modified Duke criteria. Clinical, microbiological, echocardiographic findings and treatment options were analysed. 30-day and 1-year mortality after diagnosis of IE was calculated.

Results: IE occurred in 46 out of 1717 patients (2.7%). Patients developing IE were 78.1±6.8 years of age and had a mean logEuroScore I of 21.2±14.0. According to Duke criteria, 59% and 41% of the patients had definite or probable IE, respectively. Early IE occurred in 70% and late IE in 30%. Clinically, all patients except one had fever >38.0°C, all had a predisposition, and a sepsis-related event occurred in 24%. Blood cultures (positive in all cases) included Staphylococcus in 44%, enterococci in 29%, streptococci in 7%, and others in 20%. Transoesophageal echocardiography was performed in 38 patients. There was no typical endocarditis in 25% of those patients. IE affecting another valve than the prosthetic was evident in 11%. Lead endocarditis alone occurred in 11%. The remaining 53% had echocardiographic evidence of PVE alone or in combination with multilocular IE.

Treatment included antibiotics in 78%, antibiotics and operation in 15%, and no treatment due to death immediately after admission in 7%.

Overall 30-day and 1-year mortality after diagnosis of IE was 54.3% and 71.7%, respectively. Definitive and probable IE did not differ in 30-day (51.9% vs. 57.9%, p=0.69) and 1-year mortality (74.1% vs. 68.4%, p=0.68). No difference in 30-day (42.1% vs. 47.4%, p=0.74) and 1-year mortality (68.4% vs. 63.2%, p=0.73) was detectable in patients with echocardiographic evidence of PVE compared to those without.

Conclusion: IE after TF-AVI occurred in 2.7% and was associated with a high mortality. Echocardiographic evidence of PVE was only evident in 53%. However, there was no difference in mortality between patients with echocardiographic evidence of PVE compared to those without, underlining the necessity of aggressive therapy in all TAVI patients with bacteremia.

VASCULAR BIOLOGY – NEW MOLECULAR AND GENETIC FINDINGS

2334 | BENCH

Inhibition of FGFR signaling with PD173074 ameliorates monocrotaline-induced pulmonary arterial hypertension and rescues BMPR-II expression

Y. Zheng, C.M. Xiong on behalf of State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Peking Union Medical College, Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China, People’s Republic of China

Background: Fibroblast growth factor-2 (FGF-2) signaling plays a pivotal role in the development of pulmonary arterial hypertension (PAH). PD173074 is a potent FGF receptor 1 (FGFR-1) inhibitor that displays high activity and selectivity. The aim of this study was to investigate the effects of PD173074 on monocrotaline-induced PAH. We also evaluated whether FGFR-1 inhibition could attenuate bone morphogenetic protein type II receptor (BMPR-II) down-regulation.

Methods: PAH model was established by a single intraperitoneal injection of monocrotaline. And then a daily intraperitoneal injection of PD173074 (20 mg/kg)
Vascular biology – New molecular and genetic findings 375

was administered from day 14 to day 28. Hemodynamic parameters, right ventricular hypertrophy index and morphometry were evaluated at day 28.

**Results:** The expression of FGF-2 and FGRF-1 was upregulated in lung tissue after mononuclear injection, and it was accompanied by hemodynamic changes and pulmonary vascular remodeling. PD173074 treatment significantly ameliorated PAH and vascular remodeling (Figure A). It decreased ERK1/2 activation and rescued total Akt expression, leading to a reduction in both proliferation and apoptosis in the lung. Besides, PD173074 rescued the expression of BMPR-II (Figure B).

**Conclusions:** These results suggest that PD173074 can efficiently alleviate pulmonary arterial hypertension and it may be an useful option for PAH. Our data also suggest a role of FGF-2/BMP signaling interaction in PAH.

2335 | BENCH
PI3Kalpha induced SMC migration and cell cycle progression is crucial for neointima formation following vascular injury

M. Vantler1, J. Jesus1, O. Leppaenen2, X. Chen1, M. Gerhardt1, E. Berghausen1, M. Zierden1, S. Baldus1, J.J. Zhao3, S. Rosenkranz1.

1 Université zu Köln, Köln, Germany; 2 Upsala University, UCR-Uppsala Clinical Research Center, Uppsala, Sweden; 3 Harvard Medical School, Department of Cancer Biology, Boston, United States of America

Vascular remodeling processes are the underlying cause of numerous vascular diseases like restenosis following PTCA. Receptor tyrosine kinase (RTK) induced migration and proliferation of smooth muscle cells (SMCs) critically contribute to vascular remodeling. Phosphatidylinositol 3’-kinase (PI3K) is a central downstream mediator of growth factor induced RTK signaling, but the role of PI3K isoforms in vascular remodeling remains elusive. We sought to systematically characterize the precise role of catalytic class IA PI3K isoforms (PI3Ka, PI3Kb, PI3Kd), for SMC proliferation and migration in vitro and vascular remodeling in vivo. Proliferation of rat, murine and human SMCs was determined via BrdU incorporation assays and chemotaxis by means of a modified Boyden chamber. Cells were stimulated with PDGF or diverse growth factors in the presence or absence of specific inhibitors (PI3Ka: PIK-75, PI3Kb: TGX-221; PI3Kd: IC-87114) or siRNAs (N=3). To investigate cell cycle progression, SMCs were stimulated with PDGF (50 ng/ml; 5 min, 6 h, 24 h) and phosphorylation of AKT, GSK3β and Rb as well as the expression of Cyclin D1 were analyzed by Western blotting. The absence of neointima formation was quantified 4 weeks following balloon angioplasty of carotid arteries from wild-type (WT, n=7) and SMC specific PI3Ka ko (n=5) as well as from WT and PI3Kd ko mice (n=8, respectively). Additionally, cellular proliferation was analyzed in neointimal sections by means of immunocytochemical PCNA stainings.

Western blot analyses revealed that all three isoforms are abundantly expressed in SMCs. Targeted gene knockdown as well as inhibition of PI3Ka, PI3Kb, or PI3Kd indicated that PI3Ka is crucial for RTK mediated cell cycle progression, proliferation, and migration. Surprisingly, PI3Kd exerted non-catalytic functions in SMC proliferation, as knockdown of PI3Kd significantly decreased SMC proliferation whereas inhibition of PI3Kd had no effect. Based on these results, we generated a mouse model of SMC-specific PI3Kd deficiency. Targeted deletion of PI3Kd in mice blunted growth-factor-induced cellular responses and significantly reduced SMC proliferation and thus neointima formation following balloon-injury of the carotid artery in mice (p<0.05). In contrast, PI3Ka deficiency did not affect vascular remodeling in vivo.

In conclusion, RTK-induced PI3Ka signaling plays a central role for vascular remodeling in vivo. Thus, PI3Ka represents a selective target for the prevention of neointima formation following vascular injury, whereas PI3Kd and PI3Kb expression and activity do not play a significant role.

2336 | BENCH
Targeting the paretic guanylyl cyclase receptor b with a novel agonist, c-type natriuretic peptide-53, for selective vasorelaxation

S.J. Sangaralingham1, B.K. Huntley1, A. Buglioni1, T. Ichiki1, G.E. Harders1, S.J. Sangaralingham1, B.K. Huntley1, A. Buglioni1, T. Ichiki1, G.E. Harders1.

1 Harvard Medical School, Department of Surgery, Boston, United States of America

**Background:** Endothelin-derivated C-type natriuretic peptide (CNP) possesses several cardiovascular protective actions mainly through the activation of guanylyl cyclase receptor B (GC-B) and its second messenger, cyclic GMP (cGMP).

The biologically active form, CNP-22, is known to have vasorelaxing properties, but lacks renal actions. Recently, we identified a higher molecular form of CNP, CNP-53, in the human circulation and data suggests that CNP-53 has a longer circulating half-life than CNP-22. However, it remains unknown if CNP-53 possesses biological actions through GC-B and cGMP activation and if CNP-53 is a vasorelaxant. Based on its structural similarity to CNP-22, we hypothesized that CNP-53 would: 1) have cGMP activating actions in human vascular smooth muscle cells (hVSMCs), specifically through GC-B and 2) lower blood pressure in an experimental model of hypertension.

**Methods:** HEK 293 cells over-expressing GC-A and GC-B and hVSMCs, which express GC-B, were stimulated with CNP-53 for 10 minutes at a dose of (10−8M) and cGMP was measured. Two groups of anesthetized spontaneously hypertensive rats (SHRs; n=8) received a 75-minute infusion of Vehicle (V: saline) or CNP-53, 0.264 µg/kg/min, (n=4, non-catalytic dose based on a non-catalytic dose of CNP-22). We then assessed the absolute change in mean arterial pressure (MAP), glomerular filtration rate (GFR), sodium (Na) excretion, plasma CNP-53 and plasma and urinary cGMP. Data are means±SE, *p<0.05.

**Results:** CNP-53 significantly activated cGMP in hVSMCs (0.09±0.01 vs. 0.00±0.00 pmol/well) and in GC-B HEK cells (75±9 vs. 0.41±0.1 pmol/well) compared to no treatment. In contrast, CNP-53 failed to generate cGMP in GC-A HEK cells. In SHRs, CNP-53 infusion (compared to vehicle) significantly elevated plasma CNP-53 (CNP-53: 1332±281, V: 1013 pmg/ml) as well as cGMP role in AD. In addition, activity of cGMP cycle has been described in humans. Although it is unclear exactly how IL-6 and STAT3 participate in pathogenesis of AD, or how they are related to cell cycle activation. In this study, we first performed immunohistochemical study of human AD tissue, and found that STAT3 was activated in adventitia mainly in infiltrating monocytes/macrophages. Interestingly, STAT3 was more active in the area of aortic adventitia where extracellular matrix (ECM) was more sparse, suggesting the association of STAT3 activation and ECM metabolism. In addition, Ki67 staining showed that cell cycle was more accelerated in the monocytes/macrophages. We then investigated the significance of STAT3 activation in macrophages by using macrophage-specific knockout of SOCS3, a negative regulator of STAT3 signaling (mSOCS3-KO). We created a mouse model of aortic hemodynamic stress with aortic stiffening by periarterial CaCl2 treatment and angiotensin II infusion (Ca+AngII) both in wild type (WT) and mSOCS3-KO. Both WT and mSOCS3-KO showed microscopic injuries in aorta with 40% of frequencies 1 week after Ca+AngII. In WT, the microscopic injuries healed with fibrosis in 6 weeks. However, the injuries progressed to AD in 6 weeks in mSOCS3-KO. Transcriptome analysis showed the activation of cell cycle and inflammatory genes at the stage of microscopic injury in mSOCS3-KO compared to WT before the development of AD. Flow cytometric analysis revealed the proinflammatory M1-skewed differentiation of mSOCS3-KO macrophages compared to WT, the aorta with microscopic injury. Ki67 staining and BrdU uptake study indicated the proliferative response of macrophages. These results suggest that activation of macrophage STAT3 signaling resulted in the expansion and M1 polarization of macrophages, which is presumably more active in degrading extracellular matrix; thus exacerbating the progression of AD. Deciphering such molecular events during the development of AD will be essential to develop a new diagnostic and therapeutic strategies for this lethal disease.

2338 | BENCH
Excessive sodium intake worsens aortic dissection via IL-17 pathway

N. Nishida1, H. Aoki2, S. Ohno1, M. Nishihara1, A. Furusho1, S. Hirakata1, N. Nishida1, S. Ito1, M. Hayashi1, H. Tanaka3, Y. Fukumoto1.

1 Kurume University School of Medicine, Department of Internal Medicine, Division of Cardiovascular Medicine, Kurume, Japan; 2 Cardiovascular Research Institute of the Kurume University, Kurume, Japan; 3 Kurume University School of Medicine, Department of Surgery, Division of Cardiovascular surgery, Kurume, Japan

Aortic dissection (AD) is a common disease with sudden onset and high mortality, caused by the disruption of the intimal medial layer. Recent studies showed that IL-6, a JAK-STAT3-activating proinflammatory cytokine, plays an important role in AD. In addition, activity of cGMP cycle has been described in humans. Although it is unclear exactly how IL-6 and STAT3 participate in pathogenesis of AD, or how they are related to cell cycle activation. In this study, we first performed immunohistochemical study of human AD tissue, and found that STAT3 was activated in adventitia mainly in infiltrating monocytes/macrophages. Interestingly, STAT3 was more active in the area of aortic adventitia where extracellular matrix (ECM) was more sparse, suggesting the association of STAT3 activation and ECM metabolism. In addition, Ki67 staining showed that cell cycle was more accelerated in the monocytes/macrophages. We then investigated the significance of STAT3 activation in macrophages by using macrophage-specific knockout of SOCS3, a negative regulator of STAT3 signaling (mSOCS3-KO). We created a mouse model of aortic hemodynamic stress with aortic stiffening by periarterial CaCl2 treatment and angiotensin II infusion (Ca+AngII) both in wild type (WT) and mSOCS3-KO. Both WT and mSOCS3-KO showed microscopic injuries in aorta with 40% of frequencies 1 week after Ca+AngII. In WT, the microscopic injuries healed with fibrosis in 6 weeks. However, the injuries progressed to AD in 6 weeks in mSOCS3-KO. Transcriptome analysis showed the activation of cell cycle and inflammatory genes at the stage of microscopic injury in mSOCS3-KO compared to WT before the development of AD. Flow cytometric analysis revealed the proinflammatory M1-skewed differentiation of mSOCS3-KO macrophages compared to WT, the aorta with microscopic injury. Ki67 staining and BrdU uptake study indicated the proliferative response of macrophages. These results suggest that activation of macrophage STAT3 signaling resulted in the expansion and M1 polarization of macrophages, which is presumably more active in degrading extracellular matrix; thus exacerbating the progression of AD. Deciphering such molecular events during the development of AD will be essential to develop a new diagnostic and therapeutic strategies for this lethal disease.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475/1/1833847457951/7 on 07 February 2019
although the molecular mechanism has not been fully understood. Aortic dissection (AD) is one of the fatal cardiovascular events, in which proinflammatory response is proposed to be important presumably by weakening the strength of extracellular matrix (ECM). In this study, we investigated the effect of excessive sodium intake on a mouse AD model that was induced by continuous infusion of beta-amyloid precursor protein (BAPP), an inhibitor of a collagen/ elastin cross-linking enzyme lysyl oxidase, and angiotensin II (AngII) using osmotic pumps. BAPP+AngII caused thoracic and suprarenal AD in most of the mice within 2 weeks with occasional aortic rupture and sudden death. Excessive sodium intake was achieved by giving 1% NaCl drinking water 1 week prior to and during the BAPP+AngII infusion. The lesion length of AD was significantly longer in the excessive sodium intake group than in normal water group, even though systolic blood pressure or pulse rate showed no significant changes. Because recent studies have demonstrated that excessive sodium intake activates TH17/IL-17 pathway that is central to the inflammatory response, we examined the involvement of IL-17 in AD using BAPP+AngII. Transcription analysis of aortae before the onset of AD showed that strong induction of proinflammationary genes and suppression of ECM genes precede the AD development in this model. Although IL-17 is central to inflammatory response in general, alteration of inflammatory response was not prominent in IL-17 knockout aorta. Instead, genes of ECM were upregulated in IL-17 knockout at the baseline. Furthermore, excessive sodium intake leads to the upregulation of all conditioned in our experiments. Because ECM is essential to maintain the tensile strength of aortic walls, enhanced expression of ECM genes would explain why IL-17 knockout aorta is protected from dissection. Sodium intake and IL-17 may represent important therapeutic targets for AD.

2339 | BENCH
Endothelial mesenchymal transitions do not contribute to the development of pulmonary arterial hypertension caused by a VEGF receptor inhibitor in mice
R. Okamoto1, I. Goto1, Y. Oghara1, N. Yamada1, H. Okada2, M. Ito1.
1Mie University Graduate School of Medicine, Department of Cardiology and Nephrology, Tsu, Japan; 2Saitama Medical University, Department of Neurology, Saitama, Japan.
Background: Idiopathic pulmonary arterial hypertension (IPAH) is characterized by hyperproliferation of endothelial cells and pulmonary artery (PA) smooth muscle cells that leads to plexogenic lesions. It remains unknown whether endothelial mesenchymal transition contributes to the development of IPAH.
Purpose: We aimed to use genetically engineered mice to determine whether the cells in plexiform lesions derive from endothelial cells.
Methods: To generate reporter mice, tdTomato and Tie2-Cre double transgenic mice, with a marker for endothelium-derived cells, mice homzygous for a conditional floxed tdTomato allele (Gt(RosA)262or-CAG-tdTomato) were crossed with Tie2-Cre+/- reporter mice. Adult 6-8 week-old male reporter mice were injected subcutaneously with either SU5416, a vascular endothelial growth factor (VEGF) receptor inhibitor at 20 mg/kg, or a vehicle, once a week for three weeks and were simultaneously exposed to chronic normobaric hypoxia (10% O2) in a ventilated chamber. Control mice were kept in the same room and the same light-dark cycle under normoxia. Each mouse was intubated through the mouth and anesthetized with isoflurane. Right ventricular (RV) systolic pressure was measured by right heart catheterization directly though right ventricle wall. After hemodynamic measurements, each animal was sacrificed by cervical dislocation, and lung and heart tissue samples were collected for histological and molecular profiling.
Results: The expression of tdTomato was recognized specifically in pulmonary artery endothelial cells in Tie2-Cre and Tie2-Cre-flotted double Tg mice under normoxia. Compared with control mice, mice treated with SU5416 and hypoxia showed higher RV systolic pressure (44.3 versus 21.6 mmHg; n=6, P<0.01). Histological examination showed vascular remodeling with the development of neointimal occlusive lesions. Immunofluorescence staining of frozen sections showed thickening of medial layer of arteries that highly expressed alpha smooth muscle actin but did not express tdTomato in the mice treated with SU5416 under hypoxia.
Conclusions: These results indicate that, in mice, endothelial mesenchymal transitions did not contribute to the development of plexogenic lesions associated with pulmonary artery hypertension caused by the combination of SU5416 and chronic hypoxia.

2340 | BENCH
Diastolic dysfunction in mice lacking nuclear factor (erythroid-derived 2)-like 2
R. Erkens2, C.M. Kramer1, C. Panknin1, L. Krause1, M. Weidenbach1, T. Krenz1, E. Mengis2, M. Kelm1, M.M. Cortese-Krott1, 1Heinrich Heine University, Division of Cardiology, Pneumology and Angiology, Düsseldorf; 2Ruhr University Bochum (RUB), Institute for Pharmacology and Toxicology, Bochum, Germany.
Background: The transcription factor Nr2f2 is a key master switch controlling the expression of antioxidant and protective. In this study we aimed to investigate the cardiac and vascular phenotype and systemic hemodynamics in Nr2f2 KO mice, compared with their littermates.
Methods: Male Nr2f2 KO mice and WT mice 6 month of age were studied for global changes in cardiac and vascular function and changes in biochemical parameters including redox state, eNOS/3GMP expression and NO bioavailability in the aorta and the heart. Echocardiography and Flow-Mediated-Dilation was measured. Serum IL-17 was determined in aorta and heart. IL-17 serum was assessed by calculation of pulse wave velocity. Coronary vascular function and cardiac response to β adrenergic stimulation by isoproterenol, was assessed in Langendorff hearts by measuring reactive hyperemia and changes in increase of cardiac contractility. Mean arterial blood pressure measurement was performed with a Millar catheter and responses to cardiac glycoside ouabain were detected. Expression of eNOS in the aorta and the heart was assessed by western blot analysis. The circulating NO pool was analyzed by HPLC and chemiluminescence detection. cGMP levels in plasma and aorta were measured.
Results: We found that Nr2f2 KO mice show an impaired left ventricular diastolic function, as demonstrated by prolonged isovolumic relaxation time, E-wave deceleration time and increased myocardial performance index. Accordingly, isolated perfused Nr2f2 KO hearts showed an impaired response to β adrenergic stimulation by isoproterenol, as shown by lower developed pressure and dp/dtmin as compared to WT mice, while systolic left ventricular function was preserved. Administration of the cardiac glycoside ouabain in vivo increased dp/dtmax and dp/dtmin in WT mice, but not in the KO of Nr2f2. From these findings we propose that IL-17 suppresses the effect of NaCl on the severity of AD by BAPN+AngII. Transcriptome analysis demonstrated that excessive sodium intake activates TH17/IL-17 pathway that is central to the exacerbating effect of NaCl on the severity of AD by BAPN+AngII. Transcriptome analysis of aortae before the onset of AD showed that strong induction of proinflammationary genes and suppression of ECM genes precede the AD development in this model. Although IL-17 is central to inflammatory response in general, alteration of inflammatory response was not prominent in IL-17 knockout aorta. Instead, genes of ECM were upregulated in IL-17 knockout at the baseline. Furthermore, excessive sodium intake leads to the upregulation of all conditioned in our experiments. Because ECM is essential to maintain the tensile strength of aortic walls, enhanced expression of ECM genes would explain why IL-17 knockout aorta is protected from dissection. Sodium intake and IL-17 may represent important therapeutic targets for AD.
2342 | BENCH
RNA editing is essential for vascular homeostasis in vivo and controls gene expression in patients with cardiovascular disease

K. Stellios1, A. Gatsiou2, R. Boon3, D. John2, S. Uchida4, T. Keller5, W. Chen6, H. Schwabe6, A.M. Zeiher7, S. Dimmeler7, *JW Goethe University, Department of Cardiology and Institute of Cardiovascular Regeneration, Frankfurt am Main, Germany; 2 Goethe University, Institute of Cardiovascular Regeneration, Frankfurt am Main, Germany; 3 JW Goethe University, Department of Cardiology, Frankfurt am Main, Germany; 4 Max Delbrück Center for Molecular Medicine, Laboratory of Functional Genomics and Systems Biology, Berlin, Germany; 5 JW Goethe University, Institute of Organic Chemistry and Chemical Biology, Frankfurt am Main, Germany

Background: Adenosine to inosine (A-to-I) RNA editing is catalysed by ADARs (adenosine deaminases acting on RNA) and is an important posttranscriptional regulator of RNA metabolism. Its role though in cardiovascular system remains unknown. The goal of the present study was to evaluate the role of RNA editing in human endothelial cells in vitro and in patients with coronary artery disease. Further, we addressed the role of ADAR1 in vascular development and homeostasis in mice.

Methods and results: Next generation RNA sequencing of human endothelial cells revealed that ADAR1 is the main RNA editor inducing A-to-I RNA editing events in almost 25% of transcripts, mostly in introns followed by 3′-untranslated regions (3′UTR). Among the highest ADAR1 edited targets was cathepsin S (CTSS), an extracellular matrix degradation enzyme with an established role in cardiovascular disease. RNA editing of CTSS 3′UTR was increased after hypoxia and when evaluating the clinical relevance of our bench findings, we sequenced the transcriptome of peripheral blood mononuclear cells from 4 patients after hypoxia. In order to evaluate the clinical significance of our bench findings, we sequenced the transcriptome of peripheral blood mononuclear cells from 4 patients with stable coronary artery disease and 4 patients with ischemic cardiomyopathy. RNA editing of CTSS 3′UTR was significantly increased in patients with coronary artery disease, as was the expression of CTSS in patients with heart failure, compared to healthy subjects (P < 0.001). Of interest, the extent of RNA editing in single nucleotide positions was strongly associated with cathepsin S mRNA expression (r = 0.8, P < 0.001) in our cohort. In order to investigate the underlying mechanism, we studied the role of ADAR1 in CTSS mRNA expression. Silencing of ADAR1 profoundly reduced RNA editing of the 3′UTR of CTSS mRNA and inhibited CTSS mRNA and protein expression by 60% (P < 0.001 for all). In a similar manner, ADAR1 regulated endothelial cell CTSS mRNA expression under hypoxic or inflammatory conditions. Mechanistically, RNA editing alters CTSS mRNA secondary structure and stability by regulating the binding of the stabilizing RNA-binding protein HuR to CTSS 3′UTR (P < 0.05 for all). The importance of RNA editing in vascular system was further highlighted in mice by a retinal angiogenesis defect after postnatal endothelial cell ADAR1 ablation. In adult mice, deletion of ADAR1 in endothelial cells leads to a lethal phenotype.

Conclusion: This study is the first to assign a vascular function to ADAR1 and RNA editing, and it may serve as a prototypical example for the evaluation of RNA-based mechanisms in patients with cardiovascular disease.

2343 | BENCH
Disruption of components of VEGF angiogenic signaling system in metabolic syndrome: Findings from a study conducted in rural Bangladeshi women

A. Rahman1, S. Jesmin2, S. Farzana3, S. Ahmed4, M.M. Islam5, S.N. Sultana6, O.F.S. Hossain1, A.K.M.A. Habib1, N. Shimjoo2, S. Kawano7, *K. Stellos1, A. Gatsiou2, R. Boon2, D. John2, S. Uchida4, T. Keller5, W. Chen6, *JW Goethe University, Department of Cardiology and Institute of Cardiovascular Regeneration, Frankfurt am Main, Germany; 2 Goethe University, Institute of Cardiovascular Regeneration, Frankfurt am Main, Germany; 3 JW Goethe University, Department of Cardiology, Frankfurt am Main, Germany; 4 Max Delbrück Center for Molecular Medicine, Laboratory of Functional Genomics and Systems Biology, Berlin, Germany; 5 JW Goethe University, Institute of Organic Chemistry and Chemical Biology, Frankfurt am Main, Germany

Background: Adenosine to inosine (A-to-I) RNA editing is catalysed by ADARs (adenosine deaminases acting on RNA) and is an important posttranscriptional regulator of RNA metabolism. Its role though in cardiovascular system remains unknown. The goal of the present study was to evaluate the role of RNA editing in human endothelial cells in vitro and in patients with coronary artery disease. Further, we addressed the role of ADAR1 in vascular development and homeostasis in mice.

Methods and results: Next generation RNA sequencing of human endothelial cells revealed that ADAR1 is the main RNA editor inducing A-to-I RNA editing events in almost 25% of transcripts, mostly in introns followed by 3′-untranslated regions (3′UTR). Among the highest ADAR1 edited targets was cathepsin S (CTSS), an extracellular matrix degradation enzyme with an established role in cardiovascular disease. RNA editing of CTSS 3′UTR was increased after hypoxia and when evaluating the clinical relevance of our bench findings, we sequenced the transcriptome of peripheral blood mononuclear cells from 4 patients after hypoxia. In order to evaluate the clinical significance of our bench findings, we sequenced the transcriptome of peripheral blood mononuclear cells from 4 patients with stable coronary artery disease and 4 patients with ischemic cardiomyopathy. RNA editing of CTSS 3′UTR was significantly increased in patients with coronary artery disease, as was the expression of CTSS in patients with heart failure, compared to healthy subjects (P < 0.001). Of interest, the extent of RNA editing in single nucleotide positions was strongly associated with cathepsin S mRNA expression (r = 0.8, P < 0.001) in our cohort. In order to investigate the underlying mechanism, we studied the role of ADAR1 in CTSS mRNA expression. Silencing of ADAR1 profoundly reduced RNA editing of the 3′UTR of CTSS mRNA and inhibited CTSS mRNA and protein expression by 60% (P < 0.001 for all). In a similar manner, ADAR1 regulated endothelial cell CTSS mRNA expression under hypoxic or inflammatory conditions. Mechanistically, RNA editing alters CTSS mRNA secondary structure and stability by regulating the binding of the stabilizing RNA-binding protein HuR to CTSS 3′UTR (P < 0.05 for all). The importance of RNA editing in vascular system was further highlighted in mice by a retinal angiogenesis defect after postnatal endothelial cell ADAR1 ablation. In adult mice, deletion of ADAR1 in endothelial cells leads to a lethal phenotype.

Conclusion: This study is the first to assign a vascular function to ADAR1 and RNA editing, and it may serve as a prototypical example for the evaluation of RNA-based mechanisms in patients with cardiovascular disease.

P2344 | BEDSIDE
12-lead resting electrocardiogram reveals high-risk sources of cardioembolism in young adult stroke patients

J.R.R. Pirinen1, J. Putaala1, A.L. Arko2, I. Surakka3, A. Haapaniemi4, M. Kaste5, E. Haapaniemi6, T. Tatlisumak7, M. Lehto8, *J. Ryhanen9, 1 Helsinki University Central Hospital, Department of Neurology, Helsinki, Finland; 2 Helsinki University Central Hospital, Department of Neurology, Helsinki, Finland; 3 Helsinki University Central Hospital, Department of Neurology, Helsinki, Finland; 4 Institute for Molecular Medicine Finland (FIMM), Helsinki, Finland

Background: Approximately 1.3 million patients aged 15–49 worldwide annually suffer from ischemic stroke. To our knowledge, there are no prior systematic studies on ECG in young stroke patients.

Purpose: Diagnostic work-up in a young ischemic stroke patient is challenging and resource-demanding. A special interest focuses on cardioembolism from a high-risk source, since this subtype is associated with a high early stroke recurrence and mortality. Therefore, we aimed to investigate the accuracy of plasma VEGF in MetS.

Methods: Helsinki Young Stroke Registry included ischemic stroke patients aged 15 to 49 years admitted to two hospital centers in Bangkok, Thailand, between 2003 and 2007. Of our 690 patients, 438 (63%) were male and 252 (37%) female. Atrial fibrillation (AF) was the ECG rhythm in 18 patients, 16 of whom were male. AF was only seen in the highest age groups. After AF (OR 307.1, 95% CI 33.6–2810.7), PT (terminal negative part of the P-wave having an amplitude deeper than −0.1 mm and a duration of at least 40 ms) was the ECG finding with the
strongest association with cardioembolism from a high-risk source (51.8, 12.5-214.7). A total of 27 patients had PTF, 20 of whom fell into the group of cardioembolism from a high-risk source, and 26% of the patients in this group had PTF. Furthermore, PTF was rare in patients with other etiologies. Other significant ECG findings were T-wave inversions (5.5, 2.8-10.9), a wider QRS complex (1.04, 1.02-1.06 ms), a longer corrected QT-time (1.02, 1.00-1.03 ms) and wider angle between the frontal axes of the QRS complex and the T-wave (1.02, 1.01-1.03 degree).

Conclusion: Routine 12-lead ECG provides useful information in directing the diagnostic work-up of a young stroke patient. In addition to AF, particularly PTF had statistically strong association with final etiology of cardioembolism from a high-risk source.

P2347 | BEDSIDE
Dabigatran and rivaroxaban versus warfarin in patients with high risk of stroke and embolism undergoing electrical cardioversion with persistent and long-acting atrial fibrillation
O. Kalejs1, A. Strelnieks2, M. Kovalova2, I. Sime3, M. Vikmane1, S. Sakne1, I. Cigojeva1, M. Zubunovs1, A. Lejnieks1, A. Erglis1, 1J. Stradins University Hospital, Latvian Center of Cardiology, Riga, Latvia; 2Riga East University Hospital, Riga, Latvia; 3Liepaja Regional hospital, Liepaja, Latvia

Background: The most important factor for efficacy and safety for patients with atrial fibrillation (AF) undergoing electrical cardioversion (ECV) is appropriate use of oral anticoagulant (OAC) therapy. Novel anticoagulants (NOAC) are a possible alternative to warfarin and other ECV in all pts with CHA2DS2VASc score ≥2

Methods: We have analysed the data collected before and after ECV in 1742 patients (pts) undergoing ECV. All pts had AF, 1313 persistent and 429 defined as long-lasting, CHA2DS2VASc score was 3.6±1.9, 1224 had one or two ECV procedures (n=214, 1.02-1.06 ms) and 393 were treated with dabigatran 110 mg twice daily or 312 pts 110 mg twiced daily before ECV for at least 21 days. 622 (35.6%) started warfarin therapy and 21 days start after INR was twice or 312 pts 110 mg twice or 393 rivaroxaban 20 mg daily before ECV. Patients undergoing NOAC’s have shorter time before ECV was successful after first shock in 1602 (92%) pts, total success ECV 1709 (98.1%) pts. LA thrombi were detected on TEE before ECV in 36 pts in NOAC group and 32 pts in warfarin group, so, pts continued OAC therapy for two months, and TEE had been performed again. 10 pts in dabigatran (150 mg twice), 8 pts in rivaroxaban (20 mg od) group and 7 pts in warfarin group were free of thrombus and have been referred to ECV. Average time before ECV was significantly lower for NOAC (25 days) vs warfarin (48 days, p<0.01). Stroke and systemic embolism rates at 90 days were lower in NOAC group (0.1%) vs warfarin group (1.5%), but the event in NOAC group was documented after discontinuation of the drug while 10 warfarin events were detected under the time of use of OAC. There was no difference in analysis of events between TEE and non-TEE pts in dabigatran and rivaroxaban. NOAC pts had significantly lower clinical relevant bleeding rate vs warfarin (D 110 mg 0, D 150 mg 0.47%, R 0.39% vs W 2.87%), confirming development of effective and safe NOAC’s. NOAC pts had significantly lower clinical relevant bleeding rate vs warfarin (D 110 mg 0, D 150 mg 0.47%, R 0.39% vs W 2.87%), confirming development of effective and safe NOAC’s.

Conclusion: Mean waiting time for elective DCCV was significantly shorter for patients on NOACs than on warfarin (35 days vs. 60 days). With the increasing trend in prescribing NOACs, there has been a corresponding reduction in average waiting times which likely leads to improved patient outcomes.

BEST POSTERS IN MYOCARDIAL ISCHEMIA

P2350 | BENCH
Continuous erythropoietin receptor activation reverses increased myocardial susceptibility to ischemia/reperfusion injury in chronic renal failure
K. Nishizawa1, T. Yano1, T. Miki1, M. Tanno1, A. Kuno1, H. Kozu1, T. Tobisawa1, M. Mizuno1, H. Sugawara1, T. Mura1, S. Sapporo Medical University, Department of Cardiovascular, Renal, and Metabolic Medicine, Sapporo, Japan; 2Sapporo Medical University, Department of Pharmacology, Sapporo, Japan

Purpose: Chronic renal failure (CRF) is known to increase myocardial susceptibility to ischemia/reperfusion injury (IRI). The aim of this study is to examine if epoetin beta pegol (continuous erythropoietin receptor activator, CERA) restores dysregulation of protective signaling and myocardial tolerance to ischemia/reperfusion injury in CRF.

Methods and results: The rats underwent 5/6 nephrectomy (subtotal nephrectomy, SNx) or a sham operation (Sham). Intraperitoneal administration of CERA at a dose of 0.6 μg/kg or saline every 7 days. 577 admissions (26%) proceeded to elective DCCV admissions and, more relevantly for patients, longer periods of time spent in atrial fibrillation.

Introduction: Cardiac troponin, particularly with the availability of high sensitivity assays (hs-cTnT and T), is the reference biomarker utilized in the diagnosis of myocardial infarction. Hs-cTnT has absolute specificity for the myocardium but not other organs. Infarct size and immunoreactive troponin T were significantly greater in HS-cTnT than in SNx. CERA significantly reduced the size of infarct but the size of infarct was larger in SNx than in Sham. Expression levels of Mtorc2 components (mTOR, Rictor, Sin1, and Deptor), a kinase complex promoting phosphorylation of Akt at Ser473, was higher in SNx than in Sham. CERA restored Akt-Ser473 phosphorylation in SNx. Conclusions: Continuous erythropoietin receptor activation reverses increased myocardial susceptibility to IR injury in CRF presumably by attenuation of Akt-mediated phosphorylation of Akt-Ser473.

P2351 | BEDSIDE
Use of novel oral anticoagulants results in shorter waiting times for elective DC cardioversion
D. Collison, S. Beecher, R. Walsh, Y. Smyth, J. Crowley. Galway University Hospital, Department of Cardiology, Galway, Ireland

Introduction: ESC guidelines on the management of atrial fibrillation and flutter of >48 hours duration recommend oral anticoagulation (OAC) for at least 3 weeks prior to, and 4 weeks after, direct current cardioversion (DCCV). With warfarin, an INR of 2–3 is recommended and elective DCCV is generally deferred until patients have maintained INR in the therapeutic range for this timeframe. This can result in significant delays for DCCV admissions and, more relevantly for patients, longer periods of time spent in atrial fibrillation.

Aim: To establish if changing trends in novel oral anticoagulant (NOAC) prescriptions reduce waiting times for elective DCCV.

Methods: A review of an electronic database of elective DCCV admissions at our institution was performed. Data included recorded, sex, age, booking date, procedure date, OAC prescribed and procedure outcome.

Results: There were 653 DCCV admissions from 01/01/2010 to 30/09/2014. 205 (31%) represented repeat attendances. 577 admissions (88%) proceeded to elective DCCV and of these, 512 (88%) were successfully cardioverted to sinus rhythm. Age at admission ranged from 27–86 years (mean of 63 years). 509 (78%) of patients were male. On average, female patients attending for DCCV were older than their male counterparts (Mean of 66 vs. 62 years, p<0.001). Warfarin was the prescribed OAC in 470 admissions (72%). Waiting time for admissions on warfarin was significantly longer than those on NOACs (Mean of 60 vs. 35 days, p=0.000). Of the 183 admissions on NOAC, rivaroxaban was the most commonly prescribed (102), followed by dabigatran (68) and apixaban (13). There was no significant difference in the age of patients on warfarin compared to NOAC (Mean 62.66 years vs. 62.93 years) and the trend towards older mean age in female patients was consistent in both groups. The proportion of female patients on warfarin (23.4%) was higher than in those on NOACs (18.58%) however this was not statistically significant (p=0.192). Waiving waiting time to admission reduced annually from 2011 to 2014 (66 days to 37 days). The percentage of admissions on a NOAC increased annually from 2012 to 2014 (3.2% to 72.3%). A patient admitted in the first two months of 2014 was more likely to be prescribed a NOAC than warfarin and comparison to the previous year.

Conclusion: Mean waiting time for elective DCCV was significantly shorter for patients on NOACs than on warfarin (35 days vs. 60 days). With the increasing trend in prescribing NOACs, there has been a corresponding reduction in average waiting times which likely leads to improved patient outcomes.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475 by guest on 07 February 2019
(53 ECG/echo-exercise test; 42 echo-dipyridamole test; 30 echo-dobutamine test).

Results: Plasma concentrations of hs-cTnT increased (≥10%) after stress test in 90/125 cases. Overall, hs-cTnT significantly increased from 17.5±16.92 ng/L before the test to 25.9±27.90 ng/L 6-hrs afterward (p<0.0001), without significant changes of CK-MB. Increments in hs-cTnT were documented after ECG/echo-exercise test (from 15.87±11.9 ng/L to 19.47±13.65 ng/L, p<0.0001), after echo-dipyridamole test (from 17.7±19.12 ng/L to 24.38±35.74 ng/L, p=ns) and after echo-dobutamine test (from 20.63±20.80 ng/L to 37.8±31.07 ng/L, p=0.0006), without significant changes in CK-MB according to each stress type. Out of 125 tests, 84 were negative and 41 positive for myocardial ischemia. Significant increments in hs-cTnT were detected after both negative (from 18.6±21.21 ng/L to 27.11±32.07 ng/L, p<0.0018) and positive stress tests (from 15.2±10.8 to 22.3±16.22, p=0.0005), without significant changes in CK-MB according to the test result.

Conclusions: Plasma concentrations of hs-cTnT increase in the vast majority of patients undergoing a cardiac stress test, irrespective from the result of the test. These data suggest that plasma release of hs-cTnT is caused not only by myocardial necrosis but also by other mechanisms, such as reversible ischemia and myocardial stretching secondary to increased heart rate and inotropism.

P2352 | BEDSIDE
Long term outcome following remote ischemic postconditioning during percutaneous coronary interventions
S. Lavi, N. Abu-Romeh, S. Wall, M. Alemayehu, R. Lavi. London Health Sciences Centre, London, Canada

Background: Remote ischemic conditioning reduces infarct size in animal models, but its clinical value and mode of administration is controversial.

Purpose: Assess the long-term effect of remote ischemic postconditioning (RIPost) among patients undergoing percutaneous coronary intervention (PCI).

Methods: We randomized 360 patients undergoing PCI who presented with negative Troponin T at baseline into 3 groups: two groups received RIPost (induced to arm or thigh) and a third, a control. RIPost was applied during PCI immediately following stent deployment, by three 5 minute cycles of blood perfusion (19.0±5.4 versus 0.9±0.3 U/g, P<0.01). Of note, the onset of ischemic contracture, which indicates the initiation of ATP depletion in myocardium, was earlier with phlorizin. Consistent with this finding, a significant reduction in tissue ATP content as well as glucose uptake and lactate output (indicating glycolytic flux) was observed in the phlorizin-perfused hearts.

Conclusions: Cardiac SGLTs, possibly SGLT1 in particular, represent an important protective mechanism against IRI by replenishing ATP stores in ischemic cardiac tissues via enhanced glucose availability. The present findings provide new insight into the essential role of SGLTs in optimizing cardiac energy metabolism, at least during the acute phase of IRI.

P2353 | BENCH
Expression of SGLT1 in human hearts and impairment of cardiac energy metabolism by phlorizin during ischemia-reperfusion injury in mice
Y. Kashiwagi1, T. Nagoshi1, T. Tsuchiya1, T. Tanaka1, K. Ito1, T. Harada1, H. Takahashi2, M. Iwagami3, R. Anzawa1, M. Yoshimura2, J. Iwaki University School of Medicine (Tokyo), Division of Cardiology, Department of Internal Medicine, Tokyo, Japan; 2 Jikei University School of Medicine (Tokyo), Department of Pathology, Tokyo, Japan

Purpose: Sodium-glucose cotransporter 1 (SGLT1) is thought to be expressed in the heart as the dominant isoform of cardiac SGLT, although more information is required to delineate its subtypes in human hearts. Moreover, the functional role of SGLTs in its importance to be fully elucidated. We herein investigated whether SGLT1 is expressed in human hearts and whether SGLTs significantly contribute to cardiac energy metabolism during ischemia-reperfusion injury (IRI) via enhanced glucose utilization in mice.

Methods and results: We determined that SGLT1 was highly expressed in both human autopsyed hearts and murine perfused hearts, as assessed by immunostaining and immunoblotting with membrane fractionation. To test the functional significance of the substantial expression of SGLTs in the heart, we studied the effects of a non-selective SGLT inhibitor, phlorizin, on the baseline cardiac function and its response to IRI using the murine Langendorff model. Although phlorizin perfusion did not affect baseline cardiac function, its administration during IRI significantly impaired the recovery in left ventricular contractions (%recovery of baseline; 67.3±4.5 versus 89.7±6.5, n=5 each, P<0.05) and rate pressure product, associated with an increased infarct size, as demonstrated by TTC staining (%MI; 22.1±2.7 versus 11.1±1.3%, P<0.01) and CKP activity released into the perfusate (19.0±5.4 versus 9.0±3.3 U/g, P<0.01). Of note, the onset of ischemic contracture, which indicates the initiation of ATP depletion in myocardium, was earlier with phlorizin. Consistent with this finding, a significant reduction in tissue ATP content as well as glucose uptake and lactate output (indicating glycolytic flux) was observed in the phlorizin-perfused hearts.

Conclusions: Cardiac SGLTs, possibly SGLT1 in particular, represent an important protective mechanism against IRI by replenishing ATP stores in ischemic cardiac tissues via enhanced glucose availability. The present findings provide new insight into the essential role of SGLTs in optimizing cardiac energy metabolism, at least during the acute phase of IRI.

BEST POSTERS IN CARDIOVASCULAR MAGNETIC RESONANCE
P2355 | BEDSIDE
Left ventricular global function index and left ventricular mass volume ratio by CMR: association with heart failure in thalassemia major patients
A. Meloros1, V. Positano1, C. Tudisco2, E. Chiodo3, A. Vallone4, M. G. Neri5, G. Palazzi5, D. Maddaloni6, P. Keilberg1, A. Pepe1, F. Forzani G. Monasterio CNR-Regionale Toscana, CMR Unit, Pisa, Italy; 2 Policlinico Paolo Giaccone, Istituto di Radiologia, Palermo, Italy; 3 Arcispedale Sant’Anna, Radiologia Ospedaliera-Universitaria, Ferrara, Italy; 4 Az. Osp. Garbatella, Presidio Ospedaliero Nemesia, Istituto di Radiologia, Catania, Italy; 5 Policlinico di Modena, Oncologia Medica, Modena, Italy; 6 Osp. ‘Englesi Profili’, Dip. Materno/Infantile, Fabriano (AN), Italy

Introduction: Recently two novels indicators of left ventricular (LV) performance assessed by Cardiovascular Magnetic Resonance (CMR) have been introduced: the LV global function index (LVGFI) and the LV mass/volume ratio (LVMMVR). The LVGFI combines LV stroke volume, end-systolic and end diastolic volumes, as well as LV mass, integrating structural as well as mechanical behaviour. Elevated LVMMVR is indicative of concentric remodelling. A LVGFI <37% and a LVMMVR>1 were shown to be associated with the occurrence of cardiovascular events in no-thalassemic populations.

Purpose: This retrospective cohort study aimed to systematically evaluate in a large historical cohort of thalassemia major (TM) in the CMR era whether the LVGFI and the LVMMVR were associated with a higher risk of heart failure.

Methods: We considered 812 TM patients (391 M, 30±8.6 years), consecutively enrolled in the Myocardial Iron Overload in Thalassemia (MIOT) network. LVGFI and LVMMVR were quantitatively evaluated by SSFP cine images. The T2* value in all the 16 cardiac segments was evaluated and a global heart T2* value was calculated. LVMVR is indicative of concentric remodeling. A LVGFI <37% and a LVMMVR>1 were shown to be associated with the occurrence of cardiovascular events in no-thalassemic populations.

Purpose: To systematically evaluate in a large historical cohort of thalassemia major (TM) in the CMR era whether the LVGFI and the LVMMVR were associated with a higher risk of heart failure.

Conclusion: Our study included 812 TM patients (391 M, 30±8.6 years), consecutively enrolled in the Myocardial Iron Overload in Thalassemia (MIOT) network.

LVGFI and LVMMVR were quantitatively evaluated by SSFP cine images. The T2* value in all the 16 cardiac segments was evaluated and a global heart T2* value was calculated. LVGFI <37% and LVMMVR>1 were shown to be associated with the occurrence of cardiovascular events in no-thalassemic populations.

Conclusion: Our study included 812 TM patients (391 M, 30±8.6 years), consecutively enrolled in the Myocardial Iron Overload in Thalassemia (MIOT) network.

LVGFI and LVMMVR were quantitatively evaluated by SSFP cine images. The T2* value in all the 16 cardiac segments was evaluated and a global heart T2* value was calculated. LVGFI <37% and LVMMVR>1 were shown to be associated with the occurrence of cardiovascular events in no-thalassemic populations.

Conclusion: Our study included 812 TM patients (391 M, 30±8.6 years), consecutively enrolled in the Myocardial Iron Overload in Thalassemia (MIOT) network.

LVGFI and LVMMVR were quantitatively evaluated by SSFP cine images. The T2* value in all the 16 cardiac segments was evaluated and a global heart T2* value was calculated. LVGFI <37% and LVMMVR>1 were shown to be associated with the occurrence of cardiovascular events in no-thalassemic populations.
P2356 | BEDSIDE
Troponin positive patients with unobstructed coronaries: incremental value of cardiovascular magnetic resonance
B. Raman1, B. Pathik1, N. Amin1, D. Mahadevan2, S. Rajendran3, S. Khurana4, J. Mazhar5, C. Bridgman1, A. Ganesan3, J.B. Selvanayagam1.

Background: Troponin positive chest pain patients with unobstructed coronaries are frequent in clinical practice. Cardiovascular magnetic resonance imaging (CMR) has an increasingly prominent role in the assessment of these patients, however its utility in comparison to expert clinical judgement has not been assessed. Furthermore, diagnostic accuracy of CMR in this population is unknown.

Purpose: We therefore sought to 1. Determine the heterogeneity in diagnoses amongst by experienced cardiologists when presented with blinded clinical and investigative data (without CMR) in this patient group. 2. Establish the degree of concordance between clinical panel and CMR diagnoses. 3. Demonstrate the incremental diagnostic and prognostic value of CMR.

Methods: 125 consecutive patients presenting to a tertiary centre between 2010 and 2014 with cardiac chest pain, elevated troponin (>29ng/L) and unobstructed coronaries were enrolled into the study and underwent CMR. The only exclusion criteria was the presence of CMR contraindications. A panel of three experienced (>5 years) consultant cardiologists unaware of the CMR diagnosis and blinded to each other’s assessment, each provided a clinical diagnosis based on clinical, biochemical, ECG, echocardiographic and angiographic findings. A consensus panel diagnosis was defined as two or more cardiologists sharing the same clinical diagnosis. Findings were classified into: Acute myocarditis, Takotsubo Cardiomyopathy, Non-ST elevation myocardial infarction (NSTEMI) or indeterminant.

Results: Median troponin value was 500ng/L (IQR 183,840). Consensus panel diagnosed 58 patients as CMR negative with no cardiac event in 67/125 (53%) patients. There was only moderate level of agreement between the three cardiologists (k=0.466, p<0.01) and a poor level of agreement between the consensus panel and CMR (k=0.38, p<0.01) with the most disagreement seen in patients with NSTEMI diagnosed on CMR. CMR provided a diagnosis in 87% of patients. A low incidence of major cardiovascular events was observed over a median follow up of 3.5 years.

Conclusions: 1. Clinical diagnosis of patients with non-obstructive coronaries and positive troponin remains a significant challenge. 2. CMR provides a diagnosis in majority of these patients. 3. Although concordance between CMR diagnosis and clinical diagnosis without CMR is poor, the overall incidence of major adverse cardiovascular events in these patients is low.

P2357 | BEDSIDE
White-matter-lesions as detected by 3 Tesla MRI imaging of the brain demonstrate a high association with subclinical coronary artery calcification
H. Himpen1, S. Caspers2, A.-A. Mahabadi1, N. Punth1, U. Roggenbuck1, K. Amunts2, K. Zilles2, S. Moebius1, K.-H. Joeneckel1, R. Erbel1 on behalf of Heinz Nixdorf Recall Study Investigative Group. 1University Clinic Essen, Cardiology Department, Essen, Germany; 2 Institute of Neuroscience and Medicine (INM) Research Centre Jülich, Jülich, Germany; 4 Institute of Medical Informatics, Biometry and Epidemiology, University of Duisburg-Essen, Essen, Germany; 4 Institute of Neuroscience and Medicine (INM), Research Centre Jülich, Jülich, Germany; Department of Psychiatry, Psychotherapy and Psychosomatics, RWTH University Aachen, Aachen, Germany.

Background: White-matter-lesions (WML) are a type of small vessel diseases. They are a common finding in MRI scans of the brains of elderly subjects and are suggested to be associated with brain degeneration.

Purpose: We investigated the association of WML volume with risk factors and coronary artery calcification (CAC).

Methods: Participants were drawn from the population based Heinz Nixdorf Recall study, analyzed in the 1000BRAINS study. A subsample underwent 3 Tesla MRI-imaging (FLAIR, T1-MPRAGE). Location and extent of WML were independently evaluated by 2 raters according to the qualitative Fazekas scale. WML volumes were calculated using the Analysis Segmentation Tool (LAST) for the software tool SPMM as implemented in Matlab.

Results: We included 389 individuals (61±7 years, 51% men) without known cardiovascular disease. WML were detected in all subjects. Median WML volume was 12.1 ml in men and 7.4 ml in women. Most lesions were found periventricularly and in the parietal and frontal lobes. WML was associated with age, male gender, total cholesterol, blood pressure, BMI and diabetes mellitus in univariate regression analysis. In multivariate analysis, associations remained for all risk factors except for BMI (table 1). In univariate regression analysis, we observed a strong association of WML volume (ln) with CAC-Score (lnCAC+1) (1.165 (0.91–1.4), p<0.001), which persisted after adjustment for risk factors (0.598 (0.3–0.989), p<0.001, R2=0.31).

Conclusion: WML are associated with traditional cardiovascular risk factors and CAC-score. Our results suggest that the degree of subclinical atherosclerosis may predict WML volume a few years later.

P2358 | SPOTLIGHT
Stress-cardiac magnetic resonance imaging myocardial perfusion in chronic total occlusion patients
A. Obdeninsky, V. Kurbatov, E. Kreto, E. Pokushtov. State Research Institute of Circulation Pathology, Novosibirsk, Russian Federation.

Aim: Numerous studies have shown that CMR with adenosine stress and delayed enhancement are highly sensitive and specific for myocardium perfusion evaluation. Aim of our study to detect the dynamics of myocardial viability using stress-CMR in patients with chronic total occlusion before and after PCI.

Methods and results: We present the results of prospective randomized trial of stress-CMR in isolated Right Coronary Artery Chronic Total Occlusion patients. Seventy two RCA CTO patients were randomized in two groups. In group 1 (39 patients) endovascular recanalization of RCA CTO was performed, group 2 (33 patients) received standard medical treatment. All of them had stress-CMR before and 12-month period after PCI. The endpoint was any new area of myocardial ischemia according to MRI data (defect of perfusion ≥2 segments). All participants were evaluated as a myocardial ischemia high risk patients (≥2 segments affected). In first group, 183 segments of myocardium with perfusion defect were revealed. Average number of segments (mean difference) before PCI was 4.65 (1.45). In second group, 157 segments of myocardium with perfusion defect were revealed. Average number of segments (mean difference) (mean difference) (mean difference) of segments before PCI was 4.75 (1.41). There was no statistically significant difference between the groups, mean difference (group 1 − group 2) −0.06, 95% confidence interval (CI) for difference −0.61 to 0.74, p=0.758. At 2-month follow up on 103 affected segments (56.3% of initial value) in 1st group was marked. Average number (mean difference) of segments was 2.64 (1.61), statistically significant reduction of index (mean difference) −2.05 segments, 95% CI for difference −2.58 to −1.52, p<0.001 was obtained.

Statistically significant reduction of high risk patient (≥2 segments affected) from 39 (100.0%) to 29 (74.4%), p<0.001 was noticed. In second group after 2-month period 152 affected segments (96.8% of initial value) was marked. Average number (mean difference) of segments was 4.61 (3.32), without statistically significant reduction of index (mean difference) −0.15, segments, 95% CI for difference −0.21 to −0.51, p=0.41. Number of high risk patients in 2 group remained constant in comparison with initial value 33 (100.0%). Mean difference (group 1−group 2) −0.06, 95% confidence interval (CI) for difference −2.65 to −1.27, p<0.01.

Conclusion: Recanalisation of CTO RCA statistically significant reduce the risk of myocardium ischemia according to stress-CMR data. Perfusion and myocardial viability represents an important tool for the pre-interventional decision to recalciante CTOs and follow up.

BEST POSTERS IN METABOLISM AND THE HEART

P2360 | BENCH
P21 deficiency is protective against high fat diet-induced metabolic disturbances and myocardial dysfunction

Background: Abnormal expression of tumor suppressor p53 contributes to age-associated cardiovascular and metabolic (MB) diseases. Deficiency of p53 powerfully protects against MB disturbances and cardiac dysfunction in diabetic model. However, this is of limited clinical relevance because of p53’s eminent tumor suppressive role. p21 is a p53 downstream target without any tumorigenesis role. We aimed to explore whether p21 deficiency confers protection against obesity-induced glucose intolerance and myocardial dysfunction in a murine high-fat diet (HFD) model.

Methods: p21−/− (WT, C57BL/6, n=8) and p21−/− mice (p21KO, n=9) underwent HFD (60% fat, 7% sucrose) for 16 weeks. Metabolic profiles were evaluated every 5 weeks by glucose and insulin tolerance tests (GTT & ITT, respectively). Body weight (BW) was monitored every 2 weeks and left ventricular ejection fraction (LVEF) was measured by echocardiography every 5 weeks.

Results: After initial increase in BW, p21KO stopped gaining weight at 6 weeks whereas WT continued to gain weight as compared to baseline values (figure 1). With HFD, metabolic profiles (GTT & ITT, respectively) progressively deteriorated in WT but not in p21KO mice. This protection against HFD-induced insulin resistance in p21KO mice occurred regardless of BW. Myocardial function progressively declined in WT but not in p21KO (LVEF: 65±2% vs 89±1%; p<0.05).

Conclusions: p21 deficiency carries a remarkable potential to protect from
P2361 | BENCH
The SR influences mitochondrial ATP production via IP3 mediated Ca release
L.K. Seidmayer, J. Kuhn, O. Ritter. University Hospital of Wurzburg, Wurzburg, Germany

Background: The mechanisms in cardiac myocytes to distinguish between general Ca release for contract and local Ca signaling e.g. for metabolic adaptation still need to be elucidated.

Hypothesis: Mitochondrial Ca uptake is influenced by IP3-mediated Ca release from the SR. Through this mechanism myocytes are able to adapt mitochondrial membrane potential and ATP demand of the cell.

Methods: Isolated adult mice ventricular myocytes were examined using confocal microscopy. X-Rhod was used for Ca measurements, mitochondrial membrane potential (ΔΨm) and ROS were measured using TMRM and mitoSOX, respectively. ATP concentration was measured indirectly using mag fluo-4 and directly using a luciferase assay.

Results: The stimulation of myocytes with the IP3 agonist endothelin-1 (ET-1, 10 nM) resulted in a strong increase of mitochondrial Ca by +29±13% after 20 min (n=27, p<0.01). The observed increase could be blocked completely by the IP3R antagonist 2-APB as well as in functional IP3 i.o. mice. Following mitochondrial Ca uptake, the mitochondrial membrane potential depolarized by 51±14% (20 min, n=9). Interestingly an effect on ROS production could not be seen within the first 20 min (+15%, n=8).

As a consequence of the cellular stimulation with IP3 agonists, the mitochondrial ATP production, measured indirectly by using the dye mag fluo-4, was increased significantly by 25±2% (n=9). ATP production was markedly decreased in the presence of 2-APB.

Interestingly, the stimulation of mitochondria with the beta agonist isoproterenol (iso) resulted in a faster and smaller mitochondrial Ca uptake which reached its maximum of 15±14% at 15 min (n=10). Furthermore, iso stimulation did not alter after the mitochondrial ATP concentration.

This implies two different underlying mechanisms. To explore the underlying molecular mechanisms we blocked the mitochondrial Ca uniporter (mCU) using Ru360. This did not influence mitochondrial Ca uptake following cellular stimulation with ET-1 (+31±7% after 20 min, n=11) but prevented iso induced mitochondrial Ca uptake (+12±2%, n=8). In contrast, when blocking the mitochondrialryanodine receptor (mRyR1) using dantrolene, the mitochondrial Ca uptake following ET-1 stimulation was significantly blunted (+20±4%, n=13) whereas iso mediated Ca uptake was not affected (+16±3%, n=9).

Conclusion: IP3 mediated Ca release from the SR results in mitochondrial Ca uptake via the mRyR1. This Ca uptake is followed by an increase in mitochondrial ATP production. So, here we elucidated a new pathway which enables the myocyte to adapt mitochondrial ATP production to the actual needs of the cell.

P2362 | BENCH
TIMP3 acts through apelin to maintain cardiac metabolic flexibility
R. Stoehr1, B.A. Kappel1, M. Cavaleria1, M. Mavilio1, R. Menghini1, I. Arisi2, N. Marx2, M. Federici1. 1Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy; 2European Brain Research Institute, Genomics Facility, Rome, Italy; 3RWTH University Hospital Aachen, Internal Medicine I, Cardiology, Pulmonology & Vascular Medicine, Aachen, Germany

Purpose: Tissue inhibitor of Metalloproteinase 3 (TIMP3) is an extracellular matrix bound protein, downregulated in human subjects with metabolic and inflammatory disorders. We have previously shown that loss of TIMP3 on the ApoE−/− background exacerbates atherosclerosis and leads to early mortality coupled to intracellular lipid deposition within the myocardium in mice. The aim of this study was to assess the impact of the loss of TIMP3 on cardiac lipid metabolism.

Methods: To assess myocardial metabolic regulation and lipid deposition we performed histological analysis, western blotting and RT-PCR in ApoE−/− and ApoE−/− TIMP3−/− mice. To gain further insight into total heart mRNA regulation we performed whole heart mRNA transcriptionic analysis in ApoE−/− TIMP3−/− and ApoE−/− littermates (n=5 per group). After revealing that expression of the peptide Apelin was reduced in hearts of ApoE−/− TIMP3−/− mice, we supplemented Apelin for 2 weeks.

Results: At the myocardial level, we found histological signs of lipotoxicity including lipid accumulation. RT-PCR revealed a reduction in genes encoding for lipid oxidation (PPARα, ACDVL1, ACDVL2) while western blotting showed reduced phosphorylation of AMPK and a reduction in PPARα in fasted mice. Together this suggests impaired beta-oxidation of cardiacmyocytes. Metabolic cage experiments confirmed that ApoE−/− TIMP3−/− mice rely on glucose as their main energy source during starvation.

Conclusion: Generation whole heart mRNA sequencing, we identified Apelin as being significantly downregulated in the hearts of ApoE−/− TIMP3−/− mice. This downregulation was confirmed by RT-PCR only in myocardial tissue (0.87±0.07 vs. 0.54±0.10 AU, n=5, p<0.05) but not in adipose tissue, liver and muscle. Additionally, apelin blood levels were significantly lower in ApoE−/− TIMP3−/− mice (692±308 vs. 3625±268 pg/ml, n=4, p=0.0002).

Supplementation of Apelin in ApoE−/− TIMP3−/− mice over a period of 2 weeks increased PPARα (2.4±0.1 vs. 1.7±0.1 AU, n=5, p<0.05) and pAMPK (1.3±0.2 vs. 0.75±0.1 AU, n=5, p<0.05) protein levels in the heart, thus rescuing some of the metabolic defects.

Conclusion: Apelin has recently been shown to rescue defects in insulin resistance and fatty acid oxidation in adipose tissue. Our data suggests that TIMP3 may positively affect Apelin levels within the myocardium potentially in contribution to maintain metabolic flexibility of the heart through regulation of PPARα/AMPK signaling, especially in the fasted state.

P2363 | BENCH
Identification of a glucose sensor in the heart
A. Van Steenbergen1, M. Balteau1, H. Koepsell2, G. Muccioli3, J.L. Vanoverschelde1, L. Huel1, S. Hornan1, L. Bertrand1, C. Beauloye1. 1Institute of Experimental and Clinical Research (IREC), Brussels, Belgium; 2University of Wurzburg, Institute of Anatomy and Cell Biology; Würzburg, Germany; 3Louvain Drug Research Institute (LDRRI), Brussels, Belgium

Background: In the heart, hyperglycemia (HG) stimulates reactive oxygen species (ROS) production through NOX2 activation. We previously demonstrated that NOX2 activation is independent of glucose metabolism but requires a sodium-glucose transporter (SGLT). Seven isoforms of SGLT (SGLT1 to 5 and SMIT1/2) have been described although their expression and function in heart remains elusive. Our working hypothesis is that one of SGLTs confers to the cardiomyocyte the ability to detect increased glucose concentration and acts as a glucose sensor.

Purpose: The aim of this work is to investigate the expression of SGLTs in heart and to identify the isoform responsible for hyperglycemia-induced NOX2 activation.

Methods: We systematically investigated the expression of SGLT isoforms in human and rat heart and human ex-vivo and in cardiomyocytes. NOX2 activation was evaluated, based on their substrate affinity (galactose transported by SGLT1, DODG by SGLT3 and myo-inositol by SMIT1). Genetic demonstration was performed in SGLT1−/− cardiomyocytes and after adenoviral SMIT1 overexpression in cardiomyocytes. NOX2 activation was assessed by measuring p47phox translocation to the plasma membrane and ROS production.

Results: SGLT1 and SMIT1 were expressed in mice and rat hearts as well as isolated cardiomyocytes. SGLT3b corresponding to the human SGLT3 was marginal. SGLT2, SGLT5 and SMIT2 were not detected. SGLT4 was only expressed in rat heart. The human heart expressed SGLT1 and SMIT1. Under HG background, incubation of adult rat cardiomyocytes with 16mM galactose or 1DOD did not activate NOX2. By contrast, addition of 16mM myo-inositol completely repro-duced toxic effects of HG (21mM glucose), favoring NOX2 activation and ROS production. Myo-inositol-induced NOX2 activation resulted from increased diacylglycerol and PKCζ2 activation, similar to that observed with HG. The absence of SGLT1 didn’t prevent HG to activate NOX2. Isolated cardiomyocytes from SGLT1−/− mice exhibited a similar glucose response, compared to SGLT1+/+ cells. Adenoviral SMIT1 overexpression in rat cardiomyocytes sensitized cardiomyocytes towards glucose and exacerbates glucotoxicity. Under this condition, NOX2 activation and subsequent ROS production were more than doubled at 10mM glucose, being nearly maximal (which was normally observed at 21 mM glucose).

Conclusion: Adult cardiomyocytes express SGLT1 and SMIT1. SMIT1 but not SGLT1 senses an increase in glycerol, inducing NOX2 activation. This work strongly supports that SMIT1 acts as a glucose sensor in the heart.

BEST POSTERS IN PULMONARY HYPERTENSION TREATMENT STRATEGIES

P2005 | BEDSIDE
Effect of sitelopan on long-term outcomes in patients with pulmonary arterial hypertension (PAH) receiving one, two or no PAH therapies at baseline: results from the GRIPHON study
I. Lang1, S. Gaine2, N. Galiè3, H.A. Ghofrani4, F.O. Le Brun5, V. McLaughlin6, L.J. Rubin7, G. Simonneau8, O. Sitbon8, M.M. Hoeper9 on behalf of GRIPHON Steering Committee. 1Medical University of Vienna, Dept of Internal Medicine II, Division of Cardiology, Allgemeines Krankenhaus, Vienna, Austria; 2Mater Misericordiae University Hospital, National Pulmonary Hypertension Unit, Dublin, Ireland; 3University of Bologna, Istituto di Malattie dell’Apparato Cardiovascolare, Bologna, Italy; 4University of Giessen and Marburg Lung Center (UGMLC),
Background: Selexipag is an orally available, selective IP receptor agonist target for pulmonary arterial hypertension. In the Phase III GRIFFON study, selexipag significantly reduced the risk of morbidity/mortality events (primary endpoint) up to the end of treatment vs placebo by 40% (hazard ratio [HR] 0.60; 99% CI: 0.46, 0.78; log-rank p<0.0001) in patients with PAH.

Methods: PAH patients (aged 18–75 years) were randomized 1:1 to placebo or selexipag. HRs (99% CI) were calculated using Cox regression models to determine the effect of selexipag vs placebo on morbidity/mortality events in subgroups of patients according to PAH therapy at baseline: 1) no PAH therapy; 2) endothelin receptor antagonist (ERA) monotherapy; 3) phosphodiesterase 5 inhibitor (PDE5i) monotherapy; 4) ERA and PDE5i combination therapy. Consistency of treatment effect across these subgroups was assessed using interaction tests.

Results: At baseline, of the 1156 enrolled patients, 236 (20.4%) were not receiving PAH therapy, 170 (14.7%) were receiving ERA monotherapy, 374 (32.4%) were receiving PDE5i monotherapy and 376 (32.5%) were receiving ERA and PDE5i combination therapy. Baseline characteristics were balanced between treatment arms within each subgroup. The HRs (99% CI) for the primary endpoint, for the comparison selexipag vs placebo in the subgroups were: 1) no PAH therapy at baseline: 0.57 (0.32, 1.03); 2) ERA monotherapy at baseline: 0.66 (0.32, 1.40); 3) PDE5i monotherapy at baseline: 0.58 (0.37, 0.91); 4) ERA and PDE5i combination therapy at baseline: 0.63 (0.39, 1.01). There was consistency in the treatment effect across the subgroups (tests for interactions indicated no heterogeneity; p=0.9518). Common adverse events (AEs) observed with selexipag were significantly greater in CR group than in non-CR group (+10.5±9.8 vs. +1.2±9.6%; p<0.05). Cardiac index increased from 4.5±1.3 L/min/m² to 5.3±1.8 L/min/m² in CR group whereas it increased only from 4.3±1.5 L/min/m² to 4.4±1.6 L/min/m² in non-CR group (p<0.05).

Conclusions: Selexipag is an effective and well-tolerated treatment for PAH patients with significant risk of morbidity/mortality events during follow-up. Although side effects were more frequent in CR group, the treatment effect was maintained in both groups. Thus, selexipag may be considered as a new option for PAH therapy.
functional class all significantly improved in CR group after 12-week CR, but not in non-CR group, with the concomitant increase in quadriceps isometric strength (all $P<0.05$). Importantly, any patients in CR group did not experience adverse events nor deterioration in haemodynamics (mean pulmonary arterial pressure, $25\pm4$ vs. $25\pm5$ mmHg) or right-sided heart failure (HF) (brain natriuretic peptide, $37\pm24$ vs. $45\pm60$ pg/mL) compared with non-CR group during follow up.

**Conclusions:** These results suggest that CR is a safe and effective therapy following BPA to ameliorate exercise capacity close to normal level and HF symptoms additionally in patients with inoperable CTEPH, whose haemodynamics has significantly improved after BPA.

**BEST POSTERS IN EFFECTS OF EXERCISE ON THE CARDIOVASCULAR SYSTEM**

**P2370 | BENCH**

**Differential effects of aerobic endurance, interval and strength endurance training on telomerase activity and senescence marker expression in circulating mononuclear cells**

C. Werner$^1$, A. Heckstedt$^2$, J. Zündler$^1$, M. Boehm$^1$, T. Meyer$^2$, U. Laufs$^1$.

1Universitätssklinikum des Saarlandes - Klinik für Innere Medizin III, Homburg, Germany; 2Universität des Saarlandes, Institute for Sport and Preventive Medicine, Saarbrücken, Germany

**Background:** The aim of this prospective, randomized and controlled training study was to investigate the molecular effects of physical training in circulating mononuclear cells and to test whether different training modalities exert differential effects on molecular regulators of cellular aging.

**Methods:** n=69 healthy non-smokers without regular physical activity aged 30-65 years were randomly assigned to a control group (control: no change of inactive lifestyle) or to one of three training interventions: 1) aerobic endurance training (AET, continuous running); 2) high-intensive interval training (IT, 4x4x4 method) or 3) strength endurance training (SET; circle training on 8 devices). Physical performance capacity was determined by cardiopulmonary exercise testing (CPET) on the treadmill at baseline and after the training period. The intervention consisted of 3 training sessions per week (45 min each) for a total duration of 6 months. Isolation of peripheral blood mononuclear cells (MNC) and molecular analyses were performed before the first and after the last training session.

**Results:** Telomerase activity and mRNA expression (real-time PCR) of telomere repeat-binding factor 2 (TRF2) and senescence marker p16 were measured. The training induced an increase of both, submaximal fitness parameters such as running speed on the treadmill at a pulse of 150/min (control: 0.23±0.1; AET: 0.74±0.2; IT: 1.05±0.1; SET: 0.18±0.1 km/h), and peak oxygen uptake (control: −0.21±0.6; AET: 4.74±0.8; IT: 4.22±1.1; SET: 2.44±1.2 ml/kg*min), which was higher in endurance compared to strength training. Quantification of telomerase activity (TRAP assay, compared to HEK cells as positive controls) in MNC revealed a significant 4–5-fold increase in both endurance exercise groups, but not in strength training (A ET vs. pre/post: control 45±6; AET 287±150; IT 225±85; SET −15±2 HEK cell equivalents). Expression of the telomere capping factor TRF2 was increased compared to baseline levels (pre vs.post: control 118±17; AET 59±9; IT 134; SET 348±132) and senescence marker p16 was decreased (pre vs. post: control 104±17; AET 65±17; IT 77±15; SET 54±15) in all three training groups.

**Conclusion:** The study is the first prospective randomized, controlled trial showing that physical training improves telomerase activity and reduces senescence markers in circulating cells. Cellular mediators of “anti-aging” were increased in all three training groups, however the activity of the enzyme telomerase was increased in endurance and in high-intensity interval training but not after strength training.

**P2371 | BEDSIDE**

**Perfect coronary arteries in sportsmen aged 45 years and older: the importance of lifelong exercise and ideal cardiovascular health.**

The MARC study


1Medeber Medical Center, Amersfoort; 2University Medical Center Utrecht, Department of Radiology, Utrecht; 3University Medical Center Utrecht, Julius Centre for Health Sciences and Primary Care, Utrecht; 4University Medical Center Utrecht, Department of Cardiology, Utrecht; 5University Medical Center Utrecht, Utrecht; 6St George's University of London, Cardiac and Vascular Sciences Research Centre, London, United Kingdom

**Background:** Most exercise-related cardiac arrests occur in men aged ≥45 years and are caused by coronary artery disease (CAD). Traditional cardiovascular risk scores and exercise testing do not reliably identify CAD in asymptomatic sportsmen. Lifelong physical activity and “ideal” cardiovascular health are key in preventing cardiovascular events.

**Purpose:** To determine the impact of lifelong exercise and ideal cardiovascular health on the occurrence of CAD in 283 asymptomatic sportsmen ≥45 years with a low ESC SCORE risk.

**Methods:** Coronary CT angiography was performed in asymptomatic sportsmen ≥45 years whose routine sports medical examination, including exercise testing, was normal. Those with a coronary artery calcium score of 0 AU and no plaques on CT angiography were considered to have perfect coronaries. Lifelong exercise was defined as having trained at least 2 hours per week from adolescence onward. Ideal cardiovascular health (CVH) was defined as fulfilling at least 5 out of 7 criteria of the American Heart Association (AHA) task force for survivors of cardiac arrest. A low ESC SCORE risk had perfect coronary arteries. Lifelong exercisers and those with ideal CVH were more likely to have perfect coronary arteries (see table for crude prevalence and adjusted odds ratio’s).

**Conclusion:** Among fit sportsmen ≥45 years with a low ESC SCORE risk, lifelong exercisers with ideal cardiovascular health are most likely to have perfect impact on RFV remains unknown. This observation may help tailor preparticipation screening strategies in senior athletes.

**P2372 | BENCH**

**Comparison of the cardioprotective effects of exercise training at early and late stages of experimental pulmonary arterial hypertension**


1Universidade de Aveiro, Department of Chemistry, Aveiro, Portugal; 2University of Aveiro, Department of Chemistry, Aveiro, Portugal; 3Faculty of Sport from University of Porto, CIAFEL, Porto, Portugal

**Introduction:** Right ventricular failure (RVF) is the most common cause of death in patients with pulmonary arterial hypertension (PAH). Growing evidences suggest that exercise training (ExT) is safe and beneficial for this population but its impact on RVF remains unknown.

**Purpose:** To compare the cardioprotective effects of ExT performed at early or latter stage of experimental PAH.

**Methods:** Male Wistar rats were randomly divided in the following groups: i) sedentary injected with monocrotaline (MCT; 60 mg/kg, sc) or vehicle (SED+MCT and SED+Control); ii) early ExT (4 weeks-exercise training after MCT or vehicle injection; EarlyExT+MCT and EarlyExT+Control) and iii) late ExT (2 weeks-exercise training after 2 weeks of MCT or vehicle injection; LateExT+MCT and LateExT+Control). After ending their respective protocols, animals were submitted to an exercise tolerance test, RV echocardiographic and hemodynamic evaluations. Samples from right ventricle and lungs were collected for histological, protein and RT-PCR analysis.

**Results:** ExT improved exercise tolerance and survival in all MCT-exercised groups. EarlyExT+MCT showed improved cardiac output despite the presence of elevated overload (RV Pmax and PAAT similar to SED+MCT). ExT protected against diastolic dysfunction (EDP and Tau) and prevented RV maladaptive remodeling (normal SERCA2a protein levels, beta/alpha MHC isoform, ET-1 and VEGF mRNA) and cardiac fibrosis and inflammation in both exercise interventions, but greater results were observed in EarlyExT+MCT. In contrast to SED+MCT, MCT-exercised groups also showed preserved activity and lower oxidative damage of the mitochondrial complex V. 

**Conclusion:** ExT improves exercise tolerance and survival, paralleled by improved cardiac function and modulation of cardiac remodeling, reduced neuro-humoral and inflammatory activation, and improved mitochondrial function. Our data suggests that ExT exerts cardioprotective effects, with greater benefits when started at early stages of PAH.

**P2373 | BEDSIDE**

**Screening for cardiac conditions predisposing to sudden cardiac death: the diagnostic yield and financial implications**

H. Dhuita, A. Malhotra, S. Azizi, Z. Vinnicombe, F. Gill, K. Hughes, R. Narain, M. Papadakis, S. Sharma. St George’s University of London, Cardiac and Vascular Sciences Research Centre, London, United Kingdom

**Purpose:** Sudden cardiac death (SCD) in the young is commonly due to heritable cardiomylopathies that can be detected during life. The ESC recommend preparticipation screening (PPS) with history and physical examination (H+P), and electrocardiography (ECG) in young athletes to detect those at risk. Antagonists have questioned the cost effectiveness of such practice and the ethics of confining screening to athletes when most deaths in the young affect non-athletes. This study reports the diagnostic yield and financial implications of detecting potential SCD risk in young individuals in the UK.

**Methods:** Between 2011–2013, 30,542 individuals aged 14–35 years were evaluated by a cardiologist at a cost of €44 per person with H+P and an ECG interpreted in line with 2010 ESC recommendations. On site echocardiography (TTE)
plotted TAV reduction up to unprecedented 79.4 and 60.3 mm² respectively with high level of safety and feasibility. **Methods:** The completed randomized two arm (1:1) study (NANOM-PCI) with parallel assignment (n=62) assessed (NCT01436123) the safety and feasibility of the delivery technique for nanoparticles (NP) using micro-injection catheter (with intravascular intramural injection of allogenious stem cells carrying NP after MSC-, IVUS- and OCT-guided mapping of the vessel), and plasmonicphotothermal therapy of atherosclerosis combined with stenting (Nano group, n=32) versus stenting with Xience V cage (Stenting group, n=30). The primary outcome was TAV at 12 months. **Results:** The mean reduction of TAV at 12 months in Nano group was −84.1 mm² (95% CI: SD 28.3; min −52.4 mm², max −99.1 mm²; p<0.05) versus −12.4 mm² in case of stenting (p<0.05 between groups). 42/62 patients (68%) in Nano group passed the Glagov threshold of a 40% plaque burden with mean plaque burden (PB) 36.2% (95% CI: SD 9.3%, min 30.9%, max 44.5%). We have documented 2 vs 3 cases of the definite thrombosis and 3 vs 5 cases of target lesion revascularization in groups respectively. The analysis of the event-free survival of the ongoing clinical follow-up shows the significantly lower risk of cardiovascular death in Nano group if compare with stenting (93.4% vs 86.7%; p<0.05). No evidences of nanotoxicity were revealed. The cytotoxicity manifested with increased rates on surface of erythrocytes (from 0.34 to 6.12 per cell, p<0.05) within 72 hours after exposure of NP (Fig 1).

**Conclusion:** Plasmonic resonance-mediated therapy using noble-metal NP associated with significant reduction of coronary atherosclerosis below a 40% PB and minimal nanotoxicity.

---

**P2377 | BENCH**

**Nanoenabled rapid endothelialisation of stent-grafts**


1 Mayo Clinic, Cardiovascular Diseases, Rochester, United States of America; 2 Mayo Clinic, Engineering, Rochester, United States of America; 3 University of Durham, Medicine, Pharmacy and Health, Durham, United Kingdom

**Background:** Clinically used synthetic vascular grafts are limited to diameters greater than 5 mm due to thrombosis, restenosis and incomplete endothelialisation. Stent-grafts used for emergency treatment of vascular perforations consist of bulky dual stents with a fabric sandwiched in the middle, and have high rates of reocclusion. Conduits for small caliber peripheral, coronary and neurovascular applications are currently unavailable.

**Purpose:** To demonstrate that a small caliber magnetisable stent-graft incorporating porous polyurethane nanofibers is capable of capturing magnetic nanoparticle labeled endothelial cells, and to confirm complete endothelialisation within 7 days in a porcine model.

**Methods:** Stent-grafts with 3 mm diameter were fabricated by embedding a magnetised 2205 stainless steel stent within 300 μm of electropun polyurethane nanofibers. Porcine blood outgrowth endothelial cells were labeled with superparamagnetic iron oxide nanoparticles (SPIONs) and a fluorescent marker. Stent-grafts were tested in vitro for cell capture. In vivo testing was carried out by deploying a 3.15 mm stent-graft in a porcine coronary artery, following which labeled cells were delivered locally. Endothelialisation was assessed at 7 days.

**Results:** Representative images show a widely patent stent-graft that is free of thrombus. Light microscopy (Fig 1A) and scanning electron microscopy (Fig 1C) demonstrated complete coverage by a neointima (~200 μm thick) along with confluent endothelium. Fluorescence microscopy (Fig 1B) demonstrated the presence of delivered endothelial cells within the neointima.

**Conclusions:** Magnetic endothelialisation may enable the development of small caliber synthetic vascular conduits, thereby enabling additional therapeutic revascularisation options for smaller vessels.

---

**P2376 | BENCH**

**Frontiers of plasmonic photothermal and stem cell therapy of atherosclerosis: nanotoxicity in NANOM-PCI trial**

A. Kharlamov1, J. Gabinsky2, V. Shur2 on behalf of NANOM-PCI. 1 De Haar Research Foundation, Department of Science, Rotterdam, Netherlands; 2 Ural Institute of Cardiology, Yekaterinburg, Russian Federation; 3 Ural Federal University, Modern Nanotechnologies, Yekaterinburg, Russian Federation

**Background:** Our previous bench studies PLASMONICS and NANOM-FIM trial demonstrated TAV reduction up to unprecedented 79.4 and 60.3 mm² respectively with high level of safety and feasibility. **Methods:** The completed randomized two arm (1:1) study (NANOM-PCI) with parallel assignment (n=62) assessed (NCT01436123) the safety and feasibility of the delivery technique for nanoparticles (NP) using micro-injection catheter (with intravascular intramural injection of allogenious stem cells carrying NP after MSC-, IVUS- and OCT-guided mapping of the vessel), and plasmonicphotothermal therapy of atherosclerosis combined with stenting (Nano group, n=32) versus stenting with Xience V cage (Stenting group, n=30). The primary outcome was TAV at 12 months. **Results:** The mean reduction of TAV at 12 months in Nano group was −84.1 mm² (95% CI: SD 28.3; min −52.4 mm², max −99.1 mm²; p<0.05) versus −12.4 mm² in case of stenting (p<0.05 between groups). 42/62 patients (68%) in Nano group passed the Glagov threshold of a 40% plaque burden with mean plaque burden (PB) 36.2% (95% CI: SD 9.3%, min 30.9%, max 44.5%). We have documented 2 vs 3 cases of the definite thrombosis and 3 vs 5 cases of target lesion revascularization in groups respectively. The analysis of the event-free survival of the ongoing clinical follow-up shows the significantly lower risk of cardiovascular death in Nano group if compare with stenting (93.4% vs 86.7%; p<0.05). No evidences of nanotoxicity were revealed. The cytotoxicity manifested with increased rates on surface of erythrocytes (from 0.34 to 6.12 per cell, p<0.05) within 72 hours after exposure of NP (Fig 1).

**Conclusion:** Plasmonic resonance-mediated therapy using noble-metal NP associated with significant reduction of coronary atherosclerosis below a 40% PB and minimal nanotoxicity.

---

**P2377 | BEDSIDE**

**Reduction of radiation exposure with a quality control system and influence of technological progress - comparison of a German coronary angiography and angioplasty registry and single centre data**

A. Albrecht1, B. Levenson1, N. Reifart3, G. Ringwald4, S. Goehring5.

1 Heart Failure, Universitätsklinikum Schleswig-Holstein, Kiel, Germany; 2 Deutscher Herzzentrum, Leipzig, Germany; 3 Main-Taunus-Hospital, Cardiology, Bad Soden, Germany; 4 Friedrichshapal, Cardiology, Bruchsal, Germany; 5 Health Care Consulting, Weinheim, Germany

**Introduction:** Exposure to radiation is of general concern as there is an increasing number of CT scans, procedures in interventional radiology, and interventional cardiology. Whenever possible patients and physicians exposure to radiation should be minimized. The reduction of radiation exposure can be driven by operator experience or technological progress. Can experienced interventionists still improve and reduce radiation when using a system of quality control although cases have become more complex? And which role does technological progress play, as for instance flat panel detectors and image data processing in reducing radiation exposure?

**Methods:** Since 1996 members of the Association of German Cardiologists in
Private Practice collects procedural data of coronary angiographic and interventional procedures (PCI) for quality control receiving a feedback of their data four times a year. Over 1.5 million procedures have been documented over a period of 20 years. We compared the PCI radiation data of a single centre with the values of the whole registry from 2002 to 2013. The radiation dose area product (DAP) was measured as Gy cm², the fluoroscopy time (t) as minutes (min) and the contrast medium (dye) consumption as ml.

**Results:** In a selected centre two cardiologists perform their procedures in the catheterization laboratory continuously for more than 20 years. Each of them has done more than 10,000 coronary angiographies or interventions. In 2012 a new X-ray unit was installed, allowing the assessment of the influence of technological progress. DAP (−32%) of radiation was measured using individual electronic radiation dosimeter badges and higher ones for dye consumption (+13%). The decline of DAP in the whole centre from 2012 to 2013 (from 31 to 22 Gy cm²) reflects the installation of a new X-ray unit, while fluoroscopy time and amount of dye did not change.

**Conclusion:** Even experienced interventionalists can still reduce the amounts of radiation and contrast medium when using a system of quality control, although severity of PCI cases has been increasing over time. Furthermore technological progress can reduce the amounts of radiation exposure but not contrast medium.

**P2378 | BEDSIDE**

**Comparison of right radial, left radial and right femoral approach**


**Background:** Because of a presumably increased incidence of long-term malignancies in interventional cardiologists, radiation exposure of the operator during coronary interventions is of rising concern. A few studies concerning the operator radiation exposure comparing femoral to radial or radial left access have previously been published, but no data comparing the three access sites are available to our knowledge.

**Purpose:** We sought to compare the operator radiation exposure by right femoral (RFA), right radial (RRA) and left radial (LRA) access during percutaneous catheterization for diagnostic coronary angiography (CA) with or without coronary angioplasty (PCI).

**Methods:** From September 2014 to February 2015, all consecutive patients (n=692) undergoing elective or emergency CA +/- PCI, performed at our hospital, Switzerland, were prospectively included. The selection of the percutaneous access site was left to the discretion of the interventional cardiologist. Operator radiation exposure was measured using individual electronic radiation dosimeter badges positioned externally on the sternum. Radioprotection materials and equipment was similar for all procedures. The primary endpoint was operator radiation exposure quantified as cumulative dose (CD) per dose-area product (DAP), in order to adjust for the additional amount of radiation dose.

**Results:** A total of 692 consecutive procedures (386 [56%] CA and 306 [44%] PCI) were performed, of which 380 (55%) were realized via the RFA, 232 (34%) via the RRA and 80 (11%) via the LRA. The cumulative dose of radiation received by the operators in the RFA (6.2±11.8 Sv/Gy cm²) compared to the RRA (26.4±54.1 Sv/Gy cm²), p<0.001) and the LRA (9.9±18.5 Sv/Gy cm², p<0.001). The latter approach showed a significantly lower cumulative dose compared to RRA (p<0.001). There was no difference in the DAP between LRA (34.4±23.7 Gy cm²) and RRA (40.2±28.4 Gy cm², p=0.13). The RFA however demonstrated higher levels (55.2±64.2 Gy cm²) compared to both RRA (p=0.03) and LRA (p<0.01).

The adjusted operator radiation exposure was significantly lower in the RFA (0.17±0.27 Sv/Gy cm²) compared to the RRA (0.62±0.69 Sv/Gy cm², p<0.001) or the LRA group (0.32±0.36 Sv/Gy cm², p<0.001). Operator radiation exposure was lower for the LRA compared to the RRA (p<0.001).

**Conclusions:** The RFA in percutaneous coronary angiography and percutaneous coronary intervention is associated with significantly lower operator radiation exposure when compared to the RRA or LRA. The LRA is associated with significantly lower operator radiation exposure when compared to the RRA.

**BEST POSTERS IN NEUROHORMONES**

**P2380 | BENCH**

**Deletion of osteoprotegerin gene exacerbates cardiac hypertrophy and systolic dysfunction in aged-mice**

T. Tsuruda1, I. Hato1, S. Sakamoto2, S. Kurogi3, N. Udagawa3, M. Nakamura3, K. Hatakeyama4, E. Choja1, Y. Asada1, K. Kitamura5, K. Hatakeyama1, University of Miyazaki, Department of Internal Medicine, Circulatory and Body Fluid Regulation, Miyazaki, Japan; 2University of Miyazaki, Division of Orthopedic Surgery, Department of Sensory and Motor Organs, Miyazaki, Japan; 3Matsusuto Dental University, Department of Biochemistry, Matsusuto, Japan; 4University of Miyazaki, Department of Pediatric Dentistry, Miyazaki, Japan; 5University of Miyazaki, Department of Pathology, Miyazaki, Japan

**Background:** Osteoprotegerin (OPG) is a member of the tumor necrosis factor family and is involved in bone metabolism. In the elderly, OPG mRNA is widely distributed in organs associated with bone metabolism, but is also highly expressed in the heart. In addition, serum levels of RANKL and OPG are reported to be increased in patients with heart failure. However, the role of OPG remains to be elucidated their pathophysiological roles in the development of heart failure with aging.

**Purpose:** This study aimed at addressing the roles of endogenous OPG in age-related alternation in morphology and function of left ventricle (LV), using mice genetically lacking OPG gene (OPG−/− mice) and wild-type (WT) mice.

**Methods and results:** We conducted experiments using 12-months old OPG−/− mice (n=16) to compare the morphology and function of LV with the age-matched wild types (n=12). Aged-OPG−/− mice showed significant elevations of systolic blood pressures (+103±0.03 mmHg, p<0.0001) and greater increase of heart weight/body weight (8.0±0.64 to 4.7±2.01±11 mg/g, p<0.0012), compared with the wild types. Trans-thoracic echocardiogram revealed that OPG−/− mice displayed significant increases of LV chamber size at diastole (3.22±0.20 vs. 2.08±0.09 mm, p=0.0003) and systole (2.01±0.25 vs. 0.67±0.03 mm, p<0.0003), resulting in the decrease of LV fractional shortening (42±3 vs. 67±2, p<0.0001). Real-time quantitative PCR demonstrated that OPG−/− mice exhibited the activation of myocardial gene expressions for atrial natriuretic peptide (−220%, p<0.0001), angiotensin converting enzyme (+79%, p=0.0434) and matrix metalloproteinase-2 (+61%, p=0.0132), and increased phosphorylation of ERK (+76%, p=0.0195) and JNK (+81%, p=0.0220) by Western blot. Moreover, OPG−/− mice exhibited to increase soluble form of RANKL (335±12 vs. 91±6 pmol/mL, p<0.0001) in the serum, along with decrease in trabecular bone volume/issue volume at the proximal metaphysis ofibia (2.89±0.68 vs. 7.92±1.23%, p<0.0022), assessed by micro-computed tomography.

**Conclusion:** These results suggest that OPG might play an important role to preserve myocardial structure and function with aging, interacted with RANKL. Our data support a potential cross-talk between bone and cardiovascular system in the development of heart failure.

**P2381 | BENCH**

**Hypothyroidism predicts the mortality of idiopathic dilated cardiomyopathy**


**Background:** Previous studies claiming the relationship between thyroid dysfunction and poor prognosis of heart failure (HF) had a major limitation that they included patients with different etiology. With full information of thyroid function profile from four hundred and fifty eight consecutive patients with idiopathic dilated cardiomyopathy, we tested the hypothesis that thyroid status can independently predict mortality in patients with idiopathic HF.

**Methods and results:** The original cohort consisted of 572 consecutive patients with idiopathic dilated cardiomyopathy (IDCM), and 458 patients remained at the end of follow-up. All the patients took thyroid function test and other regular examinations in hospital. The risk of mortality was evaluated based on FT3, TSH, and the whole thyroid function profile, respectively. The most frequent thyroid dysfunction was subclinical hypothyroidism (n=441), followed by subclinical hyperthyroidism (n=35), euthyroid sick syndrome (n=17), and hypothyroidism (n=12). Logistic analysis showed log-TSH and FT3 as independent predictors of exacerbated cardiac function and mortality in patients with subclinical hypothyroidism.

**Conclusion:** Hypothyroidism was the strongest predictor of mortality (HR=4.189, 95% CI: 2.118–8.283), followed by low-T3 syndrome (HR=3.147, 95% CI: 1.558–6.355) and subclinical hypothyroidism (HR=2.869, 95% CI: 1.817–4.532). Subclinical hypothyroidism showed no significant impact.

**Conclusion:** We found clear association between an increased risk of death in HF caused by IDCM and thyroid dysfunction. These results suggest that monitoring thyroid function in HF patients is necessary and further study about treatment is warranted.
similar in idiopathic (DCM) as well as ischemic (ICM) human end-stage cardiomyopathy. However, the hallmarks of cardiac remodelling typical of DCM may be helpful to identify new treatment targets. Osteopontin (OPN), a phosphoglycoprotein of cardiac extracellular matrix, is an emerging mediator of cardiac inflammation and fibrosis in failing hearts. We have investigated whether the myocardial levels of OPN were affected by etiology of heart failure in the presence of similar left ventricular ejection fraction (LVEF).

**Methods:** mRNA and protein levels of OPN were measured in LV samples from failing DCM (n=8; age: <50yrs; LVEF%=17.5±3.3; LVEDV=305.5±110ml) and ICM patients (n=8; age: <50yrs; LVEF%=19.5±5.2; LVEDV=270±97 ml), undergoing cardiac transplantation. All patients received conventional therapy for HF and underwent to cardiac function evaluation. As control (C), atrial samples of age and sex matched normal subjects (LVEF%=<50) were analyzed. Real-time PCR analysis was carried off to measure OPN gene expression and data were normalized to three genes (RPS4X, eEF1a, RPL13a). The protein levels of OPN were assessed by enzyme immunometric assay.

**Results:** Even though the extent of interstitial fibrosis in ICM was higher than DCM, OPN mRNA was significantly increased in DCM compared to C and ICM patients (C: 2.2±0.3; DCM: 31.3±7.4; ICM: 2.7±1.1, p=0.0004 C vs DCM and p=0.0002 DCM vs IC). A similarly trend was observed for OPN cardiac protein concentration (C: 1.12±0.26; DCM: 1.29±0.22; IC: 1.00±0.77 ng/ml).

**Conclusion:** We have detected higher levels of OPN gene expression in LV samples of DCM rather than ICM failing hearts in the presence of similar LVEF. Our data suggest the new role of OPN as biomarker of myocardial remodelling typical of DCM independently of the fibrosis degree.

**P2383 | BEDSIDE**

**Pro-ADM is a strong prognostic biomarker in acute heart failure with preserved ejection fraction:** from the ACE 2 Study

M.O. Perez, M.N. Lyngbakken, E.C. Langsjoen, A.D. Hoist, T. Omland, H. Rosjo. Akershus University Hospital, Akershus, Norway

**Background:** There is a need for improved patient management in heart failure with preserved ejection fraction (HFpEF). Mid-regional pro-adrenomedullin (MR-proADM) levels are reflective of left ventricular (LV) remodeling, but the prognostic utility of MR-proADM in HFpEF is unknown.

**Methods:** We measured MR-proADM levels on hospital admission in 141 patients with acute decompensated HF requiring symptoms and clinical signs of HF and either LVEF <50% (HFpEF) or echocardiographic indices of diastolic dysfunction (HFpEF). MR-proADM was measured on day 1 and MR-proADM was compared to N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels.

**Results:** MR-proADM levels were classified as HFpEF and 50% or more of NT-proBNP. MR-proADM levels did not differ between patients with HFpEF and HFpEF: 1.31 (0.99-1.98) vs. 1.32 (0.93-1.81) mmol/L, p=0.33. In contrast, NT-proBNP levels were higher in HFpEF compared to HFpEF: 4308 (2064–8738) vs. 2293 (687–4969) pg/ml, p<0.001. Patients with NT-proBNP levels ≥2947 pg/ml had a significantly greater beneficial effect on cardiac ECM turnover and deposition when compared with non-responders (R=0.875; P=0.001) as specific biomarkers for cardiac ECM turnover and fibrosis.

**Conclusion:** MR-proADM levels provide strong and independent prognostic information in HFpEF.

**Acknowledgement/Funding:** Thermo Fisher Scientific supported the study by providing reagents.

**BEST POSTERS IN SYMPATHETIC RENAL DENERVATION**

**P2385 | BEDSIDE**

**Renal norepinephrine periprocedural gradient and blood pressure response 6 months after renal denervation**

K. Tiroch, A. Sause, J. Szymanski, I. Nover, R. Leischik, M. Vorpal, M. Seyfarth. Helios Clinic Wuppertal. Department of Cardiology, Wuppertal, Germany

**Background:** No widely available “read-out” is currently available to evaluate the extent of nerve ablation by renal denervation (RDN).

**Purpose:** We prospectively evaluated the association of intra-procedural reduction of renal veno-arterial norepinephrine gradient with blood pressure (BP) response at 6 months after RDN.

**Methods:** In 46 consecutive RDN patients, pre- and post-procedural norepinephrine concentrations were measured in each renal artery and vein. The veno-arterial difference was defined as norepinephrine gradient. BP responders were defined as patients with reduction of office systolic BP ≥10mmHg at 6-months follow-up.

**Results:** We observed a reduction of the office systolic BP from 176±19mmHg to 163±22mmHg (P=0.02) at six months. There was a decrease of the norepinephrine gradient during RDN (pre: 301±1061pg/ml vs. post: 80±362pg/ml, P=0.02). BP responders showed a greater reduction of the norepinephrine gradient compared to non-responders (−340±423pg/ml vs. −18±122pg/ml, P=0.01). Patients with reduction of norepinephrine gradient in both kidneys showed the most pronounced decrease of the systolic BP (−24±14mmHg) compared to patients with reduction of norepinephrine gradient in only one kidney (−7±15mmHg) or patients without norepinephrine reduction (−3±19mmHg, P=0.03 vs. bilateral reduction).

**Conclusion:** Measuring renal norepinephrine gradient during RDN may be a method to gauge the extent of renal nerve ablation.

**P2386 | BEDSIDE**

**Influence of renal sympathetic denervation on cardiac extracellular matrix turnover and cardiac fibrosis**

O. Doerr, C. Liebetrau, H. Moellmann, L. Gaede, C. Troidl, J. Wiebe, S. Voss, T. Bauer, C. Hamm, H. Neef. Justus-Liebig University Giessen, Medical Clinic I, Cardiology, Bad Nauheim, Germany; 1 Kerckhoff Clinic, Department of Cardiology, Bad Nauheim, Germany

**Background:** Renal sympathetic denervation (RSD) represents an effective treatment option for patients with resistant arterial hypertension (HT). Extracellular matrix (ECM) turnover and deposition are essential processes in HT-related cardiovascular remodeling, fibrosis, and cardiac hypertrophy that all contribute to hypertensive heart disease (HHD). The primary aim of the present study was to examine the effect of RSD on collagen turnover by analyzing serum levels of type I and III collagen amino-terminal pro-peptides (PINP, PIIINP) and carboxy-terminal pro-peptide (PICP) as specific biomarkers for cardiac ECM turnover and fibrosis.

**Methods:** A total of 100 consecutive patients (mean age: 65.9±10.1 y) undergoing RSD were included in this study. A therapeutic response was defined as an office systolic blood pressure (SBP) reduction of ≥10 mmHg 6 months after RSD. Various blood samples for measurement of serum PICP, PIIINP, and PINP were collected prior to and 6 months after RSD.

**Results:** A significant reduction in the office SBP of 24.3 mmHg (SBP baseline: 166.9 [±14.3] mmHg; p=0.001) was documented 6 months after RSD. At this time point, the serum levels of PICP (baseline: 423.0 μg/L [IQR: 294.6; 963.9] vs. follow-up: 190.8 μg/L [IQR: 120.1; 414.5], p=0.01), PINP (baseline: 14.8 μg/L [IQR: 13.7; 17.5] vs. follow-up: 11.8 μg/L [IQR: 9.9; 14.2], p=0.01), and PIIINP (baseline: 66.3 μg/L [IQR: 55.7; 85.2] vs. follow-up: 43.4 μg/L [IQR: 29.4; 69.1], p=0.01) were significantly decreased compared with baseline values in patients with an increased collagen turnover. The linear regression model demonstrated a significant relationship between elevated PICP, PINP, and PIIINP baseline serum levels and the extent of RSD-related serum level reduction 6 months after RSD (PICP: R=0.879, PINP: R=0.821, p=0.001).

In addition, successful SBP reduction in responders was associated with a significantly greater beneficial effect on cardiac ECM turnover and deposition when compared with non-responders (p=0.02).
Methods: Fifty-eight patients with refractory hypertension (daytime systolic BP >135 mmHg on ambulatory BP measurements) underwent RSD. All patients had a stable antihypertensive drug regimen of ≥3 agents including a diuretic. All RSD procedures were performed using the Symplicity Flex Catheter. Aortic PWV was assessed invasively by simultaneous pressure recordings in the ascending aorta and femoral artery. PWV was calculated from distance between pressure recordings and wave transition time. PWV was assessed in all patients before RSD and in 29 patients before and 6 months post RSD.

Results: Mean age of the patient population was 62±10 years. There was a significant reduction in mean daytime systolic ABPM from 154.3±11.4 to 146.2±13.0 mmHg (p<0.0001). Patients with baseline PWV below the median (14.4 m/s) displayed a significantly greater reduction in mean daytime systolic ABPM as compared to patients with PWV above the median (PWV > median -12.3±10.9 vs. PWV < median -4.3±9.6 mmHg, p=0.005). Baseline PWV correlated significantly with changes in mean systolic ABPM 6 months after RSD (r=0.42, p=0.0008). Within the population of patients undergoing PWV measurements at baseline and 6 months follow-up, there was no change in PWV following RSD (from 14.2 to 14.0 m/s, p=0.86).

Conclusion: Increased aortic stiffness as assessed by PWV seems to be associated with unfavourable outcome after RSD and remains unaffected by RSD. These results warrant further study of PWV as a patient selection criterion for RSD.

P2389 | BEDSIDE

Triple site pacing improves LVPdP/dtmax compared to conventional biventricular pacing

F. Zanon1, G. Pastore1, E. Baracca1, L. Marcantonio2, D. Lanza1, C. Picariello1, L. Roncon1, S. Aggio1, F. Noventa2, F.W. Prinzen3, 1 General Hospital, Rovigo, Italy; 2 University Hospital of Padova, Padua, Italy; 3 Maastricht University, Maastricht, Netherlands

Background: Multisite stimulation of the LV has been suggested as an alternative to standard BiV.

Purpose: Aim of the study was to compare the acute hemodynamic response of tri-ventricular pacing (TRIV) with standard BiV pacing in a group of CRT pts.

Methods: Ten male pts with chronic AF, 76±9 years old, LVEF 32±8%, 6 with ischemic, 4 with non-ischemic cardiomyopathy. QRS duration 184±30 ms, were selected as candidates for CRT. A right ventricular lead was implanted in the mid septum. Two LV leads were positioned in two different branches of the coronary sinus. The first LV pacing lead was positioned based on the criterion of the latest electrically activated site during intrinsic ventricular activation and the second lead as remote as possible from the first lead. Acute hemodynamic response was evaluated as variation of LVPdP/dtmax by means of a RADI pressure wire within the LV. One-way analysis of variance (ANOVA) with repeated measures and with Bonferroni post-hoc testing was applied to evaluate differences in pacing protocols.

Results: On average, 2.8±0.6 veins and 5.8±1.8 pacing sites were evaluated per patient. During standard BiV pacing LVPdP/dtmax from the latest electrically activated LV site was 30.5±20.7% greater than during intrinsic rhythm. A small but significant further increase in acute hemodynamic response (figure) was observed when TRIV pacing was enabled (to 35.0±20.4%).

Conclusion: In pts with HF and RV pacing TRIV pacing produces a small but significant further increase in acute hemodynamic response compared to conventional BiV.
sible to find a left ventricular site with a delay >10 msec in 86% of patients in less than a minute and every patient had a very different pattern of activations.

Results: Both groups demonstrated significant improvement of NYHA functional class, reductions of left ventricular ejection fraction and LVESV. All parameters of dyssynchrony were significantly higher in super-responders group. Multiple logistic regression analysis showed that LVPEP was an independent predictor for CRT super-response (95% confidence interval [CI] 1.007–1.055; p=0.011). In ROC curve analysis LVPEP demonstrated sensitivity 73.7% and specificity 75% (AUC 0.753; p=0.002) in prediction of response to CRT.

Conclusion: Greater cardiac mechanical dyssynchrony is associated with super-response to CRT in patients with CHF. LVPEP can be used as an independent predictor of super-response. Further studies are needed to confirm these findings.

P2393 | BEDSIDE
Super-response to cardiac resynchronisation therapy in patients with congestive heart failure
V.A. Kuznetsov, N.N. Melnikov, D.V. Konochnik, A.M. Solidatova, T.N. Enina. Tyumen Cardiology Center, Tyumen, Russian Federation

Background: Some patients with congestive heart failure (CHF) have greater improvement of cardiac remodeling after cardiac resynchronisation therapy (CRT) and they are identified as super-responders. It remains unclear if echocardiographic cardiac dyssynchrony parameters could accurately predict super-response to CRT.

Purpose: To evaluate potential echocardiographic predictors related to super-response after CRT.

Methods: 59 CRT patients (mean age 52±10 years, 88% men) with CHF (54% ischemic and 46% non-ischemic etiology) and II-III NYHA functional class were enrolled. After 6 months patients were divided into super-responders (reduction in left ventricular end-systolic volume (LVESV) >30%, n=20) and non-super-responders (reduction of LVESV <30%, n=39). To assess mechanical dyssynchrony we evaluated interventricular mechanical delay, duration of left ventricular pre-ejection period (LVPEP) by Doppler ultrasound velocity measurements of blood flow, the maximum delay between peak systolic velocities of the septal and lateral walls of left ventricle by Doppler tissue imaging. Systolic dyssynchrony index was assessed by 3D echocardiography.

Results: There were no significant differences in cardiac dyssynchrony measures between groups. LVPEP (median 150 ms), LVESV (median 75 ml), and LV end-diastolic volume (median 175 ml) were significantly lower in Group I, p<0.001. All parameters of mechanical dyssynchrony were significantly higher in super-responders group. Multiple logistic regression analysis showed that LVPEP was an independent predictor for CRT super-response (95% confidence interval [CI] 1.007–1.055; p=0.011). In ROC curve analysis LVPEP demonstrated sensitivity 73.7% and specificity 75% (AUC 0.753; p=0.002) in prediction of response to CRT.

Conclusion: Greater cardiac mechanical dyssynchrony is associated with super-response to CRT in patients with CHF. LVPEP can be used as an independent predictor of super-response. Further studies are needed to confirm these findings.
sponse only amongst patients with QRS >150 ms at baseline (responders: group 1: 88.3%; vs group 2: 53.3%; p < 0.01), while in groups 3 and 4 clinical improvement occurred more often but without differences between the two groups (responders: group 3: 86.7% vs group 4: 76.5%; p = ns). 

Conclusions: In patients with a basal QRS duration >150 ms, a simple variable ("delta" QRS) can be helpful in predicting clinical response to CRT implantation. In patients where baseline QRS was >150 ms the clinical response occurred in over 75%, and "delta" QRS showed no benefit in predicting clinical response

P2396 | BENCH
The ratio of the neutrophil leukocytes to the lymphocytes predicts the outcome of chronic heart failure patients undergoing cardiac resynchronization therapy (CRT).

A.M. Boros1, P. Perge1, Z. Jen1, L. Molná1, E. Zima1, L. Geller1, Z. Prohaszka2, B. Merkely1, G. Szepelak1, S. Semmelweis University Heart Center, Budapest, Hungary; 2 Semmelweis University, Third Department of Internal Medicine, Budapest, Hungary

Background: The low lymphocyte counts and high neutrophil leukocyte fractions have been associated with poor prognosis in chronic heart failure. We hypothesized that the baseline ratio of the neutrophils to the lymphocytes (NL ratio) would predict the outcome of chronic heart failure patients undergoing cardiac resynchronization therapy (CRT).

Methods: The qualitative blood count and the serum levels of NT-proBNP (N-terminal of the prohormone brain natriuretic peptide) of 122 chronic heart failure patients and 122 controls were analyzed. We considered the 2-year mortality as primary endpoint and the 6-month reverse remodelling (<15% decrease in the end-systolic volume) as secondary endpoint. Multivariable adjusted logistic regression analysis was used and Cox regression analyses were applied and net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were calculated.

Results: The ratio of neutrophils to lymphocytes was elevated in chronic heart failure patients compared to the healthy controls (2.93 [2.12–4.05] vs. 2.21 [1.64–2.81], p < 0.0001). The baseline NL ratio exceeding 2.95 predicted the lack of the 6-month reverse remodelling (n=63, odds ratio=0.38 [0.17–0.85], p=0.01; NR=0.49 [0.14–0.83], p=0.019), the 2-year mortality (n=29, hazard ratio=2.44 [1.04–5.71], p=0.03; NR=0.63 [0.24–1.01], p=0.001; IDI=0.04 [0.00–0.08], p=0.02) of the patients independently of NT-proBNP levels or other factors.

Conclusions: The NL ratio is elevated in chronic heart failure and predicts outcome after CRT. It is related to the reclassification improvement, 4% of the patients were better categorized in the prediction models by combining the NT-proBNP with the NL ratio. Thus, a single blood count measurement could facilitate the optimal patient selection for the CRT.

P2397 | BENCH
The effect of cardiac resynchronisation therapy on cognitive function in patients with moderate to severe heart failure

C.I. Freeman1, R.A. McCarthy2, L. Fletcher2, L.A. Smith2, D. Kelly3, P.J. Cowburn2, 1 University of Southampton, Southampton; 2 University Hospital Southampton NHS Foundation Trust, Southampton; 3 Basingstoke and North Hampshire Hospital, Basingstoke, United Kingdom

Background: Cognitive impairment in heart failure is common and is associated with the severity of the disease and long-term prognosis. Cardiac resynchronisation therapy (CRT) increases systolic blood pressure (SBP) and cardiac output in patients with reduced systolic function and broad QRS.

Purpose: We hypothesised that CRT might reverse symptoms of neurocognitive decline by increasing SBP and cardiac output.

Methods: This prospective study included 16 consecutive patients undergoing CRT implantation. The participants underwent a series of cognitive and psychosocial assessments pre implantation and at 6 weeks follow up. The neurocognitive tests were chosen in order to provide a brief evaluation of areas of cognitive function that are important in daily life and which are known to be vulnerable in patients with heart failure namely attention, memory, executive function and psychomotor speed. All patients underwent transcranial doppler echo procedure and at 6 weeks follow up. The acute rise in SBP was measured using a femoral arterial line at the onset of biventricular pacing.

Results: Changes in SBP (mean difference in score 8.87, 95% CI 5.30–12.44, p = 0.0001) and change in LVEF at 6 weeks post device implantation (Beta 0.29, 95% CI 0.18–0.40, p = 0.0001) were found in speed of processing post CRT (mean difference in score 7.81, 95% CI 4.70–10.92, p < 0.0001). Significant improvements were found in speed of processing post CRT (mean difference in score 7.81, 95% CI 4.70–10.92, p < 0.0001). The acute rise in SBP was measured in 13/16 patients. The qualitative blood count and the serum levels of NT-proBNP (N-terminal of the prohormone brain natriuretic peptide) of 122 chronic heart failure patients and 122 controls were analyzed. We considered the 2-year mortality as primary endpoint and the 6-month reverse remodelling (<15% decrease in the end-systolic volume) as secondary endpoint. Multivariable adjusted logistic regression analysis was used and Cox regression analyses were applied and net reclassification improvement (NRI) and integrated discrimination improvement (IDI) were calculated.

Conclusions: In young patients with CAVB and CRT, SDE/ECG individualized optimization of V-V intervals showed at short/medium-term follow-up, a significant improvement of LV dimensions, systolic function, synchrony, and NT-proBNP class.

P2398 | BEDSIDE
Optimization of pacing parameters with 3D-echo increases response in CRT in paediatric patients

M.S. Silvetti, A. Ammirati, R. Palmieri, L.M. Santucci, S. Placidi, M. Prosperi, L. Rava, F. Drago. Bambino Gesù Children’s Hospital, Rome, Italy

Background: CRT can improve the clinical outcome of patients with left ventricular (LV) dysfunction induced by chronic right ventricular (RV) pacing.

Purpose: Aim of this study is to evaluate short/medium-term results of CRT in a paediatric population requiring optimization of atrioventricular (AV) and ventriculo-atrial (VA) intervals.

Methods: We prospectively analyzed patients (pts) who underwent CRT between 2009 and 2014 in our institution. For individualized V-V interval, QRS duration, LV end-diastolic diameter z score (2), (end-systolic volume (ESV), ejection fraction (EF), systolic dysssynchrony index (SDI)) were calculated at 1–2–3–4 years. The devices were programmed for the V-V interval with the lowest SDI and shortest QRS. Response to CRT was defined as an increase ≥5% of EF. Data are reported as median (25–75th quartiles), p < 0.05 is significant.

Results: 22 patients (7 F), aged at implantation 9 (1–28) years, with systemic LV and CABV, other congenital heart defects in 11, prior RV pacing in 15 pts, EF 39% (30–60%), underwent CRT with epicardial systems (15 pts), hybrid (2), transvenous (5). LV pacing site was free wall (epi), posterolateral basal vein (transvenous). Four patients with CAVB, narrow QRS, severe LV dilatation, normal EF, underwent 'de novo' CRT. At a follow-up of 4 (1–5) years (table 1), NYHA class decreased from 2 (2-3) to 1 (2–1) (p=0.0001). A linear regression model showed: increase of V-V intervals (coefficient 1.9, p=0.1), significant increase of EF (coefficient 3.4, p<0.0001) and decreases of QRS duration (–7.2, p=0.0001), LV end-systolic volume (ESV) (–7.1, p=0.03), SDI (–0.9, p=0.04). All patients were considered responders, but a 27 years old patient died suddenly after 1 year of CRT (EF increase 10%).

Table

<table>
<thead>
<tr>
<th>Proportions</th>
<th>Pre-CRT</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
<th>4–5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS, ms</td>
<td>150 (120–160)</td>
<td>120 (90–140)</td>
<td>110 (90–120)</td>
<td>105 (90–115)</td>
<td></td>
</tr>
<tr>
<td>EF, %</td>
<td>39 (30–50)</td>
<td>51 (46–58)</td>
<td>52 (48–60)</td>
<td>54 (50–60)</td>
<td>58 (52–60)</td>
</tr>
</tbody>
</table>
P2399 | BEDSIDE
Single center experience with transseptal endocardial left ventricular lead implantation using transseptal puncture via the subclavian vein
If left ventricular stimulation for resynchronization therapy (CRT) is not successful using a coronary sinus (CS) lead, application of alternative methods may be necessary. The aim was to investigate the implantation of transseptal endocardial left ventricular TSEC LV leads, when transseptal puncture was performed via the subclavian vein in a university heart center.
TSEC LV lead implantation was performed in 18 patients (13 male, NYHA III-IV stage) after one or more unsuccessful attempt of CS electrode implantation, in 16 cases from the left, in two patients from the right side. Transseptal puncture was done via the subclavian vein, using a special ablation wire and intracardiac echo. After the wire was positioned in the left side, steerable sheath was also forced through the interatrial septum. Active fixation bipolar lead (Medtronic 3830–98) was fixed in the late activation region of the left ventricle. Statistical data are given in median and IQR.
The lead was successfully fixed in the left ventricle in all of the left sided operations, while both right sided cases were unsuccessful. In one of the patients left sided implantation was performed later, in the other case the lead was implanted after femoral transseptal approach. In one patient lead dislocation was observed into the left atrium on the first postoperative day, the lead was extracted, and new lead was implanted. Procedure time was 65 (43; 77) min., X-ray time was 12 (8; 17) min. During implantation 12 (8; 19) mV left ventricular signal amplitude, at 0.4 mV/100 ms gain was achieved.
Conclusions: The probability of survival at 5 years from battery depletion was 54%. Modern-generation CRT-LVs displayed better longevity, and differences were additional factors associated with replacement for battery depletion.

P2400 | BEDSIDE
Conclusions: The Vereckei algorithm correctly predicted the diagnosis 65.5% and the Pava criterion (R-wave peak time in II) 51.5%. The Brugada algorithm correctly predicted the diagnosis 72.7% of the time; CHD were: 21 tetralogy of Fallot, 6 atrial septal defect, 7 transposition of great arteries, 4 complex CHD, 4 Ebstein anomaly and 9 other CHD. The mean tachycardia cycle length was 38.5±21.6 years. 62.7% were male. The mean tachycardia cycle length was 38.5±21.6 years. 62.7% were male. The mean tachycardia cycle length was 38.5±21.6 years. 62.7% were male. The mean tachycardia cycle length was 38.5±21.6 years. 62.7% were male. The mean tachycardia cycle length was 38.5±21.6 years. 62.7% were male. The mean tachycardia cycle length was 38.5±21.6 years. 62.7% were male. The mean tachycardia cycle length was 38.5±21.6 years. 62.7% were male. The mean tachycardia cycle length was 38.5±21.6 years. 62.7% were male.

P2401 | BEDSIDE
Single center experience with transseptal endocardial left ventricular lead implantation using transseptal puncture via the subclavian vein
If left ventricular stimulation for resynchronization therapy (CRT) is not successful using a coronary sinus (CS) lead, application of alternative methods may be necessary. The aim was to investigate the implantation of transseptal endocardial left ventricular (TSEC LV) leads, when transseptal puncture was performed via the subclavian vein in a university heart center.
TSEC LV lead implantation was performed in 18 patients (13 male, NYHA III-IV stage) after one or more unsuccessful attempt of CS electrode implantation, in 16 cases from the left, in two patients from the right side. Transseptal puncture was done via the subclavian vein, using a special ablation wire and intracardiac echo. After the wire was positioned in the left side, steerable sheath was also forced through the interatrial septum. Active fixation bipolar lead (Medtronic 3830–98) was fixed in the late activation region of the left ventricle. Statistical data are given in median and IQR.
The lead was successfully fixed in the left ventricle in all of the left sided operations, while both right sided cases were unsuccessful. In one of the patients left sided implantation was performed later, in the other case the lead was implanted after femoral transseptal approach. In one patient lead dislocation was observed into the left atrium on the first postoperative day, the lead was extracted, and new lead was implanted. Procedure time was 65 (43; 77) min., X-ray time was 12 (8; 17) min. During implantation 12 (8; 19) mV left ventricular signal amplitude, at 0.4 mV/100 ms gain was achieved.
Conclusions: The probability of survival at 5 years from battery depletion was 54%. Modern-generation CRT-LVs displayed better longevity, and differences were additional factors associated with replacement for battery depletion.

P2402 | BEDSIDE
P2402 Are wide complex tachycardia algorithms applicable in adults with congenital heart disease?
Z. Blazquez Bermejo, O. Salvador, J. Restrepo, P. Cepas, A. Vega, A. Gonzalez, J. Ruiz Cantartor, A. Sanchez Recalde, J.M. Oliver, R. Peinado. 1 University Hospital La Paz, Cardiology, Madrid, Spain; 2 University Hospital De La Princesa, Madrid, Spain
Background and purpose: Several criteria and algorithms have been developed to help determine the origin (ventricular or supraventricular) of wide complex tachycardias (WCT) in adults. However they have not been tested in adult patients with congenital heart disease (CHD). This study was aimed at analysing the diagnostic accuracy of them in these patients.
Methods: A retrospective review of the arrhythmia in adult congenital heart disease database at our institution, from 1996 to 2015 was performed. All patients with WCT, a 12-lead electrocardiogram (ECG) available for review, and an electrophysiological study used as the gold standard for defining VT and SVT were included. Patients with a paced rhythm were excluded. Three blinded cardiologists independently analysed the ECGs according to the Brugada and Verecke algorithms and the Pava lead II criterion. We analysed the sensitivity (S), specificity (Sp), predictive positive value (PPV), and negative predictive value (NPV) of these algorithms and that of the single criteria included in them. Interobserver agreement was evaluated.
Results: A total of 55 WCT ECGs in 51 patients were identified. Supraventricular tachycardias (SVT) were not in 78.2% and VT in 21.8% of the ECGs. The mean age was 38.5±21.6 years. 62.7% were male. The mean tachycardia cycle length was 418±215 milliseconds. CHD were: 21 tetralogy of Fallot, 6 atrial septal defect, 7 transposition of great arteries, 4 complex CHD, 4 Ebstein anomaly and 9 other CHD. The Brugada algorithm correctly predicted the diagnosis 72.7% of the time; the Verecke algorithm correctly predicted the diagnosis 65.5% and the Pava criterion 98.2%. S, Sp, PPV and NPV of them are shown in the table. The single criterion with the best S and Sp was Pava criterion (see table). The sensitivity was 0.85.

P2403 | BEDSIDE
P2403 Idiopathic ventricular fibrillation - electrocardiographic abnormalities do not predict recurrent arrhythmias
U. Chaudhry, R. Borgquist, A. Rubulis, B. Borgfelt, S.M. Jensen, P.G. Piasnow. 1 Sahlgrenska University Hospital, Department of Cardiology, Lund, Sweden; 2 Sahlgrenska University Hospital, Department of Cardiology, Gothenburg, Sweden; 3 Umea University Hospital, Department of Cardiology, Umea, Sweden
Background: In patients with cardiac arrest due to idiopathic ventricular fibrillation (VF) the prognosis is unclear. Some studies have suggested a VF recurrence...
rate of up to 10% per year. The diagnosis offers a managerial challenge when under-derlying cardiac aetiologies are excluded.

**Purpose:** We sought to assess the predictive value of abnormal baseline electrocardiogram (ECG) in relation to recurrence of ventricular arrhythmias during follow-up of a patient cohort with IVF.

**Methods:** Patients with idiopathic VF (n=52, median age at event 37 [IQR 24] years, 62% male) were followed for a median time of 8 [IQR 11] years. Structural heart disease was excluded by echocardiography and/or cardiac MR. Channelopathies and ischemic heart disease were also ruled out. All patients received an ICD and subsequent follow-up included device-based data and clinical outcome. Pre-ICD implant ECGs were available in all subjects and were analysed independently by two electrophysiologists.

**Results:** A majority, 71%, had abnormal ECG findings at baseline. 3 patients developed reduced ejection fraction during follow-up, but no patients received any definite etiologic diagnosis. 9 patients (17%) had appropriate ICD therapy at a median of 1.5 (0–13) years after implant. 9 patients had inappropriate ICD shocks. One patient had a ventricular storm. All patients survived. Neither ECG nor imaging findings and clinical factors could predict appropriate ICD therapy (table).

**Conclusion:** Contrary to earlier reports, the vast majority of patients who survived idiopathic VF in our cohort had no VF recurrence during long-term follow-up. ECG abnormalities though common were unspecific and had no predictive value for future VF events or appropriate ICD therapy.

**Acknowledgement/Funding:** Nothing

---

**Concealed sinus node dysfunction (SND) may become manifest with increasing heart rate.** A low fibrillatory wave amplitude predicts SND after catheter ablation in patients with persistent atrial fibrillation.

A. Sunaga, M. Masuda, T. Kanda, Y. Matsuda, M. Fujita, O. Iida, S. Okamoto, T. Ishihara, K. Nanto, M. Uematsu. Kansai Rosai Hospital, Cardiovascular Center, Amagasaki, Japan

**Background:** Concealed sinus node dysfunction (SND) may become manifest after restoration of sinus rhythm by ablation in patients with persistent atrial fibrillation (AF).

**Purpose:** The purpose of this study was to investigate the predictors of SND after catheter ablation of persistent AF.

**Methods:** Two hundred two consecutive patients who underwent ablation for persistent AF were enrolled. Ipsilateral pulmonary vein isolation followed by, if necessary, electrocardiographic, were performed in all patients. SND was defined when temporary and/or permanent pacemakers were needed due to sinus brady- cardia after ablation.

**Results:** SND developed in 12 (5.9%) patients. There was no difference between the patients with and without SND in terms of the age (with SND: 67±9, and without: 66±10 years old, p=0.599) and sex (male: 58% vs. 79%, p=0.186). However, the patients with SND had a lower amplitude of the fibrillatory waves (0.11±0.086 vs. 0.176±0.077 mV, p=0.009) and larger left atrial volume index (LAVI: 66±31 vs. 34±13, p=0.007) than those without. A receiver operating characteristic curve identified a fibrillatory wave amplitude of 0.145 mV (AUC=0.742; sensitivity=65%; specificity=83%) and LAVI of 47.5 ml/m² (AUC=0.837; sensitivity=82%; specificity=87%) as the optimal cutoff values for predicting SND. A multivariate analysis revealed that the amplitude of the fibrillatory waves (odds ratio=0.84 for 0.010 mV increase, 95% CI: 0.71–0.98, P=0.031) and LAVI (odds ratio=1.08 for 1.0 cm²/m² increase, 95% CI: 1.04–1.12, P<0.001) were independent risk factors for SND. The scattergram of I wave and LAVI

**Conclusions:** A low amplitude of the fibrillatory waves and large LAVI were predictors of SND after restoration of sinus rhythm by ablation in patients with persistent AF.
both groups up until discharge, when TC patients started to show significantly less leads with LORSV. In TC patients, normalization in AAQRS during hospitalization showed a positive linear association with systolic function recovery. 

**Conclusions:** LORSV and AAQRS are not reliable in differentiating ACS from TC, because of a similar trend in QRS amplitude reduction during the acute phase. However, QRS amplitude attenuation in TC is in transition, and is linearly associated with systolic function recovery.

**P2407 | BEDSIDE**

**Patients who revert to atrial fibrillation after cardioversion demonstrate impaired thrombotic status**

M. Farag1, O. Okaro2, M. Niespialowska-Steuden3, B. Artman2, V. Markides4, D.A. Gorog2, 1 University of Hertfordshire, Postgraduate Medical School, Hertfordshire, United Kingdom; 2 East and North Hertfordshire NHS Trust, Department of Cardiology, Hertfordshire, United Kingdom; 3 Imperial College London, London, United Kingdom; 4 Royal Brompton and Harefield NHS Foundation Trust, London, United Kingdom

**Background:** Patients with atrial fibrillation (AF) are at increased risk of thromboembolic events and oral anticoagulation (OAC) reduces the risk of stroke. Whether restoration of sinus rhythm (SR) through direct current cardioversion (DC) favourably improves thrombotic profile and reduces stroke risk, is unknown.

**Methods:** We enrolled 40 patients (73% men, 67±13y) with newly diagnosed non-valvular AF, on OAC and scheduled to undergo DCCV. Assessment of thrombotic status was performed before and 6 weeks after DCCV, using the Global Thrombo- sis Test. This automated, point-of-care test assesses both platelet reactivity and endothelial dysfunction from a native, non-anticoagulated blood sample. The time taken to form an occlusive thrombus under high shear stress (occlusion time [OT]), in seconds, and the time required to restore flow by endothelial thrombosis (lysis time [LT], in seconds) are measured. We compared thrombotic profiles of patients who remained in SR at follow-up (n=20) to patients who had reverted to AF (n=20).

**Results:** Amongst the whole cohort (n=40), there was no difference in OT or LT before and after DCCV. However, patients who reverted to AF demonstrated significant prolongation of LT after DCCV (2923±1770 vs. 176±2382s; P<0.009), compared to no change in LT between pre- and post-DCCV in those who maintained SR (1691±581s vs. 1480±786s; P=0.17). Between groups comparison showed significantly prolonged LT in those who reverted to AF compared to those who maintained SR after DCCV (2894±1728s vs. 1407±282s; P=0.002). No change in OT was observed in between groups. There was no difference in baseline OT and baseline LT between those who stayed in SR and those who did not. The groups were well matched for variables, including age, sex, OACs, and CHADS2-VASc score.

**Conclusion:** Patients who revert to AF after DCCV exhibit a more pro-thrombotic profile, with impaired endothelial fibrinolysis, than those who maintain SR, despite OAC. Whether more prolonged maintenance of SR improves thrombotic status, and reduces stroke risk, requires evaluation.

**Acknowledgement/Funding:** East and North Hertfordshire NHS Trust

**P2408 | BEDSIDE**

Implantable cardioverter defibrillator shock does not immediately worsen left ventricular systolic and diastolic function

T. Mine, H. Kishima, K. Ashida, T. Masuyama. Hyogo College of Medicine, Nishinomiya, Japan

**Background:** Implantable cardioverter defibrillator (ICD) shock has been reported to be associated with ventricular tachycardia storm or poor prognosis. It remains unclear whether ICD shock directly affects cardiac function. We investigated left ventricular systolic and diastolic function immediately after ICD shock.

**Methods:** Cardiac catheterizations were performed in 34 ICD patients (29 men, age 63±13 years, 14 with ventricular fibrillation and 20 with ventricular tachycardia, 17 with ischemic heart disease and 15 with cardiomyopathy, 18 with cardiac resynchronization therapy; CRT) who underwent ICD/CRT-D implantation. In each patient we measured the peak positive dP/dt (+dP/dt), minimum dP/dt (-dP/dt), LV peak systolic pressure (LVP), LV end-diastolic pressure (LVEDP) and the tau in-dex during baseline and at 1, 3, 5, 10, and 15 minutes after defibrillation threshold (DFT) test shock.

**Results:** In comparison with baseline, the +dP/dt increased at 1, 3, 5, 10, and 15 minutes after shock (796±229 vs. 1039±259, 1049±245, 1042±247, 1037±259, 1034±254 mmHg/s, P<0.001) and LVP increased at 1, 3, and 5 minutes (111±26 vs. 116±29, 114±28, 115±29 mmHg, P<0.05). The tau index decreased at 3 and 5 minutes. (65±1.8±5 vs. 62.5±16.8, 62.4±15.9 msec, P<0.05). There were no changes in the -dP/dt and LVEDP.

**Conclusion:** Implantable cardioverter-defibrillator device shocks improve left ventricular systolic and diastolic function immediately after shock. Excessive functional reaction of the LV after ICD shock might induce ventricular tachycardia storm.

**Introduction:** Brugada phenocopy (BP) is a clinical entity characterized by EKG patterns identical to those shown by true congenital Brugada syndrome (BS) but are elicited by various other factors such as hyperkalemia.

**Objective:** We aimed to describe the prevalence, clinical, electrocardiographic and arrhythmic characteristics of the BP associated to hyperkalemia.

**Methods:** We conducted a retrospective observational study of adults patients (p) admitted to a tertiary university hospital during first six months of 2013 that presented severe hyperkalemia (cutoff value: ≥6.5 mmol/l) any time during hospitalization. Clinical and EKG data were collected of all p making special attention to hyperkalemia.

**Results:** Out of 19,750 admitted p, severe hyperkalemia occurred in 125 p (0.63%). An EKG was obtained at the time of the electrolyte alteration in 49 p (39%). 2)without those findings. Baseline demographic,clinical and electrocardiographic characteristics were analyzed. Early repolarization was defined as ≥0.1mV J-point elevation of the QRS-ST junction in at least two leads in inferior leads as QRS slurring or notching, and was stratified according to the degree of J-point elevation (≥0.1mV or ≥0.2mV).

**Results:** ER was identified in 26 subjects. There was no significant difference in baseline characteristics between two groups. However, 13 subjects with more than 0.2mV J-point elevation of Group 1 had markedly lower in survival time than the Group 2 (2.3±3.3 vs. 9.7±19.1 [days]; P=0.02), and more than 5 days survival after resuscitation was significantly increased in Group 2 compared with those subjects in Group 1 (28 vs 15%); P=0.022.

**Conclusions:** Greater ascending of early repolarization in the inferior leads of ECG after resuscitation might suggest the poor outcome in the CA subjects.

**P2410 | BEDSIDE**

Early repolarization on electrocardiography in survivors after out of hospital cardiac arrest:impact and short-term outcome

Y. Hori, K. Fukushima, H. Takahashi, N. Komiya. Matsudo city hospital, Matsudo, Japan

**Purpose:** An early repolarization (ER) in inferior leads on electrocardiography (ECG) has been shown to be associated with an increased risk of arrhythmic death. However,little is known about ECG findings on ER after resuscitation of cardiac arrest (CA) subjects.

**Methods:** Of 568 consecutive subjects with out-of-hospital CA for the last 2.5 years,144 subjects were resuscitated.Among them, 67 subjects (37 male, 75±13 years) who had no evident of acute ischemia or vascular diseases were evaluated and divided into following two groups:1)with early repolarization in inferior leads 2)without those findings. Baseline demographic,clinical and electrocardiographic characteristics were analyzed. Early repolarization was defined as ≥0.1mV J-point elevation of the QRS-ST junction in at least two leads in inferior leads as QRS slurring or notching, and was stratified according to the degree of J-point elevation (≥0.1mV or ≥0.2mV).

**Results:** ER was identified in 26 subjects. There was no significant difference in baseline characteristics between two groups. However, 13 subjects with more than 0.2mV J-point elevation of Group 1 had markedly lower in survival time than the Group 2 (2.3±3.3 vs. 9.7±19.1 [days]; P=0.02), and more than 5 days survival after resuscitation was significantly increased in Group 2 compared with those subjects in Group 1 (28 vs 15%); P=0.022.

**Conclusions:** Greater ascending of early repolarization in the inferior leads of ECG after resuscitation might suggest the poor outcome in the CA subjects.
Conclusion: Hyperkalemia induced Brugada phenocopy is a non-frequent form of severe hyperkalemia but it presence must be followed for close heart rhythm monitoring and appropriate treatment.

P2411 | BEDSIDE
Can we monitor left atrial electrical remodelling with standard 12-lead ECG in patients with atrial fibrillation?

M. Wojcik1, R. Blaszczzyk1, A. Socha1, E. Rychta1, L. Lebee1, K. Oleszczak1, K. Poleszak1, J. Baszak2, A. Smolen2, A. Wysokinski2. 1Medical University of Lublin, Department of Cardiology, Lublin, Poland; 2Medical University of Lublin, Lublin, Poland

Background: P-wave terminal force (Ptf) is a product of the amplitude (Pam) and the duration (PT) of the terminal phase of P-wave in lead V1. It was suggested that Ptf is early marker of left atrial conduction abnormalities and electrical remodelling, which precedes dilatation of left atrium.

Purpose: We aimed to follow PT, Pam and Ptf changes during 5-year follow-up (5FU) and examine the relation of these changes to the number of AF episodes requiring hospitalisation (HOSP) for restoration of sinus rhythm (RSR).

Methods: We analysed 18217 elective and emergency HOSP aimed for RSR in patients with AF. The inclusion criteria were: AF, successful RSR documented in 12-leads ECG, 5FU. The exclusion criteria were: arrhythmia other than AF, unsuccessful RSR, successful RSR but missing 12-leads ECG recording, previous ablation/operation within left atrium, no 5FU. Consequently, 608 patients (52% male; median: age 65 years, CHADS 2, CHA2DS2-VASc 3, EF 55%, LA 4.6cm) were identified. Pam, PT and Ptf were calculated at inclusion (Pam0, PT0, Ptf0) and at 5 years (Pam5, PT5, Ptf5).

Results: We observed: A/significant (p<0.00001) differences (median [ICR 25:75%]) between A1/PT0 (60 [40;60]) and PT5 (80 [60;100]), PAM0 (0.075 [0.050;0.10]) and PAM5 (0.075 [0.050;0.10]), A3/Ptf0 (4.75 [2.5;6.0]) and Ptf5 (7.9 [5.0;10.0]), B/correlations between: B1/changes of PT (PT5-PT0) and number of HOSP (r=0.28, p<0.00001; B2/changes of Pam (PAM5-PAM0) and HOSP5; r=0.25, p<0.00001; B3/changes of Ptf (Ptf5-Ptf0) and HOSP5: r=0.5, p<0.00001.

Conclusions: 1. The progression of atrial electrical remodelling can be observed with changes of Pam, PT, Ptf in standard 12-leads ECG. We describe significant 5FU changes of PAM, PT, Ptf in standard 12-leads ECG in patients with AF. 2. With changes of PAM, PT, Ptf in standard 12-leads ECG, we observe significant correlations between: A1/PAM0, PT0 and number of HOSP, A2/PAM0, Ptf0 and number of HOSP, A3/PT0, Ptf0 and number of HOSP.

P2412 | BEDSIDE
QT-TQ dynamics in long QT patients during a supine-standing ECG test

V.M. Meijboer1, P.G. Postema1, H.J. Ritsema Van Eck2, A.A.M. Wilde1, R. Coronel1. 1Academic Medical Center of Amsterdam, Department of Clinical and Experimental Cardiology, Amsterdam, Netherlands; 2Erasmus Medical Center, Department of Medical Informatics, Rotterdam, Netherlands

Introduction: The diagnosis of long QT syndrome (LQTS) is difficult in the absence of QT prolongation on the baseline ECG. Previously, the supine-standing test was reported to enhance diagnostic accuracy of LQTS. Detailed analysis of the dynamics of QT and TQ (=RR-QT) during supine-standing tests may further improve the diagnostic possibilities.

Purpose: To evaluate QT-TQ dynamics in LQTS patients.

Methods: Age and gender matched subjects with LQTS1, LQTS2 and healthy relatives (controls) were studied (each group n=8). Continuous 12 lead ECGs were made during 2 minutes in supine position (baseline) followed by 3 minutes of standing. For analysis we used a custom-made program applying fiducial segment averaging. Beat-to-beat analysis of RR, TQ (=RR-QT), QT, QT/TQ ratios and QT/TQ crossover (defined as a change in QT/TQ ratio from <1 at baseline to >1 during standing) was performed at baseline, during standing (first 30s of standing) and during standing (1 min following stand-up).

Results: In all groups (mean±SD, 42±5 yrs, 63% male, before betablocker therapy, 347±36 beats per subject) QT significantly decreased during stand-up, whereas QT hardly decreased (figure). It resulted in a significant QTc increase during standing (QTc stretching) in control (442±5 to 474±11) and LQT2 (476±10 to 530±17), but not in LQT1 (495±9 to 524±25). In 6/8 controls QTc of several beats exceeded the previously established critical level of 490 ms.

Conclusion: QT and TQ dynamics during stand-up. All four LQTS patients with a normal baseline QTc < 465, and only 1 of 5 controls, demonstrated a QT/TQ crossover during standing (p<0.05). Conclusions: QT/TQ ratio crossover during standing may add to diagnosis of LQTS, and identifies LQTS patients with otherwise normal baseline QTc.

P2413 | BEDSIDE
Electrocardiogram characteristics of verapamil-sensitive fascicular ventricular tachycardia

G. Zhou, J. Ma, X. Guo, X. Liu, S. Zhang. Fuwai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Annythmia Centre, Beijing, China. People’s Republic of China

Purpose: To study the surface electrocardiogram (ECG) characteristics and related electrophysiologic features of verapamil-sensitive idiopathic ventricular tachycardia (VVT, and evaluate ECG criteria for the differential diagnosis of wide QRS complex tachycardia (WCT) in this subset of arrhythmia.

Methods: Retrospectively, a total of 51 patients who underwent radiofrequency catheter ablation (RFCA) with ILVT verified by electrophysiological study between August 2012 and March 2014 were included in this study. The ILVTs were classified into three subgroups according to the origin verified by successful ablation. During the episodes of ILVT induced in the electrophysiology study (EPS), the atrioventricular relationship was recorded. The ECG characteristics were thoroughly analyzed.

Results: 45 left posterior, 3 left anterior and 3 upper septal ILVTs were verified by EPS and successful RFCA. V-A conduction was observed in 29.4% induced ILVTs (1.5 (0.6-2.5); 49% surface ECGs exhibited evidence for atrioventricular dissociation. Regarding the ILVTs originating from left posterior fascicular, the major ECG findings were as follows: 1) Mean tachycardia cycle length was 353.7±61.1ms, 2) Mean QRS complex width was 130.3±29.2ms, 3) Mean RS interval was 57.6±9.5ms, 4) V1V1 was observed in all precordial and aVR leads, 5) Mean R wave peak time at DII was 20.4±8.7ms. 6) Left axis deviation was observed in 64.4% ECGs while 35.6% exhibited axis of “no man’s land”, 7) Lead V1 mainly exhibited R or qR pattern, 8) Lead V6 commonly presented rS or QS pattern, 9) Lead aVR predominantly demonstrated qR pattern. For the left anterior ILVTs, the ECG exhibited a right deviation of frontal QRS axis with QR pattern at lead V1 and S pattern at lead V6. Atrioventricular dissociation was observed in two of three ECGs in the subgroup of upper septal ILVT, leaving one case presenting 1:1 retrograde P wave.

Conclusion: WCT differential criteria related with conduction velocity fail to reliably predict the correct diagnosis of ILVT. Axis of “no man’s land” and morphology criteria are valuable in differentiating ILVT from wide QRS complex SVT. In addition, atrioventricular dissociation is frequently detected on the surface ECG of ILVT and represents the sole ECG finding to predict the presence of upper septal type ILVT.

P2414 | BEDSIDE
Association of right ventricular systolic function and conduction delay in patients with right bundle branch block

K.I. Cho, S.I. Im, H.S. Kim, J.H. Heo, T.J. Cha. Kosin University School of Medicine, Department of Internal Medicine, Division of Cardiology, Busan, Korea

Background: Elevated right ventricle (RV) pressure and/or volume can place stress on the right bundle branch block (RBBB) and its associated Purkinje network, which may affect its electrical properties resulting in conduction delay or block. We hypothesized that R’ wave duration in lead V1, prolonged later portion of the QRS complex, would be an indicator of reduced RV function in patients with RBBB.

Methods: A University echocardiography and electrocardiogram (ECG) database was reviewed from 2013 to 2014 to identify patients with complete RBBB. ECGs recorded closest to the time of the echocardiogram were carefully reviewed and measured QRS and R’ wave duration. RV systolic dysfunction was defined as RV fractional area change (FAC)<35%, as indicated by echocardiography guideline.

Results: Patients with RV dysfunction (n=241) showed more prolonged QRS duration (145.3±19.3 vs. 132.2±13.4 ms, p<0.001) predominantly due to R’ prolongation (4.8±13.9 vs. 1.9±12.0 ms, p<0.001) compared to the patients with normal RV function (n=123) (Table). R’ duration was significantly associated with RV FAC (r=−0.609, p<0.001), as well as RV systolic pressure (r=0.142, p=0.008), RV dimension (r=0.193, p<0.001) and RV myocardial performance index (r=0.199, p<0.001).

Conclusion: Prolonged R’ wave duration in lead V1 would be an indicator of RV dysfunction as well as pressure and/or volume overload in patients with RBBB.
P2415 | BEDSIDE
Transient manifestation of J-waves during acute pericarditis: electrophysiological abnormalities in subepicardium are possibly associated with the genesis of J-waves

I. Abe, M. Nakagawa, Y. Ikebe, S. Saito, H. Kondo, T. Shinohara, Y. Teshima, K. Yulu, N. Takahashi. Faculty of Medicine, Oita University, Department of Cardiology and Clinical Examination, Oita, Japan

Background: Experimental studies suggested that transmural differences in early phase of action potential between epicardial and endocardial surfaces are responsible for the genesis of J-wave. We investigated ECG findings in patients with acute pericarditis which may involve in the subepicardial region.

Methods: We studied 24 patients (18 males, 59.8±15.0 years) who were diagnosed with acute pericarditis based on the presence of typical chest pain, widespread ST-elevation or PR-depression, and new pericardial effusion. Twelve-lead ECGs and Holter ECGs were obtained before, during and after acute pericarditis.

The J-wave was defined as terminal QRS notching or slurring with amplitude of >0.1 mV in at least 2 leads.

Results: The J-waves were recorded with ST-elevation in 18 patients (75%) during acute pericarditis (figure, A-D). The J-waves newly appeared in 16 patients, and the already existing J-waves were augmented in 2 patients. J-waves were more prevalently observed in the inferior leads (II, III, aVF) (83%). Only 1 patient showed a few ventricular premature contractions. The amplitude of J-waves recorded in Holter ECGs showed a significant positive correlation with preceding RR-intervals.

Conclusion: The present study suggested that the J-waves manifested by acute pericarditis could be associated with electrophysiological abnormalities in the ventricular subepicardial region.

P2416 | BEDSIDE
Evaluation of Tp-e interval and Tp-e/QT ratio in patients with coronary slow flow

K. Karaman1, F. Altunkas1, M. Karayakal1, A. Arisoy2, M. Cetin1, I. Akar3, C. Zencirci, B. Aygu1, A. Celik1, K. Ceyhan1, 1. Gaziosmanpasa University, Cardiology, Tokat, Turkey; 2. Adiyaman University Training and Research Hospital, Cardiology, Adiyaman, Turkey; 3. Gaziosmanpasa University, Cardiovascular Surgery, Tokat, Turkey; 2Adnan Menderes University, Cardiology, Aydin, Turkey

Background: Coronary slow flow (CSF) is characterized by normal or near-normal coronary arteries with delayed opacification of the distal vasculature. The interval between the peak and the end of the T wave (Tp–e) is accepted as an approximation of the QRS/T vector ratio. Painful LBBB S/T was 1.483±0.16, range 1.2–1.7 while chronic LBBB S/T was 3.92±0.05, range 2.2–4.8 (p<0.001). A subset of chronic LBBB with heart rate >100 (112±5 min-1, n=179) had S/T of 3.67±0.07 (p<0.001 with painful LBBB). There was no overlap between chronic LBBB and painful LBBB at S/T cut-off of 2.

Conclusions: To characterize LBBB morphology (in particular QRS/T wave ratio) in painful LBBB syndrome immediately after LBBB onset and compare it to the chronic LBBB.

Methods and results: We analyzed electrocardiograms (EKG) of 14 patients with painful LBBB syndrome (unapparent PS and intermittent PS) and 10 published EKGs of 8 Male, age 49±14 years, heart rate 115±14 min-1 and compared it to 443 patients with chronic LBBB, 160 Male, age 77±5 years, heart rate 77±5 min-1 (all data Mean±SD). Maximal precordial S/T wave ratio (S/T) was used as best approximation of the QRS/T vector ratio. Painful LBBB S/T was 1.48±0.16, range 1.2–1.7 while chronic LBBB S/T was 3.92±0.05, range 2.2–4.8 (p<0.001). There was no overlap between chronic LBBB and painful LBBB at S/T cut-off of 2.

Conclusion: EKG pattern of the painful LBBB within seconds/minutes of onset is characterized by a very low (<1.7) precordial S/T ratio consistent with the “new LBBB” pattern. S/T ratio of 2.0 discriminated between acute onset and chronic LBBB. This finding confirms the validity of LBBB age determination based on QRS/T vectors ratio.

P2418 | BEDSIDE
Is ECG a reliable means of preexcitation syndrome diagnosis?

B. Brenbilla-Perron1, A. Olivier1, J.M. Seftal1, V. Manenti1, T. Vilemin1, D. Beurrier1, C. De Chillou1, J. Vincent1, N. Girerd2. 1 University Hospital of Nancy - Hospital Brabois, Vandoeuvre les Nancy, France; 2 Hospital Brabois of Nancy, INSERM, Centre d’Investigations Cliniques 9501, Université de Lorraine, Vandoeuvre les Nancy, France

Background: Main basis for the diagnosis of preexcitation syndrome (PS) is the ECG which associates short PR interval and widening of QRS complex with a delta wave. PS is associated with a risk of sudden death and diagnosis is important, mainly in athletes. The purpose of the study was to evaluate the prevalence of unapparent PS in sinus rhythm and intermittent PS among a population studied by electrophysiological study (EPS) for palpitations.

Methods: ECGs of 617 patients in whom PS related to an atrioventricular accessory pathway (AP) was identified at esophageal and/or intracardiac electrophysiological study (EPS), were studied. All patients had symptoms that had led to EPS. Asymptomatic PS was excluded. PS was considered as malignant and at risk of sudden death when the shortest RR interval between pre-excitation beats was <250 ms in control state (CS) or <200 ms after isoproterenol during induced sustained atrial fibrillation (AF).

Results: 85 patients (14%) had a normal ECG in SR and anterograde conduc- tion over AP at atrial pacing (unapparent PS). 24 patients had intermittent PS; 507 patients had an ECG suggestive of PS (overt PS). Gender and age (respectively 36±17, 38±19, 35±17.5) did not differ significantly. Accessory pathway (AP) was more frequently left lateral in patients with unapparent PS (62%) than in patients with intermittent PS (33%) (0.011) and overt PS (41%) (0.0003). Left posteroapical AP was as frequent (16, 16, 17%) but right posteroapical PS was less frequent in unapparent PS (12%) than in intermittent PS (58%) (p<0.0008) and overt PS (42.4%) (0.01). Data of EPS were similar in unapparent and overt
PS except the rate of malignant form higher in unapparent PS (23%) than in overt PS (14%) (P<0.03). Two patients with unapparent PS presented aborted sudden death. Patients with unapparent and overt PS differ significantly from intermitten PS except for the rate of induced atrioventricular tachycardia, similar in all patients (from 71 to 79%). Patients with intermittent PS had less induced AF and a poorer conduction on AP (108±45 bpm in CS, 168±67 bpm after isoproterenol) than in unapparent PS (191±576, 227±81) and overt PS (197±64, 241±576) (P<0.000).

Conclusion: The diagnosis of PS is not always evident and symptoms should draw attention to minor abnormalities and lead to enlarge indications of EPS that is the only means compared to home event monitors to diagnose a PS and at opposite to eliminate an antegrade conduction over AP.

P2419 | BEDSIDE
Frontal QRS-T angle as a predictor of appropriate implantable cardioverter-defibrillator therapy in ischemic and non-ischemic cardiomyopathy
S. Chandrasekharan, W. Wiatworawan, T. Yingchoncharoen, T. Ngernsritakul, S. Apiyawat, O. See, P. Siritara. Ramathibodi Hospital of Mahidol University, Bangkok, Thailand

Background: The frontal QRS-T angle is defined as the difference between vectors of QRS and T-wave vectors in the frontal plane. The patients were followed 38±26 months for development of appropriate ICD therapy (anti-tachycardia pacing and shock). The primary endpoint was analyzed using univariate and multivariate cox regression model.

Results: During follow-up, the event developed in 17 patients (18.5%). Patients with appropriate ICD therapy had wider QRS-T angle than those without ICD therapy (133±42° vs. 75±42°, P<0.001). The patients with frontal QRS-T angle ≥110° received more appropriate ICD therapy than those with QRS-T angle <110° (14.1% vs. 4.3%, P<0.001). Presence of frontal QRS-T angle ≥110° was the predictor of appropriate ICD therapy (hazard ratio 5.78, 95% confidence interval 1.85–18.06, P=0.003). T wave inversion ≥0.2 mV or fragmented QRS complex in two consecutive leads was also predictive of appropriate ICD therapy (hazard ratio 5.25, 95% confidence interval 1.78–15.44, P=0.003 and hazard ratio 6.83, 95% confidence interval 1.19–39.93, P=0.023 respectively). In multivariate analysis, QRS-T angle ≥110° remained a significant predictor of appropriate ICD therapy (hazard ratio 4.40, 95% confidence interval 1.32–14.70, P=0.016)

Conclusion: Frontal QRS-T angle ≥110° is the independent predictor of appropriate therapy in ischemic and non-ischemic cardiomyopathy patients.

P2420 | BEDSIDE
The effect of percutaneous closure of atrial septal defects on the P-wave dispersion
O. Ozturk1, U. Ozturk2. 1Diyarbakir Education and Research Hospital, Department of Cardiology, Diyarbakir, Turkey; 2Dicle University Medicine Faculty, Department of Neurology, Diyarbakir, Turkey

Objective: The aim of this study is to assess the P-wave dispersion (PD) in patients who underwent percutaneous ASD closure devices, to determine the effects of structural innovations on atrial electrical homogeneity.

Methods: We prospectively examined 22 consecutive patients who underwent percutaneous transcatheter closure of secundum ASD from June 2013 to December 2014. P wave maximum, P wave minimum, and P wave dispersion were measured in 12-lead surface electrocardiography, before the procedure and soon after procedure.SPSS 12 was used for statistical analysis.

Results: A total of 22 patients were prospectively evaluated; 5 male and 17 female. The mean age of the patients was 36.3±9.2 years. The mean diameter of the occlusive devices was 16.3±2.7 mm. Pmax, Pmin and Pd were significantly increased immediately after procedure (P<0.05). Before percutaneous ASD closure; Pmax: 79±8.41 ms, Pmin: 42±3.37 ms, PD: 37±2.27 ms. Immediate after percutaneous ASD closure; Pmax: 95±3.43 ms, Pmin: 48.7±3.9 ms, PD: 48±3.36 ms (P<0.05).

Conclusions: Pmax, Pmin and PD were significantly increased soon after atrial septal defect closure procedure in percutaneous closure of secundum ASD.

P2421 | BEDSIDE
Prevalence of early repolarization pattern in 12-lead electrocardiogram: a population-based study
M.G. Matta1, P.E. Gulayin1, S. Garcia Zamora 2, R. Poggio 1, L. Gutierrez 1, C. Ittmann 3, M.G. Matta1, P.E. Gulayin1, S. Garcia Zamora 2, R. Poggio 1, L. Gutierrez 1, C. Ittmann 3

Purpose: This study was to determine the prevalence of ER pattern in a Portuguese general population.

Methods: In this prospective, cross-sectional, population-based study, 12782 adults were enrolled from the entire geographic area of the city of Porto, Portugal. A trained nurse recorded the demographic and clinical information, performed a physical examination, and collected blood samples for biochemical analysis. The study was divided into two stages: stage 1, during which all adults were invited to participate; and stage 2, during which a random sample of invited subjects was selected for validation. The prevalence of ER was calculated as the percentage of individuals with QRS-T angle ≥110°.

Results: A total of 12782 individuals were included in the study. The prevalence of ER was 4.77% (90/1886). The inferior location was found in 70% of cases (63/1886). The most common type was the “slurring” appearance without ST elevation (type 4) represented 68.89% of cases. Type 2 was observed in 27.78% of cases (25/1886).

Conclusion: Our study found a prevalence of 4.77% of ER pattern. In Portugal, ER is a common finding. Further studies are needed to understand the clinical significance of this finding.

Acknowledgement/Funding: None

P2422 | BEDSIDE
A novel formula to predict the QT interval during intrinsically atrioventricular conduction from the ventricular paced electrocardiogram
R. Srivattanakom, A. Shvilkin. Beth Israel Deaconess Medical Center, Cardiology, Boston, United States of America

Background: The QT interval is used to monitor drug safety and arrhythmia risk. Ventricular pacing (VP) alters the QT interval through immediate QRS prolongation and time-dependent repolarization remodeling. Normal QT interval limits during VP are unknown and there exists no consensus on its monitoring.

Purpose: We sought to develop a formula to predict the QT interval during intrinsically atrioventricular conduction (IC) from the ventricular paced electrocardiogram that is the predicted QT, using established normal values, could be used for monitoring.

Methods: In 38 patients (22 men, age 69±12.8 yrs, MtsSD) with cardiac devices and preserved atrioventricular conduction, we measured QRS, QT, QT peak (QTp), and T-peak-T end (TpTe) intervals using custom-built software. We performed paired measurements in AAI (IC) and DDD (VP) modes at equal heart rates (HR) at baseline and after VP for 1 week. We fit a generalized estimating equation model to predict IC QT intervals from VP intervals.

Results: VP resulted in immediate QRS, QT, QTp, and TpTe prolongation compared to IC at baseline. After 1 week of VP, IC QT prolonged while VP QT shortened due to a decrease in the VP TpTe interval. QTp prolonged in both pacing modes at 1 week. A formula using VP QTp and HR: 0.861 x QTp ms – 1.21 x HR (beats per minute) + 205, predicted the IC-QT interval with R²=82% (P<0.001 for model and coefficients).

Conclusion: One-week VP results in repolarization remodeling as evidenced by prolongation of the QT interval during IC but shortening during VP. VP QT
shortening occurs through a decrease in the TpTe interval, indicating reduced repolarization heterogeneity. In contrast, the QTp interval at 1 week trends in the same direction during IC and VP. In patients with ventricular paced rhythms, a formula using the VP QTP interval closely predicts the intrinsically conducted QT interval.

P2423 | BEDSIDE
Identification of the anatomic location of focal atrial tachycardias using synthesized 18 lead electrocardiography

M. Ishimura, M. Ueda, K. Miyazawa, N. Hashiguchi, Y. Kobayashi.
Chiba University Graduate School of Medicine, Cardiovascular medicine, Chiba, Japan

Introduction and purpose: Atrial tachycardias (ATs) are curable arrhythmias with the current developed radiofrequency ablation (RFA) techniques and devices. However, we often have difficulty in identifying their focus because of the many patterns depending on the anatomic location. Synthesized 18 lead ECG is well known and accepted as the detector of left ventricular posterior wall ischemia. However, it is not evident that it is useful for decision of local electrical activity. This aim of study is to evaluate whether synthesized 18 lead ECG give us additional information about local electrical activity or not.

Methods: We retrospectively reviewed 68 consecutive patients (mean age 60±13 yrs) undergoing RFA and analyzed their synthesized 18 lead ECGs. The P wave morphology was classified according to each AT diagnosed by electrophysiologic studies. During them, multipolar catheters were used for recording activation. In some recurrence cases after the pulmonary vein isolation for paroxysmal atrial fibrillation, the CARTO electroanatomical system were used to define the anatomic location.

Results: The AT origin distribution was the coronary sinus (CS) ostium (n=16), crista terminalis (CT) (n=11), perinodal (n=6), right atrium (RA) posterior (n=2), tricuspid annulus (TA) (n=9), interatrial septum (IAS) (n=13), and basal left atrial appendage (n=1). The superior vena cava (SVC) (n=1), inferior vena cava (IVC) (n=1), right atrial appendage (RAA) (n=1), and right atrial family (RAF) (n=1). RA tachycardias from the SA had positive or biaxial P waves in V3R-SR. We could distinguish CT from CS ostium ATs by checking II,III, and aVF leads. RA posterior ATs had positive P waves in V3R-SR contrast to the CS ostium, which was negative. AT from the LSPV, RSPV and RIPV had positive P waves in V3R-SR, and the LSPV tended to have higher P waves than the RSPV and RIPV. The RSPV had isoelectric P waves in V7-V9.

Conclusion: Synthesized 18 lead ECGs could be helpful to identify the origin of focal ATs.

P2424 | BEDSIDE
Association of initial and terminal ventricular activation velocity ratio on 12-leads electrocardiography with myocardial scar presence

S. Priyantoro, Y. Yuniadi, M. Kasim. National Cardiovascular Center Harapan Kita, Jakarta, Indonesia

Background: Fibrotic scar tissue post infarction may potentially lead to fatal arrhythmias, recurrent ischaemia, heart failure, and sudden cardiac death (SCD). Cardiac magnetic resonance (CMR) is still a gold standard which cannot be applied to every patient. A 12-leads electrocardiography (ECCG) might be an alternative for detecting myocardial scar which is widely available.

Purpose: Initial and terminal ventricular activation velocity ratio (vi/vt) on surface ECG is a fourth step on Verecke criteria to differentiate wide complex tachycardia. The aim of this study is to evaluate the association of this criteria with myocardial scar presence.

Methods: This is a cross-sectional study. A consecutive subjects who underwent CMR during January 2013 and August 2014 were included. Myocardial scar were analyzed visually using late gadolinium enhancement CMR. Vi/vt on 12-leads ECG was measured manually on each lead and mean of each contiguous leads analyzed. The vi/vt only in mixed scar in each territory according to contiguous leads. A cut-off value ≤ 0.12 mV of vi/vt in IV-V5 leads with 71.4% sensitivity and 75.5% specificity and a cut-off value ≤ 0.12 mV of vi/vt in II, III, aVF leads with 69.4% sensitivity and 66.7% specificity were obtained by ROC analysis.

Conclusions: Vi/vt on 12-leads ECG associated with myocardial scar presence and location. A value of vi/vt 1.20–1.35 mV associated with myocardial scar presence in LAD territory and RCA territory with 69.4–71.4% sensitivity and 66.7–75% specificity.

ANTIBRADYCARDIA PACING

P2425 | REDUCTION IN BEDSIDE
Reduction in unnecessary ventricular pacing fails to affect hard clinical outcomes: A meta-analysis

M. Shurrab1, G. Bott0, S. Connelly2, B. Arouny3, D. Newman1, G. Boriani4, L. Padeletti5, J. Healey6, E. Crystal7, S.unnybrook Heart Centre, Toronto, Canada; 3SaintAnna Hospital, Como, Italy; 4Population Health Research Institute, Hamilton, Canada; 4University of Bologna, Bologna, Italy; 1University of Florence, Florence, Italy

Introduction: Several pacing modalities have been introduced to minimize unnecessary right ventricular pacing.

Purpose: We conducted a meta-analysis to assess whether ventricular pacing reduction modalities (VPMM) influence accepted hard clinical outcomes in comparison to standard dual-chamber pacing (DDD).

Methods: An electronic search was performed using Cochrane central database, Pubmed, Embase, and Web of Knowledge. References were searched manually. Only randomized controlled trials (RCT) were included. Outcomes of interest were: percentages of ventricular pacing (VP), incident of atrial fibrillation (AF)/atrial tachycardia (AT), all cause mortality (including cardiac death) and cardiovascular (CV)/heart failure (HF) hospitalizations. Continuous variables were expressed as weighted means. Odds ratios (OR) were reported for dichotomous variables.

Results: Five RCTs involving 3470 adult patients were identified. VPMM were employed in 1737 patients (MVP (Medtronic) in 1423 and SafeR (Sorin) in 314 patients). Baseline demographics and clinical characteristics were similar between VPMM and DDD groups (Age: 73±1.9 vs. 73±1.5 years, P=0.1; Male gender: 54% vs. 53%, P=0.9 and LVEF: 58±4.4 vs. 57±4.0%, P=0.7). There was no difference between 12–36 months. VPMM showed significant reduction in VP in comparison to DDD groups (7% vs. 85%, P<0.001). The incidence of AF/AT was similar between both groups (14% vs. 15%, OR 0.98 (95% confidence interval [CI) 0.61; 1.30), P=0.56). VPMM showed no significant differences in comparison to DDD for all cause mortality or CV/HF hospitalizations (5% vs. 6%, OR 0.86 (95% CI 0.62; 1.19), P=0.35; 9% vs. 9%, OR 0.94 (95% CI 0.72; 1.22), P=0.64, respectively).

Conclusion: Novel VPMM significantly reduced VP in comparison to standard DDD. When actively programmed, VPMM did not improve clinical outcomes and were not superior to standard DDD programming in reducing incidence of AF/AT, all cause mortality or CV/HF hospitalizations.

P2426 | BEDSIDE
Heart-related quality of life improvement following transcatheter pacemaker system implantation

R.E. Knops1, F.V.Y. Tjong1, J.R. De Groot1, C. Waweru2, K. Stromberg2, R.E. Knops1, F.V.Y. Tjong1, J.R. De Groot1, C. Waweru2, K. Stromberg2, M. Shurrab1, G. Bott0, S. Connelly2, B. Arouny3, D. Newman1, G. Boriani4, L. Padeletti5, J. Healey6, E. Crystal7, S.unnybrook Heart Centre, Toronto, Canada; 3SaintAnna Hospital, Como, Italy; 4Population Health Research Institute, Hamilton, Canada; 4University of Bologna, Bologna, Italy; 1University of Florence, Florence, Italy

Background: Transcatheter pacemaker systems (TPS) provide a novel, less invasive approach in which a minimally invasive, ‘leadless’ pacemaker is implanted in the right ventricle using a percutaneous transfemoral route. Compared to conventional pacing systems, TPS mitigates complications related to the lead and pocket, preserve left ventricular function, and may prompt improvements in patient Health Related Quality of Life (HRQOL) as well as reducing acute mobility restrictions. To date, the HRQOL impact from TPS therapy is unknown.

Purpose: To evaluate short-term HRQOL impact of TPS following implantation.

Methods: Between December 2013 and August 2014, 60 patients with an indication for a single chamber ventricular pacemaker were implanted with TPS and completed a 3-month follow-up visit in an ongoing global, multi-center, single-arm clinical trial. HRQOL impact of TPS was evaluated using SF-36 data collected at baseline (pre-implant) and at 3 months. Patient satisfaction with recovery, activity level, and aesthetic appearance at 3 months post-implant was assessed using a 3-item questionnaire.

Results: The mean age of the implanted cohort was 77 years (range: 21–94) and 61% were male. Of the 60 patients with a follow-up visit, 58 (97%) completed the SF-36 at baseline and at 3 months. Improvements were observed in all SF-36 domains including physical function, role function and mental health, and all attained statistical significance except for bodily pain (Table). In addition, 96.6%, 84.7%, and 69.5% of patients were satisfied/very satisfied with their aesthetic appearance, recovery, and level of activity respectively.

Conclusion: TPS resulted in HRQOL improvements, and majority of patients experienced treatment satisfaction by 3 months post-implant.
SF-36 results at baseline and at 3 month.

### SF-36 domain

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mortality (n=160)</th>
<th>Survival (n=875)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>76±17.6</td>
<td>74±11.6</td>
<td>0.062</td>
</tr>
<tr>
<td>Male gender</td>
<td>103 (64.4%)</td>
<td>562 (64.2%)</td>
<td>0.972</td>
</tr>
<tr>
<td>Dual chamber pacing</td>
<td>110 (68.8%)</td>
<td>718 (82.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>114 (71.3%)</td>
<td>631 (72.1%)</td>
<td>0.823</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>57 (35.6%)</td>
<td>248 (28.3%)</td>
<td>0.063</td>
</tr>
<tr>
<td>Heart failure, n (%)</td>
<td>54 (33.8%)</td>
<td>166 (19.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vascular disease, n (%)</td>
<td>19 (11.9%)</td>
<td>50 (5.7%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Stroke/TIA, n (%)</td>
<td>30 (18.1%)</td>
<td>66 (7.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CKD, n (%)</td>
<td>5 (3.1%)</td>
<td>55 (6.3%)</td>
<td>0.115</td>
</tr>
<tr>
<td>ESPR, n (%)</td>
<td>19 (11.9%)</td>
<td>55 (6.3%)</td>
<td>0.012</td>
</tr>
<tr>
<td>Malignancy, n (11%)</td>
<td>32 (20.0%)</td>
<td>96 (11.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHADS2 score</td>
<td>2.4±1.3</td>
<td>2.0±1.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHA2DS2-VASc score</td>
<td>3.8±1.5</td>
<td>3.2±1.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Results:

- The CHADS2 and CHA2DS2-VASc scores were significant predictors of mortality with an adjusted HR of 1.316 and 2.256 per 1 increment of the CHADS2 and CHA2DS2-VASc scores, respectively.
- The CHADS2 and CHA2DS2-VASc scores can be used for predicting long-term outcome in AVB patients undergoing PPM.

### Conclusions:

- We demonstrated that both CHADS2 and CHA2DS2-VASc scores can be used to predict the long-term outcome in AVB patients undergoing permanent pacemaker implantation.

**P2427 | BEDSIDE**

Using the CHADS2 and CHA2DS2-VASc scores for prediction of long-term outcome in patients with atrioventricular block undergoing permanent pacemaker implantation

J.-N. Liao1, T.F. Chao2, T.C. Tsai3, S.A. Chen1, T. Taipeh Veterans General Hospital, Taipei, Taiwan, ROC

**Background:** Long-term survival for patients with atrioventricular block (AVB) undergoing permanent pacemaker (PPM) has been discussed and several risk factors were found. However, a comprehensive model for risk stratification is lacking. Therefore we aim to test whether the CHADS2 and CHA2DS2-VASc scores could be used to predict the long-term outcome.

**Methods:** From 2000 to 2013, a total of 1,035 patients with AVB undergoing PPM implantations were followed with a duration of 46.5±43.2 months. The study enrolled patients submitted to the hospital for the first time and not submitted to prophylactic pacemaker implantation.

**Results:** The mean ages were 74.9±11.0 years and 64% were men. During the follow-up, 160 patients expired with an annual incidence of 4.0%. The CHADS2 and CHA2DS2-VASc scores were higher in subjects with mortality. Besides, patients with AVB undergoing PPM implantation among pts submitted to LT. Kaplan-Meier and multivariate Cox regression analysis were considered for the decision making of PPM implantation.

**Conclusions:** We demonstrated that both CHADS2 and CHA2DS2-VASc scores can be used for predicting long-term outcome in AVB patients undergoing PPM.

**P2428 | BEDSIDE**

Progression of cardiac conduction abnormalities in patients with familial amyloid polyneuropathy after liver transplantation


**Background:** Amyloid infiltration often leads to disturbances of cardiac conduction in patients with V30M transthyretin familial amyloid polyneuropathy (FAP). Liver transplantation (LT) inhibits the hepatic production of the abnormal protein and attenuates the progression of neurological dysfunction, but its impact on cardiac involvement remains controversial.

**Methods:** To evaluate the progression of cardiocentric cardiac tissue dysfunction by analyzing the need of pacemaker implantation during long-term follow-up in PAF patients (pts) submitted to LT.

**Results:** From a total population of 284 PAF patients, 101 underwent LT during follow-up (51% males). Of these, 58 pts underwent prophylactic pacemaker implantation prior to LT. Prophylactic pacemaker implantation did not influence the perioperative or long-term mortality (log rank P=0.451). Among the 43 pts not submitted to prophylactic pacemaker implantation, 15 (35%) had the implant performed during follow up due to new onset cardiac conduction defects and the probability of being required pacemaker implantation reached 42% at 10 years follow-up. No patient remained free of pacemaker at 20 years after the LT.

**Conclusion:** LT does not prevent the progression of cardiacocentric tissue dysfunction. However, the prophylactic pacemaker implantation is not widely justified. Indeed, the probability of cardiac conduction dysfunction occurrence during the lifetime of the pacemaker generator (assuming a median battery longevity of 10 years) will only be 42%. Better risk markers are needed to identity PAF pts at risk of perioperative bradycardiasms.

**P2429 | BEDSIDE**

Independent predictors of permanent atrioventricular block after transcatheter aortic valve replacement

N. Badenho1, R. Frank1, C. Maupain1, C. Nguyen2, G. Dutho1, P. Leprin1, G. Lebret1, O. Barthelyami2, E. Gandjbakhch1, J. Collet1, A.P.-HP - Hospital Pitie-Salpetriere - Institute of Cardiology, Rhythmology Department, Paris, France

**Introduction:** Atrioventricular block (AVB) is common after transcatheter aortic valve replacement (TAVR) and permanent pacemaker (PPM) implantation is needed in up to 30% of patients. Whether these high degree periplicative AVB are permanent or transient and PPM implantations clinically relevant remains debated.

**Purpose:** To identify periplicative electrocardiographic predictors of long term AVB.

**Methods:** Patients who underwent TAVR at our center between 2013 and 2014 were considered. Patients with PPM at the time of TAVR were excluded. His bundle recording was performed before and after TAVR and repeated at day 2 for Edwards Sapiens (ES) valves and day 5 for Medtronic Corevalue (CV), indication for PPM was high degree AVB occurring before day 5 or prolonged HV interval >80 ms at the last recording. Occurrence of high degree AVB after discharge was evaluated on pace maker interrogation, clinical and electrocardiographic findings at 1 month and 6 months.

**Results:** Data was obtained in 86 patients (66% CV and 34% ES). PPM were implanted in 29 patients (34%) who already documented AVB (n=11, 18.7%), or prolonged HV interval (n=8) or sick sinus syndrome (n=3). High degree AVB was observed after discharge in 12 patients (13.9%). The only periplicative predictive factor for AVB was the presence of RBBB (p=0.001). The occurrence of AVB during the procedure and the implantation of CV model were the other periplicative factors associated with long term occurrence of high degree AVB on multivariate analysis (p=0.001 and p=0.03 respectively). Post-operative ECG findings were not associated with the occurrence of late AVB including post TAVR LBBB (p=0.8) and repeated EPS findings (last HV interval, p=0.91). The absence of AVB and narrow GRS at the end of the TAVR was correlated with an absence of delayed post-operative AVB.

**Conclusion:** Preoperative RBBB, the use of Corevalue model and periplicative high degree AVB are the 3 independent factors for late AVB and should be considered for the decision making of PPM implantation.

**P2430 | BEDSIDE**

Left ventricular only pacing is a feasible and safe way to avoid tricuspid valve injury in patients with pre-existent tricuspid valve disease or surgery

T.W. Lim, W.T. Yeo, D. Singh, S.C. Seow, P. Kojodjojo. National University Hospital, National University Heart Centre, Singapore, Singapore

**Background:** Conventional right ventricular pacing is increasingly recognised to cause tricuspid valve (TV) injury or dysfunction, in part due to the need to pass the lead through the valve. This may be especially problematic in patients with pre-existing TV disease or prior TV surgery. Contemporary left ventricular (LV) pacing leads used in biventricular pacemakers or defibrillators have much reduced dislodgement rates and may be a viable alternative for ventricular pacing in these patients without having to pass a lead through the TV.

**Purpose:** We aimed to demonstrate the safety and feasibility of implanting an LV lead in place of a conventional right ventricular pacing lead.

**Methods:** We report a series of 13 patients (age 69±10 years old, 7 female) who had moderate or severe tricuspid regurgitation (TR, n=10), TV repair or annuloplasty (n=2) or a bioprosthetic TV (n=1) requiring annuloplasty. No patient had moderate or severe tricuspid regurgitation (TR, n=10), TV repair or annuloplasty (n=2) or a bioprosthetic TV (n=1). Three patients underwent TV repair (n=2) or annuloplasty without a right atrial lead (n=6). Patients were followed for a median of 297 days (IQR 96–454 days) to determine lead performance.

**Results:** The LV lead was placed in the lateral (n=5), posterolateral (n=2), anterolateral (n=4) or middle cardiac vein (n=2) branches of the coronary sinus. LV lead sensed R wave amplitude was 11.8±7.1mV, impedance was 983±278 Ω and lead threshold was 1.2±0.3V @ 0.5ms at implantation and duration of TV injury was not associated with the occurrence of late AVB including post TAVR LBBB (p=0.8) and repeated EPS findings (last HV interval, p=0.91). The absence of AVB and narrow GRS at the end of the TAVR was correlated with an absence of delayed post-operative AVB.

**Conclusion:** Preoperative RBBB, the use of Corevalue model and periplicative high degree AVB are the 3 independent factors for late AVB and should be considered for the decision making of PPM implantation.
stable. One patient had phrenic nerve capture that was managed successfully by adjusting the pacing output. LV dimensions were unchanged with a trend towards improved LV ejection fraction 6 months after implantation (51±7% vs. 56±19%; p<0.09).

Conclusion: LV lead only pacing is feasible and appears safe on short term follow up. In patients with significant TV disease or prior TV surgical repair who require pacing, this may be a viable alternative to standard right ventricular pacing leads. It may reduce the risk of TV injury and does not appear to degrade LV function.

P2431 | BEDSIDE
Eight years experience in permanent pacemaker implantation after open heart surgery
K.O. Yazdani, A. Yaminsharif, A. Shafee, A. Kazemisaedeh, H.A. Tafti. Tehran Heart Center, Tehran, Iran (Islamic Republic of)
Purpose: This study aimed to evaluate the prevalence of permanent pacemaker (PPM) implantation among patients who underwent open heart surgery and its predisposing factors.

Methods: We reviewed data of 25115 patients undergoing open heart surgery between 2006 and 2014 in our heart centre in Iran. Totally, 18070 (72%) patients had coronary bypass graft surgery (CABG), 3598 (14.5%) valvular surgery and 3447 (13.5%) redo surgery or congenital repair procedures. Patients requiring PPM implantation in the same admission were included. Patients who underwent PPM implantation had record of their indication before surgery and those who underwent the implantation of other devices after surgery were excluded.

Results: One hundred and thirty-five (0.53%) patients required PPM implantation (mean age= 58±15.3 years). Mean hospitalization time after surgery was 19.7±10.03 days, and waiting time for PPM implantation was 11.3±6.24 days. Cross-clamp time and bypass time were 84.4±44.9 and 132.6±64.4 minutes, respectively. The incidence of mechanical complications between the isolated CABG group (0.13%) and the CABG group with concomitant isolated valvular (2.6%) or isolated CABG and valvular (2.6%) groups in PPM requirement after surgery. Prevalence of PPM implantation had no significant difference between the two subgroups of mitral valve replacement (MVR) and aortic valve replacement (AVR) (2.5% vs. 2.7%), and nor was there any significant difference when AVR was added to MVR (3.6%).

Purpose: To compare the hemodynamic and electrocardiographic response to RVOTp, RVAp and LVp.

Methods: Prospective observational study in patients with permanent atrial fibrillation and left ventricular ejection fraction <40%, undergoing cardiac resynchronization therapy implantation. One RV lead was implanted conventionally in the RVA and another in the RVOT under fluoroscopic guidance to ensure proper lead positioning in the septum wall (RVS). An LVC epicardial lead was implanted through the coronary sinus. Within 1 month after implantation, all patients underwent minimum invasive hemodynamic assessment using the VigileoTM/Flotrac IIITM (Edwards Lifesciences, Irvine, USA) for the determination of cardiac output in the following pacing configurations: RVS, RVAp or LVp. Mean QRS width was also calculated for each configuration.

Results: We included 35 patients (91% males, 71±10 years old) and a total of 91 hemodynamic and 93 electrocardiographic evaluations were performed. In the paired-samples analysis, RVS significantly increased the cardiac index when compared with RVAp (p=0.001) – table. There was no significant hemodynamic difference between RVS and LVp or between RVAp and LVp. Pairwise analysis showed that RVSp significantly decreased the mean QRS duration when compared to RVAp and LVp (p<0.001, for both) - table.

Hemodynamic and ECG results

<table>
<thead>
<tr>
<th>RVS</th>
<th>RVA</th>
<th>LV</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVESDd (cm)</td>
<td>2.40±0.46</td>
<td>2.40±0.42</td>
</tr>
<tr>
<td>LVEF (EF)</td>
<td>60.1±10.7</td>
<td>60.2±10.7</td>
</tr>
<tr>
<td>Longitudinal strain</td>
<td>2.4±0.3</td>
<td>2.4±0.3</td>
</tr>
<tr>
<td>P-value</td>
<td>0.01</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusion: In patients with atrial fibrillation and LV dysfunction, RVSp is hemodynamically superior to conventional RVAp and is associated with narrower QRS complexes, which may translate in improved electro-mechanical synchrony.

P2434 | BEDSIDE
Procedural safety and long-term follow-up after pacemaker implantation in nonagenarians

Background: The rate of pacemaker (PM) implantations is continuously growing. Given that life expectancy of the population is projected to increase, a large number of nonagenarian patients will be implanted in the future.

Purpose: We aimed at analyzing the short and long-term outcome after PM implantation in this population.

Methods: Patients aged ≥90 yo referred for PM implantation from 2004 to 2014 were retrospectively included. The primary clinical endpoint was total mortality. Secondary endpoints included early and delayed-procedure related complications, and predictive risk factors of total mortality.

Results: 113 patients were included (92±6.2±10yo). Duration of the procedures was 53±11±7 min. Most of the patients had VVI devices implanted (89 pts, 78.8%). Mean hospital stay was 4.9±3.9 days. Five patients (3.5%) had short-term device-related complications (3 pocket hematoma, 1 lead displacement and 1 hemorrhax), and 16 patients (14.2%) had post-procedural complications, non-

Table 1

<table>
<thead>
<tr>
<th>RVS vs. RVA</th>
<th>RVS vs. LV</th>
<th>RVA vs. LV</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS width (msec)</td>
<td>159±21.7</td>
<td>189±18.9</td>
</tr>
<tr>
<td>P-value</td>
<td>0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: PM implantation in nonagenarians.
related to the implantation (acute heart failure, confusion, stroke, pulmonary infection, renal failure). During the follow-up, 48 patients (42.5%) died. Survival rates were 77.4% (95% CI: 67.4–84.7%), 68.7% (95% CI: 57.4–77.6%) and 36.4% (95% CI: 23.3–49.7%) after 1, 2 and 5 years, respectively (Figure). Atrial fibrillation (OR 3.5, 95% CI: 1.6–7.2) and a cardiomyopathy (OR 2.3, 95% CI: 1.2–4.4) at the time of implantation were independent predictors of mortality.

**Conclusion:** PM implantation in nonagenarians is safe, with a low risk of procedural complications. However, many comorbidities-related complications can occur in this old and frail population.

**P2435 | BEDSIDE**

Standardised patient referral pathway improves outpatient waiting times for elective brady pacemaker implants in a tertiary care hospital

M. Jawad Ul Qamar. Sandwell and West Birmingham Hospitals NHS Trust, University of Birmingham Center for Cardiovascular Sciences, Birmingham, United Kingdom

**Background:** There are no established ESC/NICE guidelines for acceptable waiting times for elective pacemaker implants in bradyarrhythmias. A delay in elective pacemaker implant that is indicated per 2013 ESC guidelines for cardiac pacing can lead to potentially serious or life threatening implications such as syncope and serious injury, myocardial and cerebral ischemia due to low cardiac output, malignant ventricular arrhythmias andystolic cardiac arrest.

**Purpose:** An audit was conducted to look into the delays in the brady pacemaker implants that are indicated per ESC guidelines. Further objectives were to understand the reasons for delay and to formulate local guidelines to standardise the referral system for this patient population.

**Methods:** A total of 382 patients were assessed for pacing delays from 1st April 2012 to 31st October 2013. Out of these 162 received elective pacemaker implants (study population for the audit). Delay in pacing was counted from the day evidence to implant was recorded in the form of 12 lead ECG, holter, event recorder or implantable loop recorder. Delay was assessed in different steps as the delay in interpretation of evidence, the delay in referral to pacing cardiologist and the delay between referral and actual implant. An acceptable audit standard was devised as 90% of patients having the pacemaker implant with a total delay of less than 21 days.

**Results:** It was found that only 42 out of 162 patients (26%) achieved the audit standard of 21 days or less. In 85 (71%) of the 120 patients who did not meet the audit standard the main point of delay was in the referral and decision to implant the pacemaker. A standardisation patient referral pathway was hence devised to improve upon the waiting times. This involved designating the on call cardiologist to flag up the abnormal patient reports requiring brady pacing. An electronic referral system was also devised with alerts to the pacing consultants and the procedure booking team. A re-audit following the implementation of recommendations was done between 1st December 2013 to 30th April 2014 during which it was found that out of 25 patients receiving elective pacing implant for bradyarrhythmia 23 (92%) met the audit standard of 21 days or less. A discussion to improve upon the waiting times. This involved designating the on call cardiologist to flag up the abnormal patient reports requiring brady pacing. An electronic referral system was also devised with alerts to the pacing consultants and the procedure booking team.

**Conclusion:** The incorporation of audit recommendations in local cardiology guidelines has led to significant improvement in patient quality of care and potential reduction in risk of serious outcomes due to unnecessary delay in pacemaker implants.

**DEVICE COMPLICATIONS**

**P2436 | BEDSIDE**

Impact of catheter ablation for atrial tachyarrhythmias on inappropriate shocks in patients with implantable cardioverter defibrillator and cardiac resynchronization therapy-defibrillator


**Background:** An implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy-defibrillator (CRT-D) are effective in reducing mortality among patients with fatal arrhythmias, but inappropriate shocks are associated with an increased risk of all-cause mortality.

**Aims:** To evaluate the efficacy of catheter ablation (CA) of atrial tachyarrhythmias causing inappropriate shocks.

**Methods and results:** We retrospectively analyzed 502 patients who underwent ICD or CRT-D implantation in our institution between January 2004 and June 2016. Sixty-two patients (12.4%; mean age 65±13 years; 35 males; structural heart diseases in 41) experienced inappropriate shocks: 54 atrial tachyarrhythmias, 3 sinus tachycardias, 3 T-wave oversensings, 1 electrical noise due to lead fracture, and 1 other cause. Among 54 patients with atrial tachyarrhythmias (38 paroxysmal atrial fibrillations [AFs], 8 atrial tachycardias [ATs], 6 atrial flutter [AFLs], and 2 paroxysmal supraventricular tachycardias [SVTs]), 23 patients underwent RFCA (RFCA group). No procedure-related complications occurred. During a mean follow-up of 56±24 months after the last procedure, 22 (95.7%) out of the 23 patients did not experience any inappropriate shocks. In 31 patients without RFCA for atrial tachyarrhythmias (non-RFCA group), the factors for inappropriate shocks were managed by changing device mode and optimizing medical therapy. The Kaplan-Meier analysis and log-rank test that the survival rate from inappropriate shocks after the last ablation procedure in RFCA group and after management of inappropriate shock-related factors in non-RFCA group was shown below (Figure 1).

**Conclusions:** RFCA is a safe and effective management option for inappropriate shocks due to atrial tachyarrhythmias among patients with an ICD or CRT-D.

**P2437 | BEDSIDE**

Ambulatory pacemaker Implant and ablation procedures: A risk worth taking?

G. Varnero. Casmu Arrhythmia Service, Montevideo, Uruguay

**Background:** There are no guidelines recommending how long a patient should stay in observation and disposition after a standard pacemaker implant or a standard ablation procedure.

**Aims:** We designed a protocol to evaluate the safety of an ambulatory procedure after a pacemaker implant or after an AVNRT or typical flutter ablation versus in hospital observation for 24 hours.

**Methods:** 633 patients underwent first single or dual-chamber pacemaker implantation from Jan 2009 to Dec 2013. 62 (10.8%) were ambulatory procedures: We divided the population into two groups: Group A, patients were sent home after 3 hours of observation with a previous pacemaker check-up. Group B: patients were admitted and monitored for 24 hs. In both groups the implant technique was identical.

We performed 306 standard ablations (PVI- AF ablation were excluded from analysis), 68 (27%) patients were discharged after 4-hour observation period (group C). (98% of the ablations were AVNRT and typical atrial flutter) The rest of the patients 73% (group D) were admitted and monitored for 24 hs. After pacemaker implant, 15 min manual compression a regular dressing was placed on the homolateral shoulder. In the ablation group, a compressive dressing on the right groin was prepared after 15 min of manual compression. Follow-up was performed at 15 days, 3 and 6 months after procedure. Patients in groups A and C were carefully selected and a brochure and safety recommendations were given, including to family members. End-points: were: lead displacement, elevated pacing thresholds and pocket complications. In the ablation group: the presence of groin hematoma, and early arrhythmia recurrence.
Right heart vegetations (RHV) are the main signs of lead dependence and have been associated with morbidity and mortality. The aim of this study was to evaluate the influence of size of RHV on early effect of transvenous lead extraction (TLE) and long-term mortality after TLE. The comparative analysis of efficacy and safety of TLE in patients with RHV ≥2 cm (LDIE) and patients with smaller RHV (≤2 cm) was performed using data from videos and images. The analysis revealed that the presence and size of vegetations appear to be most important. Among patient-dependent factors, female gender was significantly associated with lower RHV size. Other factors like: patient’s age, kind of indications (infectious/non-infectious), NYHA class, EF, presence of permanent AF, previous inappropriate implantation strategy were also considered. The analysis showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for complications and worse outcome after TLE. The risk of complications was significantly higher in patients with RHV ≥2 cm (LDIE) compared to patients with smaller RHV. The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of lower survival rate after TLE. The analysis of long-term mortality after TLE revealed that the presence of RHV ≥2 cm (LDIE) was associated with a decreased survival rate. The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for adverse events (AAE) after TLE. The analysis of AAE revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for AAE, including systemic (18%) or local (45%) infection (Inf), lead malfunction (24%) (Malfx), or other indications (3%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for clinical complications (Clinical complications) after TLE. The analysis of clinical complications revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for clinical complications, including infectious (43%), venous (6%), and other (3%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for follow-up data collection (Follow-up data collection) after TLE. The analysis of follow-up data collection revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for follow-up data collection, including infective (45%), non-infectious (25%), and other (5%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for system activity (System activity) after TLE. The analysis of system activity revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for system activity, including infective (75%), non-infectious (25%), and other (0%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for other complications (Other complications) after TLE. The analysis of other complications revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for other complications, including infectious (45%), non-infectious (25%), and other (30%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for partial follow-up (Partial follow-up) after TLE. The analysis of partial follow-up revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for partial follow-up, including infective (45%), non-infectious (25%), and other (30%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for complete follow-up (Complete follow-up) after TLE. The analysis of complete follow-up revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for complete follow-up, including infective (75%), non-infectious (25%), and other (0%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for device complications (Device complications) after TLE. The analysis of device complications revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for device complications, including infectious (45%), non-infectious (25%), and other (30%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for other device complications (Other device complications) after TLE. The analysis of other device complications revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for other device complications, including infectious (75%), non-infectious (25%), and other (0%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for system activity (System activity) after TLE. The analysis of system activity revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for system activity, including infective (75%), non-infectious (25%), and other (0%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for other complications (Other complications) after TLE. The analysis of other complications revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for other complications, including infectious (45%), non-infectious (25%), and other (30%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for partial follow-up (Partial follow-up) after TLE. The analysis of partial follow-up revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for partial follow-up, including infective (45%), non-infectious (25%), and other (30%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for complete follow-up (Complete follow-up) after TLE. The analysis of complete follow-up revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for complete follow-up, including infective (75%), non-infectious (25%), and other (0%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for device complications (Device complications) after TLE. The analysis of device complications revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for device complications, including infectious (45%), non-infectious (25%), and other (30%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for other device complications (Other device complications) after TLE. The analysis of other device complications revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for other device complications, including infectious (75%), non-infectious (25%), and other (0%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for system activity (System activity) after TLE. The analysis of system activity revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for system activity, including infective (75%), non-infectious (25%), and other (0%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for other complications (Other complications) after TLE. The analysis of other complications revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for other complications, including infectious (45%), non-infectious (25%), and other (30%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for partial follow-up (Partial follow-up) after TLE. The analysis of partial follow-up revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for partial follow-up, including infective (45%), non-infectious (25%), and other (30%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for complete follow-up (Complete follow-up) after TLE. The analysis of complete follow-up revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for complete follow-up, including infective (75%), non-infectious (25%), and other (0%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for device complications (Device complications) after TLE. The analysis of device complications revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for device complications, including infectious (45%), non-infectious (25%), and other (30%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for other device complications (Other device complications) after TLE. The analysis of other device complications revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for other device complications, including infectious (75%), non-infectious (25%), and other (0%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for system activity (System activity) after TLE. The analysis of system activity revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for system activity, including infective (75%), non-infectious (25%), and other (0%). The analysis also showed that the presence of RHV ≥2 cm (LDIE) could be an indicator of higher risk for other complications (Other complications) after TLE. The analysis of other complications revealed that the presence of RHV ≥2 cm (LDIE) was associated with a higher risk for other complications, including infectious (45%), non-infectious (25%), and other (30%).
P2441 | BEDSIDE
Exterenalization of ICD leads, not only riata problem
A. Maciag1, P. Syka1, M. Sterlinski1, A. Kolodzinska2, A. Przybylski1,
K. Kusmierski1, A. Oreziak1, H. Szwed1. 1 National Institute of Cardiology, Warsaw, Poland; 2 Medical University of Warsaw, Warsaw, Poland

Introduction: The increasing number of patients (pts) with implantable cardioverter-defibrillators (ICD) causes a rise in the absolute number of patients qualifying for a transvenous lead extraction (TLE) because of infectious, vascular or lead failure related indications. One of the mechanisms of lead failure is externalization of conductor in ICD leads. Early diagnosis before surgery may help in planning of TLE.

Purpose: Authors provide the retrospective analysis of the occurrence of externalization in TLE patients.

Methods: Between 2012 and 2014 we performed TLE of 428 electrodes in 259 pts. Out of these, 143 (33.4%) leads in 137 (52.9%) pts were ICD leads. Indication for TLE in the subgroup were infection in 37 pts., lead failure 84 pts., other including late perforation, venous system obstruction, dislocation in 16 pts. We reviewed ICD patients records looking for externalization of conductor in extracted ICD leads.

Results: Externalization was revealed in 8 ICD leads (5.6%) in 8 pts (5.8%) (Fig. ABC). The mean dwelling time for externalized electrodes (8 items) was 87.8 months (55 to 132) compared to the rest of the ICD leads (129 items) 59.9 months (3 to 246). There were (dwelling time in brackets - months): one SPL (132 m.), one Kainox RV (126 m.), one Linox (57 m.), one Riata ST (71 m.) and four Riata (98, 35, 33, 57 m. respectively) leads. All externalized leads were successfully extracted using device traction, mechanical telescopic sheaths and autotomization cutting sheaths.

Conclusion: Externalization is rather rare mechanism of lead failure and is met in different type of leads from different manufacturers. Transvenous lead extraction with the use of various endovascular techniques can be safely performed in this type of lead related complication.

P2442 | BEDSIDE
Clinical features and changes in epidemiology of infective endocarditis on pacemaker devices over a 27-year period (1987-2013)
University Hospital Reina Sofia, Cardiology, Cordoba, Spain

Background and aim of the study: Use of cardiac pacing devices has grown in recent years, leading to a notable increase in the rate of infection related to these devices, a complication with a high impact on morbidity and mortality of these patients. Our aim was to evaluate changes in epidemiology and clinical features of infective endocarditis involving pacemaker devices (IE-PM) in a large series of IE over the last 27 years (1987–2013).

Methods: From 1987 to December 2013, 413 consecutive IE cases were diagnosed in our hospital, according to Von Reyn and Durack criteria. During this period, 7424 PM devices were implanted (6917 PM, 239 AIDs, 158 CRT devices and 110 CRT/AID). All consecutive cases of IE-PM were selected. Changes in incidence, clinical features, management and prognosis were analyzed.

Results: IE-PM incidence was revealed in 8 ICD leads (5.6%) in 8 pts (5.8%) (Fig. ABC). The mean dwelling time for externalized electrodes (8 items) was 87.8 months (55 to 132) compared to the rest of the ICD leads (129 items) 59.9 months (3 to 246). There were (dwelling time in brackets - months): one SPL (132 m.), one Kainox RV (126 m.), one Linox (57 m.), one Riata ST (71 m.) and four Riata (98, 35, 33, 57 m. respectively) leads. All externalized leads were successfully extracted using device traction, mechanical telescopic sheaths and autotomization cutting sheaths.

Conclusion: Externalization is rather rare mechanism of lead failure and is met in different type of leads from different manufacturers. Transvenous lead extraction with the use of various endovascular techniques can be safely performed in this type of lead related complication.

P2443 | BEDSIDE
Detection of Cardiovascular Implantable Electronic Device Infections with Sonication Following Lead Extraction and Generator Change
B.L. Nguyen1, H. Olivera1, A.L. Di Giambartolomeo1, M.T. Mascellino2, A. Cipolla3,
N. Alessandri2, C. Gaudio1, A. Ciccaglioni1, C.M. Mastroianni2, V. Vulli3,
1 Umberto I Polyclinic of Rome, Department of Cardiovascular, Respiratory, Nephrological & Geriatric, Rome, Italy; 2 Sapienza University of Rome, Infectious Disease, Rome, Italy; 3 Sapienza University of Rome, Latina Polo Pontino Sapienza University of Rome, Latina, Italy

Introduction: Cardiovascular implantable electronic device (CIED) infections are increasing, and often associated with a previous CIED-related procedure. They are not well characterized and their clinical presentation deserves further studies. Symptoms of cardiac devices showed higher sensitivity than traditional culture in the diagnosis of CIED infections.

Purpose: The aim of the study was to assess the role of sonication to detect the causative agents of CIED infections after explantation of infected devices and “non-infected” generator changes.

Methods: Patients who underwent complete CIED explantation because of infection (36) and who removed cardiac devices for generator change in the absence of infection (43) were prospectively included in the study. All patients received anti-tibiotic prophylaxis at the time of device removal. Diagnosis of CIED infection was made based on clinical findings. After collection, devices were processed and BactoSonıc was used for sonication. Anaerobic and aerobic blood agar plates were incubated at 37°C for 10 days and microorganisms were identified using conventional methods. The number of CFU/mL was obtained for each collected device.

Results: A definite microbiological diagnosis was achieved in 77.8% of patients with infection whereas 9% of subjects without infection showed bacterial growth. Coagulase-negative Staphylococci (CoNS) (75%), Staphylococcus aureus (10%), Gram-negative bacilli (13%) and fungal infection (10%) were found in the subjects with infection. The specificity of sonication method was 91% with a positive predictive value of 87%. Subjects with infection had higher CFU/mL compared to subjects without infection (5x10^4 vs. 2x10^3 CFU/mL, p < 0.001). A cut-off value of 5x10^2 CFU/mL better identified subjects with infection from those without infection (AUC 0.83; 95% CI 0.73–0.93, p < 0.0001).

Conclusions: Sonication before culture was able to identify CoNS as the most represented pathogens, asymptomatic bacterial colonization, a bacterial amount cut-off that might differentiate infection and non-infection. The role of sonication to assess the risk of future infections following CIED-related procedures and improve preventive antibiotic therapy requires extensive validation.

P2444 | BEDSIDE
Risk factors, presentation, treatment and consequences of cardiac device infections; a retrospective analysis
A. Eksi, S. Yuksel, S. Demircan, A. Erbay, H. Zengin, K. Soylu, O. Yilmaz,
M. Sahin. Ondokuz Mayis University, Faculty of Medicine, Department of Cardiology, Kurupelit-Samsun, Turkey

Background: the rate of cardiac device implantations is increasing with aging of the general population and expanding indications. Along with the increase in device implantation, the incidence of cardiac device infection (CDI) has also been increasing, but at a faster rate. In the current literature; the rate of infections ranged from 0.8 to 5.7%.

Purpose: In this study, the risk factors, presentation, procedural and clinical data and follow-up results of patients with CDI were analyzed retrospectively.

Methods: Between 2005–2014, cardiac device implantations were performed in 1705 patients. The demographic, clinical and laboratory data of these patients were reviewed from the patient database. Patients with CDI were compared with a control group with similar demographic characteristics for further risk factor analysis.

Results: Seventy-one (4%) patients with CDI (mean age 70±13, 53 (75%) male) were identified from the patient database. Compared to control group, the number of patients with heart failure (72% vs. 46%) and implanted CRT devices (54% vs. 30%) were significantly higher in patients with CDI (p values 0.008 and 0.015, respectively). The Charlson Comorbidity indexes of both groups were not significantly different (p = 2.5; p=0.14). The most common site of infections was pacemaker pocket. Localized erythema, edema and temperature increase were the most common symptoms on admission. Positive blood and exudate cultures were found in 32 (45%) CDI patients. The most common microorganism isolated was Staphylococcus species (mainly S. epidermidis) from the cultures. The history of recent manipulation of device and leads was present in 22 (26%) patients. The recurrent infections (23%) were also more common in patients with heart failure and CRT devices. The patients in whom device systems were completely explanted had a higher risk for recurrent infections (23%) than patients with infected leads (18%). The recurrent infections (23%) were also more common in patients with heart failure (72% vs. 46%) and implanted CRT devices (54% vs. 30%).

Conclusion: In this retrospective analysis, the presence of heart failure and implantation of a CRT device were found as important risk factors for development of CDI. In conclusion, appropriate antibiotic therapy should be taken before TLE and it is recommended to consider the cardiac device implantations. In patients with CDI, extraction of the whole device system with administration of proper antibiotics were found to be best measures to prevent recurrent infections.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475 by guest on 07 February 2019
P2446 | BEDSIDE
Transvenous leads extraction- analysis of factors influencing long-term mortality after procedures
A. Polewczyk1, W. Jachec2, G. Opolski3, M. Grabowski3, M. Janion1, A. Kutarski1, S. Swietokrzyskie Cardiology Center II Cardiology Dept, The Jan Kochanowski University, Dept of Health Sciences, Kielce, Poland; 2Silesian Medical University II Department of Cardiology, Zabrze, Poland; 3Medical University of Warsaw, 1st Department of Cardiology, Warsaw, Poland; 4Medical University of Lublin, Department of Cardiology, Lublin, Poland
Background: Transvenous leads extraction (TLE) is a procedure increasingly performed in patients with infectious complications or dysfunctions of the leads.
Methods: Analysis of clinical data of 1426 patients underwent TLE in single Center in years 2006-2013 was conducted. Demographic, comorbid, and procedural risk factors potentially influenced on mean 2.78 years mortality after procedures were assessed.
Results: Univariable Cox regression analysis showed that statistically significant negative survival impact presented: older age - increased mortality by 2.5% per each year, diabetes [HR=1.719; 95% CI 1.300–2.274], renal failure [HR=2.524; 95% CI 1.925–3.310], artificial valve [HR=1.012; 95% CI 1.001–1.023] LDIE presence [HR=1.925; 95% CI 1.501–2.468], the need of remove of ICD leads (due to its dysfunction or LDIE): [HR=1.298; 95% CI 0.990–1.701], CS lead [HR=1.489; 95% CI 1.112–1.992] previous pocket interventions [HR=1.200; 95% CI 1.019–1.413] and amount of the leads [HR=1.195; 95% CI 1.038–1.382; p=0.013]. Female gender and loop of the lead in atrium (as a reason of TLE) were associated with better prognosis (reduction of risk of death by 25.4% and 44.1% respectively. In multivariable Cox regression analysis was shown the key negative role of LDIE [HR=1.860; 95% CI 1.431–2.419], ICD lead [HR=1.588; 95% CI 1.167–2.161], older age at time of TLE [HR=1.035; 95% CI 1.027–1.049], artificial valve [HR=1.017; 95% CI 1.005–1.028], diabetes [HR=1.392; 95% CI 1.046–1.853], and renal failure [HR=2.168; 95% CI 1.624–2.890]. The presence of loop of the lead in atrium was connected with better prognosis by (41%).
Conclusions: The most important factor determining long term mortality after TLE was presence of cardiac device infection, especially LDIE. The significant role of older age and comorbidities: diabetes, renal failure, artificial valve presence was also demonstrated. Better prognosis in patients with loop of the lead in the atrium showed that TLE due to noninfectious complications is a procedure potentially improving survival.

P2447 | BEDSIDE
Five-years microbiologic characteristic of patients with complications of electrotherapy
R. Mlynarski1, A. Mlynarska2, R. Kaczkowski2, E. Pilai1, J. Wilczek1, J. Biernat1, M. Sosnowski2, K.S. Golba2. 1Upper-Silesian Cardiology Center, Katowice, Poland; 2Medical University of Silesia, Katowice, Poland
Infective complications of electrotherapy are still the problem. Knowledge about pathogens, place of infections and response pathogens for antibiotics are analyzed.
Methods: During 5 years 875 microbiological tests were taken in 293 patients (3.41% population). In 302 (34.5%) tests pathogens were identified. The most frequent pathogens were: Staph. epidermidis (9,14%), Staph. aureus (4,22%), S. pneumoniae (2,37%), H. influenzae (1,87%). Staph. aureus (1,48%), and Enterococcus fecalis (1,37%), 20 pathogens (2,51%) were found incidentally (1–2 times during 5 years). Cumulative response of 7 of the most frequent pathogens for selected antibiotic is presented in the table. Changes in the timeline were found for Staph. epidermidis (Chi2 p=0.002), Staph. hominis (Chi2 Yates p=0.032) and Enterococcus fecalis (Chi2 Yates p=0.045). Most of pathogens were sensitive for Vancomycin and Tigeceycin and some of them for Trimethoprim with Sulfametoksazol.
Conclusions: Constant monitoring of variation of the sensitivity of pathogens to antibiotics over the time in individual cardiac pacing centers seems to be necessary.

NON-INVASIVE STUDIES

P2448 | BEDSIDE
A novel 3-directional magnetocardiographic approach can disclose left ventricular intraventricular conduction delay in dilated cardiomyopathy patients with narrow QRS
S. Kawakami1, H. Takaki2, S. Hashimoto1, T. Aiba1, K. Kusano1, H. Ogawa1, S. Yasuda1, S. Kamakura1, M. Sugimachi2, 1National Cardiovascular Center, Suita, Osaka, Japan; 2National Cerebral and Cardiovascular Center Research Institute, Suita, Japan
Background and purpose: Dilated cardiomyopathy (DCM) patients exhibit abnormal LV intraventricular conduction, possibly further deteriorating hemodynamics. However, there is no non-invasive tool for accurately estimating the electrophysiological abnormalities. Multi-channel magnetocardiography (MCG) is potentially useful for noninvasively evaluating cardiac activation with high spatiotemporal resolution. However until now, in most of the previous studies on MCG, measurements have been obtained only from the anterior side of the thorax or the subject supine. We hypothesized that using novel MCG approach with 3-directional recordings capable of delineating the whole heart activation and detect LV intraventricular conduction delay that is hardly discernible on ECG in DCM patients with narrow QRS duration (GRS<120ms). Methods: Using a 64-channel MCG system (Hitachi), we repeated 3 measurements with sensors placed close to anterior, posterior, and left lateral chest wall (supine, prone, and lateral positions, respectively) in 33 Controls (Cont) and 64 DCM patients with narrow QRS (GRS<97±10ms; LVEF, 30±12%). Results (Figure): Cont consistently showed initial septal activations followed by
two different electrical propagations (probably through left anterior and poste-
rior fascicles) leading to prompt completion of LV activation (LV conduction time; 
LVCT 54±5ms, QRS 91±10ms). Contrarily, DCM represented prolonged LVCT 
(78±12ms, p < 0.001; QRS 101±10ms, p = 0.001) and occasionally exhibited ap-
parently abnormal conductions. LVCT/QRSd in DCM was significantly larger than 
in control (78±12 vs 60±6%, p < 0.001).

Conclusion: Our new MCG approach may allow to evaluate abnormal intra-
ventricular conduction delay which is not discernible on ECG.

P2449 | BEDSIDE

The relationship between the repolarization parameters and serum electrolyte levels in patients with J-wave syndrome

N. Sato1, R. Sasaki2, M. Imahashi2, K. Saito2, A. Talib3, N. Sakamoto1, K. Akasaka4, S. Fuji4, Y. Kawamura5, N. Hasebe1. 1Asahikawa Medical University, Dept Internal Medicine, Cardiovascular, Respiratory & Neurology Div., Asahikawa, Japan; 2Asahikawa Medical University Hospital, Medical Laboratory, 1Asahikawa Medical University Hospital, Medical Laboratory, 4Asahikawa Medical University Hospital, Medical Laboratory, 5Asahikawa Medical University Hospital, Medical Laboratory

Background: The heterogeneity of ventricular repolarization across the ventric-
ular wall is reported to be important to initiate and perpetuate polymorphic ven-
tricular tachyarrhythmias, and intravenous magnesium (Mg) is effective for poly-
morphic ventricular tachycardia via homogenization of the transumeral ventricular 
repolarization. However, the relationship between the repolarization parameters 
and electrolyte levels in patients with J-wave syndromes is unknown. We hypothesized 
that Mg has some role or contributes to the heterogeneity of the repolarization in 
J-wave syndromes.

Objective: To investigate the relationship between the repolarization parameters 
and serum Mg, K, and Ca levels in J-wave syndromes.

Methods: Thirteen patients who met the diagnosis of J-wave syndrome (Bru-
gada and early repolarization [ERV] syndromes) with documented episodes of VF 
and thirteen ER pattern (ERP) or Brugada type ECG patients were enrolled (25 
males, mean age 48±15 years). The 12 lead ECG-derived parameters including 
the QT, QT dispersion (QTD), Tpeak-Tend (Tp-e) interval, Tp-e/Ca ratio, were calculated using the QT observer Version 3.0 
(Nihon Kohden, Tokyo, Japan). Then the correlation between those parameters 
and electrolytes including Mg, K, and Ca were analyzed. As for the cases whose 
electrolytes just after ventricular fibrillation (VF) could be measured, those values 
were also evaluated.

Results: The average QT maximum (max), QT minimum (min), QTd, Tpe-max, 
T-pe, and Tp-e/QTD were 405±35ms, 350±35ms, 54±19ms, 102±17ms, 20±11ms, 
and 0.25±0.04, respectively. The average serum K, Ca, and Mg concentrations 
were 4.10±0.27mEq/L, 9.4±0.28mg/dL, and 2.1±0.16mg/dL, respectively. Although 
there was no correlation between the serum K and Ca or TQd, there was a 
tendency for a negative correlation between the serum Mg and QTD in J-wave 
syndrome patients who had a history of VF (r=-0.513, p=0.072, n=13). On the 
other hand, in 13 patients with a Brugada type ECG or ERP, no correlation 
was observed between the serum Mg and QTD or Mg and Tp-ed. Furthermore, the 
serum K and Mg had relatively low values just after VF (3.2±0.4mEq/L, and 
1.97±0.6mg/dL, respectively).

Conclusion: The serum Mg and potassium levels may play an important role in 
the cardiac repolarization process in J wave syndromes.

Conclusions: TWD in non-aberrant PAC is common in LQTS patients and asso-
ciated with elevated TWA and a history of VTA.

P2450 | BEDSIDE

Noninvasive epi-endocardial imaging of cardiac arrhythmias

M.S. Klyshin, S.V. Popov, R.E. Batalov, S.N. Krivolapov. Research Institute of Cardiology SB of RAMS, Tomsk, Russian Federation

Aim of the study: The aim of this study was to compare the accuracy of the 
noninvasively obtained activation (using only epicardial and combined epi-
endocardial mapping) as compared with that of standard invasive procedure 
in patients with different arrhythmias.

Patient population: 94 patients in the age from 20 to 67 years with ventricular ar-
rhythmias and 8 patients in the age from 21 to 65 years with atrial arrhythmias 
were examined. All patients underwent noninvasive electrophysiological exami-
nation, which was performed with Amycard System (epicardial and endocardial 
imaging) and subsequent intracardiac mapping and radiofrequency catheter ab-
lation.

Results: According to the results of the combined epi-endocardial mapping 56 
patients had an arrhythmogenic substrate (AS) in the right ventricle outflow tract 
(RVOT); 3 - in the anterior-lateral wall; 7 - in the anterior wall of the RVOT; 20 - in 
the anterior-septal position of the RVOT; 3 - in the posterior-septal position of 
the RVOT; 23 - in the septal position of the RVOT; and 11 patients had AS in 
in the left ventricle outflow tract (LVCT); 2 - in the boarder of the right and the left 
sides of Valsalva; 3 - in the noncoronary sinus of Valsalva; 2 - in the right sinus 
of Valsalva; 4 - in the left sinus of Valsalva. The separate epicardial imaging had 
lower results. Only in 55 cases we accurately determined AS and in 12 patients 
we could suppose that AS was located in LVOT or RVOT. 6 patients had AS in 
in the right ventricle (RV); 2 - in the RV free wall; 1 - in the anterior-septal position 
of the RV middle parts and 3 - under the Tricuspid annulus, near the His bundle.

The separate epicardial imaging was correct in only 3 cases and in patients with 
parasite localization it was impossible to determine AS. 10 patients had AS in 
the left ventricle (LV) according to the results of the separate epicardial and 
combined epi-endocardial mapping: 4 - in the interventricular septum; 1 - in 
the anterior wall of the LV basal parts; 1 - in the posterior-septal wall of the LV 
basal parts and 3 - in the posterior wall of the LV basal parts. The same results we 
found during intracardiac mapping. In 11 patients we had discrepancies. In patients with atrial arrhythmias we didn’t have 
discrepancies (3 patients had the atrial extrasystole from the right atrium, 1 - from 
the anterior wall of the left atrium, and 4 had the atypical ishimum-dependent atrial 
flutter.

Conclusions: The accuracy of the noninvasive combined epi-endocardial map-
ing is 89.2%.

P2451 | BEDSIDE

T-wave deformation in non-aberrant premature atrial contractions: a novel indicator associated with T-wave alternans and a history of life-threatening arrhythmias in patients with long QT syndromes

N. Takasu1, H. Goto1, T. Kuwahara1, M. Takasugi2, H. Toyoshi1, T. Nakashima1, T. Kubota1, M. Kasakawa1, K. Nishigaki1, S. Minagouchi1, 1Gifu University Hospital, Division of Cardiovascular Medicine, Gifu, Japan; 2Gifu Prefectural General Medical Center, Gifu, Japan; 3Matsunami General Hospital, Gifu, Japan

Background: We hypothesized that the response of ventricular action potential duration (APD) to premature stimulus is intramurally heterogeneous in patients with long QT syndrome (LQTS), hence the T-wave morphology in premature atrial 
contractions (PAC) becomes deformed.

Purpose: To elucidate prevalence of T-wave deformation (TWD) in PAC and its 
relationship with T-wave alternans (TWA) and a history of life-threatening ventric-
ular tachyarrhythmias (VTA) in LQTS patients.

Methods: 24-hour 12-lead continuous electrocardiogram was recorded in 32 
LQTS patients. PACs with coupling intervals <80% of preceding sinus cycle 
length and without aberrant ventricular conduction were analyzed. Peak TWA 
was generated by the modified moving average method. The lead with the peak TWA 
values and with the greatest TWD was termed “max TWA lead” and “max 
TWD lead”, respectively.

Results: 3 patients were excluded from the analysis due to absence of analyzable 
PAC. Out of a total of 29 patients (12 male; 1 infant, 10 children, 10 adolescents, 8 
adults) with congenital LQTS types 1 (n=16), 2 (n=3), 3 (n=4), unclassified (n=1), 
and acquired (n=5) LQTS, 20 (69%) exhibited TWD in PAC. Moreover, 70% of max 
TWD lead was coincident with max TWA lead. In the 
conclusion: TWD in non-aberrant PAC is common in LQTS patients and asso-
ciated with elevated TWA and a history of VTA.

P2452 | BEDSIDE

Relationship between the sinoatrial conduction time and the occurrence of Mobitz II sinoatrial exit block

K. Makowski, E. Kramarz. Military Institute of Health Services, Warsaw, Poland

The purpose of the study was to test the hypothesis that the sinoatrial conduction 
time (SACT) assessed by the Holter method may be useful in identifying patients 
at high risk of developing Mobitz II sinoatrial block (M-block).
Methods: In the group of 217 patients (mean age 63±11 years, 58% men) with symptoms that might be related to cardiac arrhythmias, SACT was measured from 24-hour ECG Holter monitoring using spontaneous premature atrial beats.

Results: During a mean follow-up period of 39±8 months, the occurrence of M-block was noted in 28 patients (13%). Patients with one or more sequences of M-block had greater values of SACT than those without M-block (149±47 ms vs. 93±38 ms, p<0.0001). Univariate predictors of M-block included advanced age of patients (>60 years), underlying heart disease, episodes of syncope and SACT >150 ms. Multivariate analysis using the Cox proportional hazard model showed two independent predictors of M-block occurrence during follow-up (Table): SACT >150 ms (hazard ratio: 13.38; 95% confidence interval: 5.46–32.78) and syncope episodes (hazard ratio: 3.46; 95% confidence interval: 1.15–10.35).

Rank:多变量分析

<table>
<thead>
<tr>
<th>Hazard ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SACT &gt; 150 ms</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Syncopal episodes</td>
<td>0.0067</td>
</tr>
<tr>
<td>Age &gt; 60 years</td>
<td>0.0653</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>0.75 (0.21–2.69)</td>
</tr>
</tbody>
</table>

SACT, sinoatrial conduction time.

Conclusions: The results indicate that the prolonged SACT calculated from non-invasive Holter method is associated with an increased risk of M-block occurrence in patients with symptoms that might be caused by cardiac arrhythmias.

P2453 | BEDSIDE
Arhythmicogenic region of premature ventricular contraction relates early left ventricular systolic dysfunction
H. Yamamoto, H. Katoh, M. Kunishige, M. Kosugi, Y. Mizukami, S. Beppu. Osaka Bay Central Hospital, Internal Medicine, Osaka, Japan

Background: High burden of premature ventricular contraction (PVCs) induces left ventricular systolic dysfunction (LV-dys), but there are few systematic studies about the influence of the region of PVC focus on LV-dys. Recently, global longitudinal strain (GLS), which is measured by echocardiographic speckle tracking analysis, has been widely used to detect fine LV-dys and reported a superior longitudinal strain (GLS), which is measured by echocardiographic speckle tracking analysis, has been widely used to detect fine LV-dys and reported a superior

Methods: Consecutive 40 patients with normal EF without underlying cardiac diseases, having more than 1000/day of PVC by 24hour Holter ECG were enrolled. GLS was measured in all patients and control with no PVC (n=8). The relationships between GLS and previous risk factors for PVC-induced LV-dys were evaluated. The patients were divided into 6 groups depending on the region of PVC focus by12-lead ECG, including right ventricular outflow tract of septum or free wall (RV-OT), near His bundle (His), left coronary cusp or LV epicardium (LCC+Epi), RV non outflow tract (RV-nOT), LV outflow and non outflow tract (LV-OT and LV-nOT). GLS for each groups were evaluated.

Results: GLS of patient was significantly higher (worse) than that of control (Hazard ratio: 13.38; 95% confidence interval: 5.46–32.78) and syncopal episodes (Hazard ratio: 3.46; 95% confidence interval: 1.15–10.35).

Conclusion: Region of PVC focus is one of the significant risk factors for prediction of PVC-induced early LV-dys. Strain analysis is useful method for detecting fine LV-dys.
gram and reveals arrhythmogenic ventricular abnormalities by abnormal depolarization at the end of the QRS complexes. A positive LP gives one minor point for diagnosing Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia (ARVC/D) according to the Revised Task Force Criteria (TFC). LP can also be caused by myocarditis, infarction or other inherited cardiac diseases and these pathologies may also be visualized by cardiac MRI (cMRI). Therefore we investigated the correlation between LP and cMRI findings in patients with verified sustained ventricular tachycardia/cardiomyopathy/arrhythmia (VT/VF).

Methods: We retrospectively collected data from 41 patients examined with LP and who had been hospitalized with ventricular arrhythmia at the University Hospital of Copenhagen. LP was considered positive if the task force criteria for ARVC/D were met. Measures of the cMRI scans relevant for ventricular size and abnormal tissue were noted and reviewed by 2 independent investigators. The cohort was split according to the LP result.

Results: 26/41 (63%) of the patients had aborted sudden cardiac death and 29/41 (71%) had idiopathic VT/VF. LP was positive in 18/41 patients (44%). Of the seven ARVC/D patients in the cohort 5 (71%) were LP positive. Between the LP groups no significant differences could be found according to positive late gadolinium enhancement (LGE) (LP-Positive 31% vs. LP-Negative 36%, p-value=1.00), dilated right ventricle according to major TFC (33% vs. 29%, p-value=0.73), RVEDV/BSA (97 vs. 99 ml/m² p-value=0.85) or RV ejection fraction (56% vs. 58% p-value=0.57).

Conclusions: The group of VT/VF patients, there were no significant differences in RV size or function or LGE between patients with or without positive LP. This suggests that LP may carry information about arrhythmic susceptibility beyond that which may be obtained from cMRI and is therefore an important independent marker in revealing arrhythmogenic abnormalities.


P2457 | BEDSIDE
Rapid diagnosis and management of symptomatic arrhythmia - the role of telemedicine
A. Roth1, Y. Shacham1, M. Golovner2. 1Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel; 2Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel

Background: One disadvantage of current loop recorders is the long ‘time lag’ between recording an electrocardiogram (ECG), establishing a diagnosis, and taking appropriate medical measures. Cellular communication with the Cardio R® loop recorder (introduced in 2009), which uses digital technology to transmit cardiac recordings and symptom descriptions, easily overcomes this problem.

Purpose: To assess the Cardio R® device’s efficacy in detecting arrhythmias which may account for symptoms that were not observed on regular office ECGs or on traditional 24-hour Holter cardiac monitoring.

Methods: Cardio R® recordings are almost immediately diagnosed by the on-duty medical team at SHL-Telemedicine’s call center. Users can concurrently relay symptom descriptions from a prepared list, thereby providing a symptom/cardio-rhythm correlation. The users and/or their physicians receive updates or instructions, or a mobile intensive care unit (MICU) is dispatched, depending upon the displayed rhythm, the described symptoms and the referring physician’s orders.

Results: Between January 2009–December 2014, a total of 80,272 ECG transmissions were received from 2,847 patients (mean±SD age 59±19 years, range 10–95; 62% females) who completed a 1-month trial with the Cardio R® device. There were 28±45 transmissions per patient. The leading complaints were palpitations (n=2,179 patients), pre-syncope (n=558 patients) and chest pain (n=110 patients). There were 28±45 transmissions per patient. The leading complaints were palpitations (n=2,179 patients), pre-syncope (n=558 patients) and chest pain (n=110 patients). A total of 41,788 (52%) transmissions were made by patients who were admitted to hospital. The Cardio R® device displayed a confirmatory disturbance in rhythm 9 minutes (range 6–20 minutes), and 2±4 days elapsed until pending upon the displayed rhythm, the described symptoms and the referring physician’s orders.

Conclusions: The cardio-rhythm correlation and the pre-syncope (n=558 patients) and chest pain (n=110 patients). A total of 41,788 (52%) transmissions were made by patients who were admitted to hospital. The Cardio R® device displayed a confirmatory disturbance in rhythm 9 minutes (range 6–20 minutes), and 2±4 days elapsed until presentation of the first symptomatic episode.

STEMI I

P2458 | BEDSIDE
Is there any benefit with beta-blocker therapy in patients with myocardial infarction with left ventricular systolic dysfunction and atrial fibrillation?
R. Gonzalez Ferreiro, S. Raposeiras Roubin, E. Abu-Assi, A. Redondo Dieguez, A. Roth1, Y. Shacham1, M. Golovner2. 1Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel; 2Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel

Introduction and objectives: β-blockers are indicated in acute myocardial infarction (AMI) patients with depressed left ventricular ejection fraction (LVEF). The efficacy of β-blockers in these patients with atrial fibrillation (AF) is uncertain. We aim to analyze the efficacy of β-blockers in AMI patients with depressed LVEF and AF.

Methods: We conducted a retrospective cohort study of 753 patients admitted with diagnosis of AMI with LVEF<40%. Using Cox regression, we analyzed the prognostic role of β-blockers comparing patients in AF with those in sinus rhythm (SR), and adjusting by confounding variables.

Results: 98 patients had AF (13.0%). During the follow-up (3.0±2.8 years), 362 (48.1%) patients died. Patients treated with β-blockers (n=436; 66.6%) and in SR had a lower mortality rate (30.1±vs.70.0%; P=0.001), but not those in AF (53.3±vs.55.3%; P=0.852). Kaplan Meier curves are shown for patients with AF/SR according to the use or not β-blockers (figure). After adjusting by age, female sex, hypertension, diabetes, peripheral artery disease, chronic obstructive pulmonary disease, history of prior AMI, creatinine, STEMI, Killip class, peri- nontaneous coronary intervention, complete revascularization and medical therapy, we found that β-blockers were an independent protective factor in the multivariate Cox regression analysis in those patients with SR (hazard ratio [HR]=0.59; 95% confidence interval [CI], 0.45–0.77; P<0.001) but not in AF patients (HR=0.96; 95% CI,0.47–1.92; P=0.903).

Conclusions: β-blockers have not shown to improve prognosis in AMI patients with LVEF<40% and AF. The benefit of β-blockers in these patients is limited to those with SR. Probably this involves a change in clinical practice guidelines regarding to the recommendation of β-blockers in AMI patients with depressed LVEF and AF.
P2460 | BEDSIDE
A risk score for predicting cardiac arrest requiring defibrillation or cardiopulmonary resuscitation for patients admitted with suspected non-ST-elevation acute coronary syndromes

J. Faxen¹, J. Ternberg¹, J. Sundstrom², B. Lindahl³, K. Szumauer¹. ¹Karolinska Institute, Department of Cardiology; Karolinska University Hospital, Stockholm, Sweden; ²Uppsala University Hospital, Department of Medical Sciences, Uppsala, Sweden; ³Uppsala University, Uppsala Clinical Research Centre, Uppsala, Sweden

Purpose: The aim of this study was to develop a risk score from baseline risk factors known on admission that could be used to predict the individual risk for cardiac arrest (CA) requiring defibrillation or cardiopulmonary resuscitation (CPR) and that could be used to guide the need for in-hospital cardiac monitoring.

Methods: Consecutive patients (n=333,278), 18 years or older who were admitted with suspected non-ST-elevation acute coronary syndromes (NSTE-ACS) 2003–2010 were identified through the nationwide SWEDHEART registry. Patients with CA/CPR prior to admission were excluded.

Baseline characteristics on admission and in-hospital CA were recorded as part of the registry. Logistic regression models were used to assess the association between baseline characteristics (24 candidate variables) and in-hospital CA. Multiple imputations (m=20) were performed to include patients with missing data.

Results: CA occurred in 4788 (1.4%) patients. A point score for potential clinical use was developed with a maximal sum of 12 points. Six variables independently predicting in-hospital CA were included with an in-hospital risk of CA between 0.3–22.6% (see figure). The identified variables were: age≥50 years (1 point), male sex (1 point), ST-T abnormalities (2 points), Killip Class ≥2 points (2 points), heart rate >100 bpm (2 points), and systolic blood pressure <100 mmHg (4 points).

A higher risk score was associated with higher in-hospital mortality. Patients with a final diagnosis of NSTE-ACS (n=96,838) had a higher risk than those without NSTE-ACS (n=236,440).

Conclusion: On admission a simple risk score including six clinical variables can be used to predict the risk of in-hospital CA and thereby identify patients who need a higher degree of cardiac monitoring regardless of final diagnosis.

Acknowledgements: Funding: This work was supported by a grant from the Swedish Foundation for Strategic Research and the Swedish Heart and Lung Foundation.

P2461 | BEDSIDE
Safety and efficacy of the esc 0h/3h-protocol for rapid rule-out of myocardial infarction among women and men

M. Rubini Gimenez, T. Bergholt, A. Hjalmarson, H. Hammar, T. Svedager, S. Osswald. University Hospital Basel, Department of Cardiology, Basel, Switzerland

Background: We aimed to prospectively evaluate the safety and efficacy of the new ESC rapid 0h/3h-rule-out protocol for AMI based on the 99th percentile of high sensitivity cardiac troponins (hs-cTnI), among women and men in order to assess potential gender-inequalities.

Methods: We enrolled consecutive patients presenting to the ED with suspected AMI in a prospective international multicenter study. Excluded were patients with ST-segment elevation, no available baseline hs-cTnI levels, and no available data about onset/peak of pain. Among the remaining 2727 patients, 32% were women and 68% men. The final diagnosis was adjudicated by two independent cardiologists. The safety and efficacy of the ESC 0h/3h-rule-out protocol was evaluated among women and men.

Results: AMI was the final diagnosis in 17% of patient (15% of women and 19% of men (p=0.001)). Using the 99th percentile of hs-cTnI (14ng/l), the ESC 0h-rule-out protocol correctly ruled-out 99.4% (95% CI, 98.8–100%) of late presenters (-6h from chest pain onset) among women and 100% (95% CI, 99.8–100%) among men (p=ns). The ESC 3h-rule-out protocol correctly ruled-out 100% (95% CI 98.3–100%) of early presenters (-6h from chest pain onset) among women and 99% (95% CI, 98.1–100%) among men (p=ns). Overall, the ESC rule-out protocol classified about 44% of women and 43% of men with suspected AMI.

Conclusions: The current ESC 0h/3h-rule-out protocol using the 99th percentile of hs-cTnI in conjunction with clinical assessment is safe and effective and provides comparable results among women and men. A common strategy for both genders seems to be the most appropriate choice.

P2462 | BEDSIDE
Hyponatremia at discharge as a predictor of 12-month clinical outcomes in hospital survivors after acute myocardial infarction


Purpose: Hyponatremia in the early phase of acute myocardial infarction (AMI) is a well-known predictor of poor prognosis. However, little is known about the clinical implication of sodium levels at discharge in hospital survivors after AMI.

Methods: The study included 1,290 consecutive patients (64±12 years; 877 men) who survived the index hospitalization after AMI. We determined the 12-month mortality rates of these patients.

Results: The 12-month mortality rate showed a U-shaped curve, with the lowest event rate at 137–139 mmol/L of serum sodium at discharge. Patients who died during the 12-month follow-up had lower sodium levels at discharge than those who had survived (137±6 mmol/L vs. 139±4 mmol/L; P=0.014). Hyponatremia at discharge, defined as a serum sodium level ≤135 mmol/L, was present in 210 patients (16.3%). In the Cox-proportional hazard model, hyponatremia at discharge (hazard ratio, 2.352; 95% confidence interval, 1.033–5.094; P=0.041) was an independent predictor of 12-month mortality. Moreover, hyponatremia at discharge had an incremental prognostic value over conventional risk factors (chi-square = 6, P=0.018), and conventional risk factors and log N-terminal Pro-B-type natriuretic peptide combined (chi-square = 7, P=0.008). In the subgroup analysis, the 12-month mortality rate of patients with hyponatremia at discharge was significantly higher than in those without, irrespective of age, Killip class, left ventricular ejection fraction, percutaneous coronary intervention at index hospitalization, and prescription of diuretics at discharge.

Conclusion: Hyponatremia at discharge is an independent predictor of 12-month mortality in hospital survivors after AMI.

P2463 | BEDSIDE
High event rate in patients with acute coronary syndromes and atrial fibrillation: Results from the prospective EPICOR Registry

U. Zeymer¹, L. Annemans², N. Danchin³, S. Pocock⁴, F. Van De Werf⁵, J. Medina⁶, H. Bueno⁷, ¹Klinikum Ludwigshafen and Institut für Herzinfarktforschung Ludwigshafen, Ludwigshafen, Germany; ²T–CHER Interuniversity Centre for Health Economics UGent, VUB, Ghent, Belgium; ³Hôpital Européen Georges Pompidou, & René Descartes University, Paris, France; ⁴London School of Hygiene and Tropical Medicine, London, United Kingdom; ⁵University of Leuven, Department of Cardiovascular Sciences, Leuven, Belgium; ⁶Observational Research Centre, Global Medical Affairs, AstaZeneca, Madrid, Spain; ⁷Hospital General Universitario Gregorio Marañón, Madrid, Spain

Background: Known or new onset atrial fibrillation is observed in around 5% of patients with acute coronary syndromes (ACS). Guidelines recommend revascularization therapies and intense antithrombotic therapies, including oral anticoagulation in these patients. We sought to determine acute treatments and the long-term event rate in patients with and without atrial fibrillation discharged after ACS in clinical practice.

Methods: EPICOR (NCT01171404) has been conducted in 555 hospitals in 20 countries.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No AF</th>
<th>n=9954</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>15.1</td>
<td>5.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Bleeding</td>
<td>7.2</td>
<td>3.2</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 1

Conclusions: In patients with AHF caused by ACS, BB therapy had no effect on in-hospital mortality after balancing of overt confounders.
countries and enrolled a total of 10 568 patients with ACS with and without ST-segment elevation. Patients were prospectively followed up over 2 years.

Results: A total of 497 (5%) patients had atrial fibrillation at baseline. The baseline characteristics, treatments for the index event, discharge medication and 2-year event rates for patients with and without atrial fibrillation are given in the table above.

Conclusions: In clinical practice, patients with ACS and atrial fibrillation are less often treated with revascularization therapies, do not receive oral anticoagulation in over 50% of cases and have a high event rate at 2-year follow-up. Therefore, all efforts must be made to increase the rate of guideline-adherent therapies in these high-risk patients after ACS.

P2464 | BEDSIDE
Clinical and angiographic characteristics of patients with acute coronary syndromes without cardiovascular risk factors
A. Correia, R. Rodrigues, B. Silva, M. Neto, S. Gomes, A. Drumond, D. Pereira, Hospital Funchal, Funchal, Portugal

Introduction: Cardiovascular risk factors are well known by the scientific community. Nevertheless some acute coronary syndromes (ACS) occur in patients without any cardiovascular (CV) risk factors.

Purpose: To describe the clinical and angiographic characteristics in patients with ACS without any CV risk factors.

Methods: Prospective, single-center study, of 1055 patients admitted for ACS between October 2009 and September 2013. The CV risk factors were defined as prior ACS, hypertension, Diabetes Mellitus, dyslipidemia, smoking, peripheral arterial disease and family history of CV disease. They were divided into 2 groups: Group A, without any CV risk factor, n=84; Group B, with one or more CV risk factors, n=971. The groups were compared regarding composite endpoint (non-fatal myocardial infarction, cardiovascular death or stroke) and mortality from any cause during hospitalization and at 1-year follow-up.

Results: The groups did not show any difference regarding age, sex and time between onset of symptoms and first medical contact. At admission group B had higher values of creatinine [I= 1.176 (standard deviation (SD)= 0.327) vs II=1.299 (SD=0.878); p<0.01] and higher values of troponin I [I= 0.080 (SD=0.229) vs II=0.103 (SD=0.318); p<0.01]. Group B had more episodes of ischemic arrhythmias (A=23.8% vs B=13.4%; p=0.01), cardiac arrest (A=14.3% vs B=6.1%; p<0.01), diabetes mellitus (A=16.9% vs B=11.3%; p=0.01), and use of inotropics (A=15.5% vs B=7.9%; p<0.05). During hospitalization group B had a higher composite primary endpoint (A=19.7% vs B=7.7%; p<0.01) and mortality (A=16.7% vs B=6.6%; p<0.01). At 1-year follow-up there were no differences in the composite primary endpoint (A=20.2% vs B=17.8%; p=0.13) and mortality (A=19.0% vs B=14.4%; p=0.2).

Conclusions: Patients with ACS without CV risk factors have more single-vessel disease and a worse clinical profile, with more complications during hospitalization, which influences the mortality of the initial event. However, at one year follow-up, the prognosis is similar.

P2465 | BEDSIDE
Clinical impact of multivessel disease with or without chronic total occlusion in non-infarct-related artery on five-year outcomes in patients with STEMI undergoing primary PCI
H. Watanabe, H.S. Shimoi, T.K. Kimura on behalf of Credo-kyoto investigators. Kyoto University, Department of cardiology, Kyoto, Japan

Background: The long-term impact of a concurrent chronic total occlusion (CTO) in a non-infarct-related artery (IRA) on patients with ST-segment elevation acute myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) is not still clear.

Objectives: The aim of this study was to investigate the clinical impact of CTO in IRA on long-term cardiovascular outcomes in STEMI patients undergoing primary PCI.

Methods: The CREDO-Kyoto AMI registry is a large-scale cohort study of acute myocardial infarction (AMI) patients undergoing coronary revascularization in 2005–2007 at 26 hospitals in Japan. Among 5429 patients enrolled in the registry, 1524 patients suffering from STEMI with IRA and CTO undergoing primary PCI within 24 hours after the symptom onset. Patients were classified as having single-vessel disease (SVD), multi-vessel disease (MVD) without CTO in IRA and multi-vessel disease (MVD) with CTO in IRA. In addition to comparing clinical outcomes through overall 5 years, 30-day landmark analysis was performed to evaluate clinical outcomes between 30 days and 5 years.

Results: Of 3892 patients, 1847 patients (48%) had SVD, 1662 patients (43%) had MVD without CTO, 383 patients (10%) had MVD with CTO. The cumulative rate of all-cause mortality was 37% in the MVD-with-CTO group, 22% in the MVD-without-CTO group, 15% in the SVD group respectively. Both 5-year and 30-day-to-5 year all-cause mortality was significantly higher in the MVD-with-CTO group than in the other groups (log-rank P=0.0001). After adjusting for confounders, both CTO and multi-vessel disease are an independent predictor of all-cause mortality through 5 years (hazard ratio[HR]: 1.5, 95% confidence interval [CI]: 1.2–1.9, P=0.0003, HR: 1.4, 95% CI: 1.1–1.6, P=0.0077). Similarly, the two factors are independent predictor of all-cause mortality between 30 days and 5 years (HR: 1.6, 95% CI: 1.2–2.0, P=0.0005, HR: 1.3, 95% CI: 1.1–1.6, P<0.0001). On the contrary, CTO is a significant predictor of cardiac death through 5 years and between 30 days and 5 years (HR: 1.7, 95% CI: 1.3–2.2, P=0.0004, HR: 2.1, 95% CI: 1.5–3.0, P<0.0001) while multi-vessel disease is a significant predictor only in 5-year cardiac mortality, but not in 30-day-to-5 year cardiac mortality (HR: 1.4, 95% CI: 1.1–1.8, P=0.008, HR: 1.3, 95% CI: 1.1–1.6, P=0.006, HR: 1.3, 95% CI: 1.0–1.8, P=0.08).

Conclusions: The presence of CTO and multi-vessel disease are an independent predictor of 5-year all-cause mortality in STEMI patients. The presence of CTO is an independent predictor of 5-year cardiac mortality in STEMI patients even when early deaths are excluded.

Acknowledgement/Funding: the Pharmaceuticals and Medical Devices Agency

P2466 | BEDSIDE
Incidence rates and predictors of major adverse cardiovascular outcomes occurring before vs. after 1-year following discharge after acute coronary syndrome

Long-term disease progression following acute coronary syndrome (ACS) is not well understood. We examined the risk of subsequent cardiovascular events in patients discharged after ACS.

Methods and results: 4,858 patients who survived a primary ACS between December 2003 and September 2012 were studied with a median follow-up period of 4.7 years (~56 months).

The primary composite endpoint of risk for non-fatal MI, non-fatal stroke, or cardiovascular death (CVD) was estimated for the first year post-index ACS. Risk and risk factors were assessed by Kaplan-Meier analysis and competing-risks (non-cardiovascular death was classified as a competing risk) regression based on Fine and Gray's proportional subhazards modeling, respectively.

In-hospital cardiovascular angiography was performed in 90.3%, PCI 64.5%; and CABG in 4.5%. Mean age was 67±13 years; 28.7% were women. At the end of follow-up (median 4.7 years), there were 915 events (18.8%). During the first year post-index ACS, the risk of developing the composite endpoint was 6.8% (number of events=326). When only analyzing MI patients (both STEMI (n=1524) and NSTEMI (n=2416); excluding unstable angina (n=937) patients), the risk of developing the composite endpoint was unchanged: 7.5%.

After adjusting for more than 20 related covariables, the significant (p<0.05) independent predictors for the occurrence of ischemic events or death from cardio-vascular death during the first year following discharge were: prior history of heart failure [subhazard ratio (sHR)=1.6], age (sHR=1.03) and multivessel coronary artery disease (sHR=1.4), diabetes mellitus (sHR=1.4), no-revascularization (sHR=3.7), drug eluting stent placement and female sex (sHR=0.7 for each) and STEMI vs NSTEMI (sHR=0.8).

For patients who did not develop the combined endpoint during the first year, composite endpoint risk was 13.6% in the following 44 months. Increased age, diabetes mellitus, peripheral arterial disease, prior stroke, Killip class I at admission, multivessel coronary artery disease, renal dysfunction, chronic atrial fibrillation, STEMI (vs. NSTEMI) were each significantly (p<0.05) associated with the occurrence of the composite end-point.

Conclusions: Risk of cardiovascular events is high beyond the first year post-ACS, indicating a need for prolonged surveillance. Predictors of cardiovascular events occurring within the first year after an ACS are practically the same to those predicting cardiovascular events occurring beyond the first year, except for chronic atrial fibrillation which become a predictor of ischemic events or CVD beyond the first year.

P2467 | BEDSIDE
Cardiovascular risk in post-myocardial infarction patients: nationwide real-world data on distribution and impact of combination of risk factors in a real-life setting
T. Jernberg1, L.P. Hasvold2, H. Hjelm3, M. Thuresson4, M. Janzon5, 1Karolinska University Hospital, Department of Medicine, Stockholm; 2AstraZeneca, Lund, Sweden; 3Medical department, Karolinska University Hospital, Stockholm; 4Nyköping Hospital, Nyköping; 5Statisticon AB, Stockholm; 6Linköping University, Linköping, Sweden

Background: The PEGASUS-TIMI 54 trial studies effect of dual antiplatelet treatment in high risk prior MI patients (age ≥65 years, diabetes, history of ≥1 prior myocardial infarction (MI) or renal disease). Prevalence of combinations and impact of these risk factors in post-MI patients in clinical practice has not been previously described.

Methods: A cohort study linked Swedish National registry data on morbidity, mortality and medication for patients (NCT01984307). 44,993 prior MI patients without recurrent MI or stroke after one year were included. Impact of combination of
cardiovascular risk factors on incidence of a end point of MI, stroke or all cause death was estimated at third year follow-up. Analyses were age stratified.

**Results:** In post-MI patients at 1 year, diabetes (28%) and history of >1 MI (21%) were the most common risk factors in all age categories, whereas previous renal disease diagnosis (4%) was less common. Risk was strongly associated with age: >75 years double risk vs younger patients. For >75 years one additional risk factor approximately doubled the event rate vs no additional risk factors. 7% of the patients had >2 risk factors; which approximately doubled the risk for patients >75 years, compared with 1 risk factor patients.

**Conclusions:** Diabetes and history of >1 MI are prevalent risk factors in post-MI patients. Distribution of risk factors in PEGASUS-TIMI 54 trial and in this observational study is broadly comparable. Risk was strongly associated with age. One or more additional risk factor when >75 years more than doubled the event rate outcomes. This indicates the need of careful management of post-MI patients with increased risk, regardless of age.

**Acknowledgement/Funding:** Sponsored by AstraZeneca

---

**STEMI II**

**P2468 | BEDSIDE**

**Zwolle risk score: the missed opportunity for early discharge after primary percutaneous intervention**

A. Arabi1, J. Alswaidi1, A. Gehani1, A. Alqhtani1, A. Alnabti1, S. Aboujalala1, I. Rafie1, O. Altameemi1, M. Yacoub2, S. Aboujalala1

**Purpose:** We aimed to assess long term prognosis prediction capability of TIMI risk score and CHA2DS2-VASc in ACS patients.

**Method:** We performed a retrospective analysis of consecutive 1571 STEMI patients treated with primary PCI in 3 Hospitals in Qatar between December 2011 and December 2016. The analysis was based on the data collected prospectively from the patients medical records. The end-point was the mortality at 3 years follow-up. The following data were included: age, gender, type of STEMI, previous cardiovascular events, diabetes, hypertension, dyslipidemia, smoking, family history of MI, body mass index, Killip class at hospital admission, PCI with stent or no stent, TIMI flow grade at PCI, Heart rate at hospital admission, mean arterial pressure, in-hospital clinical events (MI, stroke, death), discharge medications (ACE inhibitors, beta blockers, aspirin, clopidogrel, statins). The patients were divided into 3 groups: Group A ≤1 risk factor, Group B 1 to 2 risk factors, Group C >2 risk factors. The outcomes were analyzed by Cox regression and area under the ROC curve (AUC).

**Results:** The Zwolle score was significantly associated with 3-year mortality (p<0.001). The AUC of the ROC curve was significantly higher for CHA2DS2-VASc, compared to TIMI score (0.698 vs 0.593, p=0.001). In a Cox regression model, both Zwolle score (hazard ratio [HR] 1.078; 95% confidence interval [CI] 1.02–1.13; p=0.008) and CHA2DS2-VASc (HR 1.143; 95% CI 1.376–1.514; p<0.001) were found to be predictors of the primary endpoint. A CHA2DS2-VASc cutoff value of 3 was found to have a 72.35% sensitivity and a 60.42% specificity for predicting death at follow-up.

**Conclusions:** Both scores predicted long term mortality in our ACS population. However, CHA2DS2-VASc performed significantly better, and shows promising results as a risk stratifying tool for long term prognosis in an unselected ACS population.
coded in ICD-10 as I21 or I22. Deaths after discharge from AMI were categorized as in-hospital and out-of-hospital. Additionally for in-hospital deaths the causes were analysed by ICD-10 codes. Results: In 2009 a total of 75,054 AMI cases were hospitalized with 10.5% of in-hospital case-fatality, that was strongly age-related but not gender-related. The 3-year mortality after discharge was 19.9% and was increasing with age and was higher in men than in women. A large proportion (43%) of deaths occurred out-of-hospital and it was particularly high in men aged >64 years. More deaths from cardiovascular than other causes were noted in older patients, particularly in women. The most frequent cause of in-hospital cardiovascular death was heart failure. Conclusions: High proportion of out-of-hospital deaths after discharge from AMI in younger men is alarming and indicates a need for intensifying secondary prevention programmes.

P2472 | BEDSIDE
Primary angioplasty in multivessel disease: what to do after PRAMI results?
M. Madeira, F. Caetano, I. Almeida, M. Costa, L. Goncalves on behalf of National Registry of Acute Coronary Syndromes of the Portuguese Society of Cardiology. Hospital and University Center of Coimbra; Faculty of Medicine, University of Coimbra, Department of Cardiology, Coimbra, Portugal

Purpose: About 50% of patients (P) with ST elevation myocardial infarction (STEMI) have multivessel coronary disease (MVD). Primary angioplasty (P) of only the culprit artery (CA) is advised by current guidelines, except in cardiacogenic shock. PRAMI trial defied this concept. We aimed to evaluate the prognostic impact of different revascularization (Rv) strategies in P with STEMI and MVD.

Methods: From 2007-2013 P included in a national multicenter registry of ACS, we studied 703 P (78% male; 64±13 years) submitted to pPCI, with MVD amenable to percutaneous Rv. Cardiogenic shock P were excluded. P were divided in 3 groups: CAO – CA Rv only (69%); CR1 – complete Rv during pPCI (17%); CR2 – complete Rv in two different time points during the same admission (14%). We evaluated and compared clinical variables, treatment strategies and major end points. One year follow-up (FU) concerning mortality and cardiovascular hospitalization was done.

Results: CAO P were older (66±13 vs 62±13 vs 61±12, p<0.001); with no differences regarding cardiovascular risk factors or past medical history of coronary artery disease (CAD). At admission, Killip-Kimball class and analytical parameters were similar, except for BNP which was higher in CAO (442±663 vs 157±253 vs 29±43pg/mL, p<0.01). CAO had more extensive CAD (3 vessels: 30% vs 9% vs 4% for CAO, multivessel Rv and staged PCI, respectively; p<0.01). No differences in CAO, Femoral vascular access (36% vs 19% vs 32%, p=0.01) and bare metal stents (46% vs 23% vs 41%, p<0.01) were more often in CAO; but, Gp IIb/IIIa inhibitors were less used (32% vs 80% vs 56%, p=0.01). CAO presented lower left ventricle ejection fraction (49±12% vs 58±14% vs 53±10%, p<0.01) and more often evolved to heart failure (19% vs 12% vs 9%, p=0.01); with no differences between the groups with complete Rv. In multivariate analysis, complete Rv in two different time points was associated with a lower number of adverse events in FU (HR 0.1, p<0.01).

Conclusion: Incomplete Rv might have lead to the poor prognosis of P with more severe CAD and systolic dysfunction. On the other hand, complete Rv in two different time points seems to be effective and safe, and may justify the extension of hospital stay.

P2473 | BEDSIDE
Validation of the ProACS risk stratification score for acute coronary syndromes
A.T. Timoteo, S. Aguiar Rosa, M. Alonso Nogueira, T. Pereira Silva, P. Rio, R. Carvalho, M.L. Ferreira, R. Cruz Ferreira. Hospital Santa Marta, CHLC, Lisbon, Portugal

Background: The ProACS risk score is an easy, early and simple risk stratification score for hospital all-cause mortality in acute coronary syndromes (ACS) that was developed from a population of patients included in nationwide registry of ACS. Only recently our centre participated in the registry and was not included in the cohort used for the score development. Our objective was to externally validate this risk score both for short-term and longer-term follow-up.

Methods: All consecutive patients admitted at our centre with an ACS were included in our centre registry. Demographic and admission characteristics, as well as treatment and outcome was collected. The ProACS risk score variables are age ≥72 years (2 points), systolic blood pressure <116 mmHg, Killip class 2 or 3 and 1ST-segment myocardial infarction (STEMI) (1 point each) and Killip class ≥4 (3 points). We calculated for each patient both the ProACS and the GRACE risk scores. We used ROC curve analysis to assess the discriminative capacity of each model and calibration was assessed by Hosmer-Lemeshow (H-L) test.

Results: We included 3170 patients, with a mean age of 64±13 years, 71% males and 62% with a STEMI. All-cause in-hospital mortality was 5.7%, 7.2% at 30-day and 10.3% at 1-year follow-up. The ProACS score showed good discriminative capacity for all considered outcomes (Area Under ROC curve ≥0.75) with good calibration (p=0.05) but lower than GRACE risk score (Table) and slightly lower than the original development cohort (Area Under ROC curve ≥0.75). In both models a good discrimination between patients at low risk (score ≤0), intermediate risk (score 1–2) and high risk (score ≥3) in both short and mid-term follow-up (p<0.001 for all comparisons).

Conclusions: ProACS risk score is an easy and simple risk stratification score for ACS that is valid in external cohorts. It can be applied very early at the first medical contact, but later on, GRACE risk score can complement risk stratification.

P2474 | BEDSIDE
The effect of PCI strategy on 1-year mortality in STEMI patients with multi-vessel CAD who present without cardiacogenic shock
G.W. Wilberg1, S. Matezky 2, I. Goldenberg3, N. Shlomo2, D. Hasdai4, R. Kornowski3, Z. Iakovitch3, on behalf of ACSIS Study Group. 1 Rabin Medical Center, Department of Cardiology, Petach Tikva, Israel; 2 Sheba Medical Center, Lievir Heart Center, Tel Hashomer, Israel

Background: The optimal revascularization strategy for STEMI patients without cardiacogenic shock who present with multivessel CAD (CAO) has not been fully determined. In 2009 a total of 75,054 AMI cases were hospitalized with 10.5% of in-hospital case-fatality, that was strongly age-related but not gender-related. The 3-year mortality after discharge was 19.9% and was increasing with age and was higher in men than in women. A large proportion (43%) of deaths occurred out-of-hospital and it was particularly high in men aged >64 years. More deaths from cardiovascular than other causes were noted in older patients, particularly in women. The most frequent cause of in-hospital cardiovascular death was heart failure. Conclusions: High proportion of out-of-hospital deaths after discharge from AMI in younger men is alarming and indicates a need for intensifying secondary prevention programmes.

Conclusions: ProACS risk score is an easy and simple risk stratification score for ACS that is valid in external cohorts. It can be applied very early at the first medical contact, but later on, GRACE risk score can complement risk stratification.

Methods: A retrospective study using data from a national ACS survey (complying with data from 19 PCI centers), we compared 1-year mortality rates for patients who underwent primary PCI due to STEMI and were found to have multi-vessel CAD during 2008–2013 and were not in cardiogenic shock.

Results: A total of 826 patients (688 culprit lesion only, 79 premature and 59 early staged PCI were included. The 3 groups were well matched regarding all major demographic and clinical characteristics except Killip class on admission (20.3% Killip ≥1 for the preventive PCI group compared to 17.1% in the culprit lesion only and 16.9% staged PCI groups p=0.001). At 1-year follow up, patients treated by preventive PCI had higher mortality rates compared to patients treated by culprit lesion only or staged PCI (15% vs 7% vs 6% in culprit lesion only and 16% for staged PCI, p=0.01). In a group of 236 propensity score matched patients (2:1 ratio of culprit lesion only, preventive and staged PCI), patients treated by preventive PCI again had higher 1-year mortality rates that did not reach statistical significance due to the smaller sample size (16.8% vs. 6.1% for culprit lesion only and 6% for staged PCI, p=0.061).

Conclusion: Our data shows that under current practice, in STEMI patients with multivessel CAD, who present without cardiacogenic shock, culprit lesion only and staged PCI strategies are associated with similar 1-year mortality rates, although a preventive PCI strategy is associated with increased mortality. Larger randomized trials are needed to confirm the optimal revascularization strategy in STEMI patients with multivessel CAD.
**P2476 | BEDSIDE**

The impact of high D-dimer levels on in-hospital mortality in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention

K. Minami¹, M. Kurobe¹, S. Furudono¹, Y. Uchida¹, T. Nonohiro¹, S. Takeshita¹, H. Nakashima¹, K. Maemura¹. ¹ Nagasaki Harbor Medical Center City Hospital, Nagasaki, Japan

Aims: Acute coronary syndrome (ACS) can occur when a vulnerable plaque ruptures and results in platelet aggregation and coagulation at the rupture site. Plasma D-dimer, a primary degradation product and circulating marker of fibrin turnover, serves as a direct marker of ongoing fibrinolysis at the site of coronary artery occlusion. The aim of this study was to investigate the prognostic value of D-Dimer in patients with STEMI undergoing primary percutaneous coronary intervention (STEMI).

Methods: In total, 349 consecutive patients with STEMI who underwent primary percutaneous coronary intervention were included in this study. The plasma D-dimer level was measured on admission. Patients were divided into two groups based on median D-dimer levels (1.08 μg/ml).

Results: In-hospital death occurred in 21 patients (6.0%). Patients with high D-dimer levels (≥1.08 μg/ml) had increased in-hospital mortality (10.2% vs. 1.7%, p=0.001) compared to patients with low D-dimer levels (<1.08 μg/ml). Multivari-able logistic regression analyses showed that high D-dimer levels were positively correlated with in-hospital death (OR=2.49, p=0.04).

Conclusions: A high D-dimer level independently predicts in-hospital mortality in patients with STEMI.

**P2477 | BEDSIDE**

Mechanical chest compressions during prolonged resuscitation for reperfusion ventricular fibrillation that complicated coronary intervention for STElevation myocardial infarction

M.M. Demidova¹, H. Wagner², D. Eriline², P.G. Platnov². ¹ Federal Medical Research Center, S.Petersburg, Russia and Lund University, Lund, Sweden; ² Lund University, Lund, Sweden

Purpose: Ventricular fibrillation (VF) during reperfusion for STEMI is an infrequent event, but it complicates percutaneous coronary interventions (PCI) and subsequent hospital stays. We aimed to assess the demand in mechanical chest compressions for VF and its outcome in patients with VF during reperfusion.

Methods: Consecutive STEMI patients admitted to a tertiary care hospital for primary PCI during 2007–2012 were retrospectively assessed for the presence of VF during reperfusion. Medical records were analysed for circumstances of VF in relation to infarct-related artery opening and for details of CPR protocol.

Results: Among 3,224 patients with STEMI admitted for primary PCI from 2007 to 2012, 71 (1.9%) had VF during reperfusion. Prolonged chest compressions using mechanical assist device were used in 10 (14%) of them. Indications for prolonged mechanical chest compressions were pulseless electrical activity after mechanical assist device and left ventricular ejection fraction (LVEF) <20%. They did not differ in clinical presentation, lack of left ventricular ejection fraction or MI localization. Two out of 10 patients who received prolonged CPR were discharged alive from hospital with normal neurological deficit and were alive at 1-year.

Conclusion: Prolonged CPR demanding mechanical chest compressions is not uncommon in patients who develop reperfusion VF during primary PCI for STEMI, especially those with pre-procedural VF or advanced ischemic heart disease. Despite the generally poor outcome, mechanical chest compressions can enable maintenance of circulation during PCI and may lead to saving lives without neurological deficit in patients who survive PCI procedure.

**P2478 | BEDSIDE**

Prognostic implication of creatinine clearance and hemoglobin composite index in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention


Background: A creatinine clearance (CCR) and Hemoglobin (Hb) is a readily-available routine laboratory test that can predict clinical outcomes in patients with acute coronary syndrome.

Purpose: We sought to evaluate the impact of a CCR and Hb composite index (CHI) on clinical outcomes in patients with STEMI undergoing primary PCI with drug-eluting stents.

Methods: We analyzed 805 consecutive STEMI patients. The Cox regression analysis determined the optimal combination of CCR and Hb into a CHI. The discrimination ability of CHI, CCR, and Hb in predicting 12-month MACE, composite of cardiac death, nonfatal MI and stent thrombosis were compared using area under the receiving operating characteristic curve. Patients were divided into quintiles according to the CHI.

Results: The optimal weighting of CCR and Hb to form the CHI to predict a 12-month MACE was Hb + CCR/12. The area under the curve for the CHI was significantly greater (0.857) than for Hb (0.777, p=0.003) and CCR (0.802, p=0.003). A positive trend was observed between a 12-month MACE and CHI quintiles: 39.4%, 9.4%, 6.1%, 0.0%, 1.5% of MACE occurrence from quintiles 1 to 5 (p<0.001). In the multivariate setting, the lowest quintile was an independent predictor of 12-month MACE (HR: 23.15, 95% CI: 2.40–222.87, p=0.007) after adjusting for age, gender, left ventricular ejection fraction, Killip class, creatinine clearance, and other factors included in the TIMI risk score for STEMI. MACE-free survival analysis indicated the best discriminatory ability of the CHI.

**P2479 | BEDSIDE**

Clinical and angiographic predictors of microvascular dysfunction in ST-segment elevation myocardial infarction


Aims: We sought to find differences of clinical and angiographic characteristic in STEMI patients with or without coronary microvascular dysfunction by index of microcirculatory resistance (IMR).

Methods: STEMI patients who underwent primary percutaneous coronary intervention (PCI) were enrolled. Baseline characteristics including clinical and angiographic characteristics were investigated in all patients. The IMR, parameter of hyperemic microvascular resistance, was measured with a pressure sensor/thermistor-tipped guidewire after primary percutaneous coronary intervention (PCI).

Results: 113 STEMI patients (age=56±11 years, M:F=95:18) were analysed. The patients were divided into tertile IMR groups: Low-IMR (n=38, IMR=12.9±2.6 U), Mid-IMR (n=38; IMR=23.9±4.0 U) and High-IMR group (n=37; IMR=48.1±17.1 U). Mean age of Low-IMR was significantly younger than Mid-IMR and High-IMR. Mean door-to-balloon times were under 90 minutes in all IMR groups, and there were no significant differences among each IMR groups. However, symptom-onset-to-balloon time was significantly longer in High-IMR than Mid-IMR and Low-IMR (p<0.001). The high IMR group included the more frequent proximal location of culprit lesion than non-proximal location (p=0.008). In multivariate regression analysis, age and symptom-onset-to-balloon time were independent determinants of higher IMR (p=0.013 for age, p=0.003 for symptom-onset-to-balloon time).

Comparison of IMR according to variable
Conclusion: The CCR and Hb composite index is a useful and powerful marker to predict a 12-month MACE in patients with STEMI who underwent primary PCI with a superior discriminative ability than CCR or Hb.

P2479 | BEDSIDE
Circadian rhythms in patients with ST-elevation myocardial infarction
D.J. Severino, B.S. Santos, D.D. Durao on behalf of Portuguese National Registry of Acute Coronary Syndromes. Hospital of Santarem (HDS), Santarem, Portugal

Background and introduction: Circadian rhythms with regard to time of symptoms onset for patients with acute myocardial infarction have been observed, although their relationship to outcomes has been debated.

Purpose: Evaluate the circadian rhythms in patients with ST-elevation myocardial infarction.

Methods: A total number of 4367 patients included in the national registry of ACS, from 1st of October 2010 and until 20th October 2014 were divided in four groups: Group A (0–6h), Group B (6–12h), Group C (12–18h) and Group D (18–24h). We evaluate the relationship between the onset of symptoms during the 24 circadian cycle and the prehospital delay, timelessness of reperfusion and in-hospital death.

Results: There was a significant association between time of onset and the circadian cycle, with the greatest percentage of patients (32.4%) experiencing the onset between 6–12h. Time of onset was associated withprehospital delay and timeliness of reperfusion. Patients with onset from 0–6h and 18–24h had a median prehospital delay of 328 and 324 min vs 261 min from 12–18h (p < 0.001). Patients with onset time from 0–6h had median door-to-balloon time of 420 min vs 291 min from 12–18h (p < 0.001). Patients with onset from 0–6h had a higher prevalence of inferior ST-elevation myocardial infarction (54.9%, p < 0.001) and those with onset from 6–12h and 12–18h a higher prevalence of inferior ST-elevation myocardial infarction (53.1, and 52.3%).

Conclusion: Patients with ST-elevation myocardial infarction exhibit significant circadian patterns in symptom onset, prehospital delay and timeliness of reperfusion. Patients who develop symptoms from 0–6 present with longer prehospital delays and have longer door-to-balloon times. Those with onset from 18–24h had a higher incidence of heart failure (24.4%, p < 0.001) and cardiogenic shock (8.7%, p=0.007). There was no significant association between the time of symptom onset and the in-hospital death.

P2480 | BEDSIDE
Morphine and reperfusion success in ST-elevation myocardial infarction - insights from cardiac magnetic resonance imaging
S. De Waaha, I. Este1, S. Desch1, G. Fuemau1, P. Lurz2, G. Schuler2, H. Thiele1.1. University of Lübeck, Medical Clinic II, Lübeck, Germany;2. University of Leipzig, Heart Center, Department of Internal Medicine and Cardiology, Leipzig, Germany

Background: Intravenous (IV) morphine has been shown to be independently associated with adverse clinical outcome in patients with non-ST-elevation myocardial infarction. Although regional and global longitudinal strain (GLS) derived by cardiac magnetic resonance imaging (CMR) in patients with STEMI have been strongly linked with primary PCI, its role as a predictor of reperfusion success has not been thoroughly investigated.

Methods: STEMI patients reperfused by primary PCI (n=276) within 12 hours after symptom onset underwent CMR 3 days after the index event (interquartile range [IQR] 2–4). A detailed set of clinical, therapeutic and laboratory parameters was assessed in all patients. IV morphine administration was recorded in all patients.

Results: IV morphine was administered in 44.7% (n=123) of all patients. Patients in the IV morphine group displayed larger infarct size, higher extent of microvascular obstruction and lower myocardial salvage index (MSI) in comparison to the non-IV morphine group (all p < 0.05). In multivariable logistic regression analysis adjusted for parameters such as TIMI-flow pre- and post-PCI, time from symptom onset to PCI and left ventricular ejection fraction, IV morphine was identified as an independent predictor for MSI.

Conclusion: In patients with STEMI, IV morphine administration prior to PCI appears to be independently associated with suboptimal reperfusion success. These findings warrant randomised clinical trials assessing the effect of IV morphine on clinical outcome.

P2481 | BEDSIDE
Independent association of longitudinal strain of left anterior ascending artery territory and TIMI frame count after acute anterior STEMI

Background: Although regional and global longitudinal strain (GLS) derived by 2D speckle tracking echocardiography (STE) has been successfully used after STEMI for predicting left ventricular (LV) dysfunction and outcome, no information is available about relations between strain components and coronary angiographic scores.

Purpose: To evaluate the relationship between regional longitudinal strain with currently available coronary angiographic scoring systems in acute anterior STEMI.

Methods: Consecutive 37 patients with acute anterior STEMI (mean age = 61 years, 11 women) underwent standard echo and STE-derived Automated Function Imaging at admission, early before coronary angiography. A group of 37 normal volunteers, matched for age and sex, were the control group for echocardiographic parameters. LV ejection fraction (EF), the ratio of transmural E velocity to pulsed tissue Doppler annular e’ velocity (E/e’ ratio) and global longitudinal strain (GLS, % - average of 18 regional longitudinal strain in the apical views) were calculated. Longitudinal strain of left anterior descending (LAD) territory (LSlاد) was also calculated as the average of 8 myocardial segments (middle and apical posterior septum, basal, middle and apical anterior septum, basal, middle and apical anterior wall). By coronary angiography TIMI flow grade and TIMI frame count (TFC) were calculated before LAD percutaneous angioplasty. Laboratory biomarkers of myocardial necrosis were also determined.

Results: The two groups were comparable for blood pressure, heart rate and body mass index. STEMI patients had lower EF and high E/e’ ratio (both p < 0.0001) than controls. GLS was -10.4±3.4% in STEMI and -21.0±2.2% in controls (p < 0.0001). In STEMI group, LSlاد (−6.9±3.9%) was negatively related with TFC (r=−0.40, p<0.01), TIMI grade (r=0.33, p=0.04) and troponin peak levels (r=−0.45, p=0.005) but not to CK-MB peak. LSlاد was also related with E/e’ ratio (r=0.41, p=0.02) but not with EF. By a multiple linear regression analysis, after adjusting for troponin levels and E/e’ ratio, TFC was independently associated with LSlاد (standardized β coefficient = −0.375, p=0.02) (cumulative RR=0.381, SE=2.39%, p<0.0001) in STEMI group.

Conclusion: Our study is the first to demonstrate an independent association between the extent of LV myocardial functional damage - testified by regional longitudinal strain of LAD regions - and the angiographic scores of perfusion deficit in the culprit lesion after acute anterior STEMI. Pre-angioplasty regional longitudinal strain can be useful to predict successful primary percutaneous intervention.

P2482 | BEDSIDE
Prognostic impact of female gender on a contemporary cohort of Spanish patients with acute myocardial infarction

Introduction: Differences between women and men with acute myocardial infarction (AMI) have been reported, but available data are controversial. Given the older age of onset of coronary artery disease, AMI has a worse cardiovascular risk profile, that justify its worse outcomes compared to men. The poorer female outcome has been traditionally explained by lower likelihood of admission to hospitals for acute AMI, lower likelihood of admission to main units, lower likelihood of angiography and lower likelihood of angioplasty. However, in the last years, this has been challenged. Actually, the sex differences in AMI are now more attributed to differences in disease severity, rather than disease presentation. Our aim was to evaluate sex differences in 971 consecutive patients of the Portuguese registry of Acute Coronary Syndromes.

Methods: We conducted a retrospective cohort study with 4,196 patients admitted to our hospital with the primary diagnosis of AMI (2004–2010). We performed a propensity-score matched analysis to draw up two groups of 971 patients paired according gender. The prognostic differences between men and women in terms of mortality after admission were analyzed using Cox regression model; survival Kaplan-Meier curves were also plotted.

Results: In the pre-matched cohort (n=4,196), women (28.6%) were older and had a lower prevalence of smoking and higher parity. They have higher GRACE risk score values; they also underwent PCI in a lower percentage and received less commonly clopidogrel, beta-blockers and statins in comparison with men. Women had also a higher mortality rate (33.9% vs. 28.8%, p<0.001). By using propensity score matching analysis 971/4,196 patients were successfully matched. Mortality during follow-up was lower in women (31.5% vs. 37.8%; p=0.004). Therefore, female gender was associated with better long term prognosis after adjusting for confounding variables in the multivariate Cox regression analysis (HR=0.83; p=0.016).

Conclusions: In this cohort of real-life patients with AMI, less than 50% of women are matchable with men in terms of similar baseline cardiovascular risk profile and risks factors used. After adjusting for multiple different factors and the undertaken treatments between both genders –using propensity score matching analysis, women showed lower follow-up mortality.
P2483 | SPOTLIGHT
Serial improvement of early mortality of acute myocardial infarction in the whole metropolitan area: progress of direct PC coronary network system

Background: Acute myocardial infarction (AMI) is known crucial disease causing rapid deterioration and death. Therefore early admission to cardiac center enabling emergency percutaneous coronary intervention (PCI) is essential. On this reason emergency ambulance transport to appropriate hospital in shortest time is needed as cooperation system to cover the huge population area.

Objective: To clarify recent trend of emergency system (Tokyo CCU network) in Tokyo Metropolitan area.

Methods: Tokyo CCU network established in 1978 by 12 CCU centers and emergency selective coronary reperfusion started in 1983, then emergency PCI in 1992. The network expanded to 71 CCU centers which are available emergency PCI anytime everyday within 60 minutes to cover 13,017,000 people in 2013. The system has been conducted by Tokyo Metropolitan Government and its acute care results have been stored as registered database.

Results: Early mortality (30 day) are showed in attached figure from 1982 to 2013. The mortality in 1978 reached to 20.5%, however it declined to 5.1% in 2013 (n=4,587). The network system covers 95% of AMI patients requiring hospital admission, and median time from onset to emergency call (EC) to balloon time were 63 minutes and 93 minutes respectively (n=1,128, in 2011).

Conclusion: Tokyo Metropolitan area appears well covered by modern AMI care system for the whole population with remarkable low mortality.

Acknowledgement/Funding: Tokyo Metropolitan Government

P2484 | BENCH
Physical activity as a trigger of myocardial infarction and long-term survival following primary percutaneous coronary intervention

Limited evidence is available about effect of physical activity as a trigger of myocardial infarction and clinical outcomes following primary percutaneous coronary intervention in STEMI.

Methods: From January 2009 till December 2012 a total of 2793 patients with STEMI underwent primary PCI within 12 hours from symptom onset in a single high-volume centre. Level of physical activity at the time of symptom onset was determined using standardized questioner at the time of patient arrival. Mortality was assessed at a mean follow-up of 32±24 months.

Results: 533 patients (19.1%) had physical activity at the time of symptom onset (Group 1) and 2260 patients with chest pain at rest served as a control group (Group 2). Group 1 patients were younger (59±11 vs 60±12; p < 0.01), more frequently male (75.0% vs. 69%; p=0.005), presented earlier (mean total ischemic time 2.9±3.1 vs. 3.7±3.2 hours; p < 0.001), had first MI (89% vs. 84%; p < 0.01), with higher rate of TIMI 0 baseline flow (78% vs. 73%; p=0.04), and had bigger infarct size (2542±2113 vs. 2281±2164; p=0.015). In-hospital and long-term mortality was similar between Groups 1 and 2 respectively (3.8% vs. 3.8%; p=0.97; 13.8% vs. 14.5%; p=0.704). Adjusting the outcome to quartiles of total ischemic time yielded only a trend for higher mortality in Group 1 with longer reperfusion times (p=0.054).

Table 1:

<table>
<thead>
<tr>
<th>Mortality (%) per group vs ischemic time</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=2793</td>
</tr>
<tr>
<td>0-3 h</td>
</tr>
<tr>
<td>4-6 h</td>
</tr>
<tr>
<td>7-9 h</td>
</tr>
<tr>
<td>10-12 h</td>
</tr>
<tr>
<td>Group 1: physical activity-related (533 pts)</td>
</tr>
<tr>
<td>Group 2: at rest (2260 pts)</td>
</tr>
</tbody>
</table>

Conclusion: Physical activity as a trigger of myocardial infarction occurs in approximately one fifth of STEMI patients undergoing primary PCI, more frequently in first presenters, younger and male patients but has no impact on in-hospital and long-term mortality.

P2485 | BENCH
Association between hyperglycemia at admission and microvascular obstruction in patients with ST-segment elevation myocardial infarction
S. Ota, M. Yokoyama, H. Kawai, K. Komukai, T. Imanishi. Hidaka General Hospital, Cardiovascular Medicine, Gobo, Japan

Background: Blood glucose level at admission in ST-segment elevation myocardial infarction (STEMI) is a predictor of heart failure and mortality. Previous study showed the association between hyperglycemia and microvascular dysfunction during percutaneous coronary intervention (PCI). LGE cardiovascular magnetic resonance imaging (CMR) can demonstrate microvascular obstruction (MVO) as the area with hypointense core within LGE.

Purpose: This study was performed to investigate the association between hyperglycemia at admission in patients with STEMI and microvascular obstruction (MVO). The authors hypothesized that hyperglycemia influences microvascular dysfunction in STEMI patients.

Methods: We analyzed 5,641 patients with acute STEMI (<12 hours) from the Korea Acute Myocardial Infarction Registry undergoing primary PCI between December 2007 and December 2012. Patients receiving fibrinolysis and coronary intervention in STEMI remains uncertain.

Conclusion: These data indicate that, in discordance with common belief, STEMI patients with ACS remain at high risk of long-term recurrent ischemic events, but tend to be undertreated compared with the relevant ACS guidelines during, and more importantly, after the acute episode.
perglycemia at admission and MVO using CMR in patients with STEMI.

Methods: Ninety-three patients with first STEMI who were treated by percutaneous coronary intervention (PCI) were included. CMR was performed within 7 days after PCI. Venous blood was collected routinely immediately after admission for plasma glucose determination before intravenous injection of some medications. Samples were analyzed in the hospital’s central laboratory. We performed LGE-CMR to assess the presence of microvascular obstruction (MVO).

Results: MVO was found in 34 (37%) of all 93 patients; their glucose level at admission was significantly higher than that of patients who did not exhibit MVO (204 [153–267] mg/dl vs. 157 [127–200] mg/dl, p=0.002). There were no differences in glycosylated hemoglobin and incidence of diabetes mellitus between the two groups. A multivariable logistic regression analysis showed that glucose level at admission was an independent predictor of MVO (odds ratio, 1.01; 95% confidence interval 1.004 to 1.019; p=0.003). The occurrence of MVO was significantly higher in patients who present at admission ≥190mg/dl compared with the patients with glucose level <190mg/dl (18 [53%] vs. 16 [27%], p=0.023).

Conclusions: Hyperglycemia at admission in STEMI patients who were treated by PCI was associated with the presence of MVO assessed by LGE-CMR.

STEMI IV

P2488 | BEDSIDE

Early versus late diagnosis in patients with ST-elevation-myocardial infarction: clinical characteristics and long-term-survival


1 Wilhelminen Hospital, Vienna, Austria; 2 SMZ-South, Vienna, Austria; 3 Medical University of Vienna, Vienna, Austria; 4 Rudolfstiftung Hospital, Vienna, Austria; 5 Donaupital, Vienna, Austria; 6 Hietzing Hospital, Vienna, Austria

Background: Pre-hospital delay results in impaired outcome after ST-Elevation-Myocardial Infarction (STEMI). Pain-to-First Medical Contact (FMC) strongly depends on recognition of symptoms by the patient and willingness to attend medical help. Aim of the study was to identify factors associated with late diagnosis in STEMI.

Methods and results: Pain-to-FMC and long-term-outcome were documented in 2492 individuals presenting with STEMI from 2003 to 2009. Baseline parameters of patients with pain-to-FMC <60 minutes (“early presenters”) were compared to patients in whom diagnosis was made later than 60 minutes of onset of pain (“late presenters”).

Late presenters were characterized by higher age (62±14 years vs. 59±13 years; p<0.0001), higher prevalence of female sex (31.9% vs. 25.1%; p=0.002), diabetes mellitus (25.1% vs. 19.9%; p=0.02) and hypertension (57.6% vs. 50.5%; p=0.07), but lower rates of smoking (50.6% vs. 58.3%; p=0.02), hyperlipoproteinemia (52.0% vs. 57.3%; p=0.05) and cardiac shock (8.8% vs. 11.8%; p=0.042) in univariable analysis.

After multivariable adjustment, female sex (OR 1.348; CI 1.013–1.792) and diabetes mellitus (OR 1.355; CI 1.001–1.835) were independently associated with delayed FMC in STEMI, whereas cardiac shock (OR 0.582; CI 0.366–0.921) was a predictor of early diagnosis.

Three-year-survival was 90.4% and 88.7% (p=0.289) for early and late presenters, respectively. After patients with cardiac shock were excluded from outcome analysis, three-year-survival was significantly higher in patients with early compared to late diagnosis (96.0% vs. 93.0% in early and late presenters, respectively, p=0.017).

Conclusion: In this real-world cohort of STEMI-patients, female sex and diabetes mellitus (OR 1.355; CI 1.001–1.835) were independently associated with delayed diagnosis, whereas cardiac shock was a predictor of early diagnosis. Long-term-survival is strongly affected by an excess of cardiac shock in patients presenting soon after onset of pain. Special attention should be paid to avoid diagnostic delays in females and diabetics with STEMI.

P2489 | BEDSIDE

Is the predictive ability of GRACE risk score for mid-term mortality identical in all age groups?

A.T. Timoteo, S. Aguila Rosa, M. Alonso Nogueira, P. Rio, R. Carvalho, M.L. Ferreira, R. Ferreira. Hospital Santa Marta, CHLC, Lisbon, Portugal

Background: GRACE risk score is the risk stratification score in acute coronary syndrome (ACS) with the highest predictive accuracy and presently the most widely used. It was developed for in-hospital and 6-month all-cause mortality. We sought to evaluate if this score is equally effective for different age groups both for short and longer-term follow-up.

Methods: Analysis of consecutive patients admitted at a single-centre with ACS and included in a dedicated database of ACS. Patients were divided into three groups according to the age group: Group 1 (<50 years), Group 2 (50–79 years) and Group 3 (>80 years).

Results: Predictive ability of GRACE score was evaluated for hospital, 30-day, one-year all-cause mortality by ROC curve analysis (area under curve - AUC) and calibration by Hosmer-Lemeshow (H-L) analysis.

Conclusion: For short and longer-term follow-up.

P2490 | BEDSIDE

The association of epicardial fat thickness with stress hyperglycemia in patients with ST elevation myocardial infarction


Introduction: Stress Hyperglycemia (SH) as a well-defined prognostic indicator in patients with ST elevation myocardial infarction (STEMI) is associated with larger infarct size, pathologic cardiac remodeling and mortality. Beyond the insulin resistance, increased inflammatory and neurohormonal response have been postulated in the pathophysiology of SH. As a source of various inflammatory cytokines and neurohormonal mediators, epicardial fat tissue might contribute to the occurrence of SH. We aimed to evaluate the association of epicardial fat tissue thickness (EFT) with SH in STEMI patients.

Methods: Total of 200 patients who admitted with STEMI and performed primary PCI between 2013–2015 were included. Patients were followed-up median 14 months. Patient group composed of 100 patients with SH and control group consisted of 100 patients without SH. Patients with DM and BMI>25 were excluded.

Results: In patients with SH, EFT was significantly higher than the control group (7.45 mm ±1.46 vs. 6.79 mm ±1.15 p=0.013). EFT was correlated with admission glucose (r=0.362 p<0.001), CRP levels (r=0.291 P=0.003) and peak CKMB (r=0.288 p=0.004). In multivariate analysis, EFT was demonstrated as an independent predictor of SH (OR: 1.495 95% CI: 1.074-2.066 p=0.017). A cut-off value of 6.85 mm for EFT had 72% sensitivity and 64% specificity for prediction of SH (AUC: 0.671, p=0.003). According to this cut-off value, patients were divided into two groups. In Kaplan Meier analysis, patients with EFT > 6.85 mm demonstrated a higher incidence of MACE.

Conclusion: EFT, related with miscellaneous neurohormonal and inflammatory mediators, is associated with SH and MACE in STEMI patients. This noninvasive, simple echocardiographic measurement may utilize risk categorization of these patients.

P2491 | BEDSIDE

Intravascular ultrasound guidance versus angiographic guidance in primary percutaneous coronary intervention for ST-segment elevation myocardial infarction

K. Nakatsuma1, H. Shiomi1, T. Morimoto2, K. Ando3, K. Kadota4, T. Yamamoto5, Y. Furukawa2, Y. Nakagawa2, M. Horie3, T. Kimura4 on behalf of the CREDO-Kyoto AMI registry. 1Kyoto University, Department of Cardiovascular Medicine, Kyoto, Japan; 2Hyogo College of Medicine, Division of General Medicine, Hyogo, Japan; 3Kokura Memorial Hospital, Division of Cardiology, Fukuoka, Japan; 4Kurashiki Central Hospital, Division of Cardiology, Kurashiki, Japan; 5Shiga University of Medical Science, Department of Cardiovascular and Respiratory Medicine, Otsu, Japan; 6Kobe City Medical Center General Hospital, Division of Cardiology, Kobe, Japan; 7Tenri Hospital, Division of Cardiology, Nara, Japan

Background: In the setting of elective percutaneous coronary intervention (PCI), the use of intravascular ultrasound (IVUS) guidance was suggested to be associated with a reduction in the incidence of target vessel revascularization (TVR). The utility of IVUS on long-term clinical outcomes in the setting of emergency PCI for ST-segment elevation acute myocardial infarction (STEMI) is still unclear.

Table 1. Results

<table>
<thead>
<tr>
<th>AUC (95% CI)</th>
<th>Total (n=3170)</th>
<th>Group 1 (n=428)</th>
<th>Group 2 (n=2218)</th>
<th>Group 3 (n=334)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital</td>
<td>0.86 (0.83–0.89)</td>
<td>0.90 (0.89–0.96)</td>
<td>0.85 (0.80–0.89)</td>
<td>0.75 (0.68–0.82)</td>
</tr>
<tr>
<td>30-day</td>
<td>0.83 (0.80–0.86)</td>
<td>0.90 (0.89–0.95)</td>
<td>0.81 (0.77–0.85)</td>
<td>0.74 (0.67–0.80)</td>
</tr>
<tr>
<td>One-year</td>
<td>0.80 (0.78–0.83)</td>
<td>0.91 (0.86–0.95)</td>
<td>0.78 (0.74–0.82)</td>
<td>0.69 (0.61–0.73)</td>
</tr>
<tr>
<td>H-L (p-value)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td>0.263</td>
<td>0.470</td>
<td>0.059</td>
<td>0.227</td>
</tr>
<tr>
<td>30-day</td>
<td>0.098</td>
<td>0.079</td>
<td>0.057</td>
<td>0.638</td>
</tr>
<tr>
<td>One-year</td>
<td>0.633</td>
<td>0.015</td>
<td>0.013</td>
<td>0.066</td>
</tr>
</tbody>
</table>

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475/57415 by guest on 07 February 2019
Purpose: We sought to investigate the utility of IVUS guidance on clinical outcomes in patients with STEMI undergoing primary PCI.

Methods: An observatory study was implemented among 12 STEMI patients and 12 age-matched healthy volunteers. After the hospitalization, the enrollers were divided into the IVUS group and the non-IVUS group. The QoM was measured in every patient using transoral ultrasonic. The patients who underwent IVUS-guided PCI and those who underwent angiography-guided PCI. The primary outcome measure in the current analysis was TVR for the culprit lesions in STEMI.

Results: Among 3028 patients eligible for the current analysis, 932 patients (31%) who underwent IVUS-guided PCI. Compared with the angiography-guided PCI, the IVUS-guided PCI was associated with significantly lower incidences of TVR (22% versus 27%, log-rank P<0.001) and definite stent thrombosis (ST) (1.2% versus 3.1%, log-rank P=0.003). The cumulative incidence of all-cause death, heart failure, recurrent MI, and MACE (death, heart failure, recurrent MI, target vessel revascularization) were not significantly different between the 2 groups. After adjusting for confounders, however, there were no significant differences between the 2 groups in the risk for TVR (adjusted hazard ratio [HR]: 1.14, 95% confidence interval [CI]: 0.86–1.51, P=0.36), definite ST (adjusted HR: 0.58, 95% CI: 0.19–1.72, P=0.33), and all-cause death (adjusted HR: 0.82, 95% CI: 0.57–1.19, P=0.31).

Conclusion: IVUS-guided PCI was not associated with a lower risk for TVR as well as ST in STEMI patients who underwent primary PCI.

Acknowledgement/Funding: The study was supported by the National Natural Science Foundation of China (81130065, 81072981, 30971101, 31171130, 81473445, 81400336 and 30900528).

P2493 | BENCH

Bioresorbable vascular scaffolds for ST-segment elevation myocardial infarction treatment

A.V. Khrigun, M.V. Malevanny, Y. Kulkovskikh. Regional vascular center, Rostov-on-Don, Russian Federation

Purpose: Everolimus-eluting bioresorbable vascular scaffolds (BVS) have been shown to be safe and effective for stable coronary artery disease treatment. The current data on the use of BVS in ST-segment elevation myocardial infarction are very limited. Short-term and mid-term outcomes of PCI with bioresorbable vascular scaffolds in STEMI were evaluated.

Methods: The prospective single-center registry was initiated to evaluate feasibility and performance of everolimus-eluting bioresorbable vascular scaffolds in STEMI setting. From 1 October 2013 to 31 December 2014 a total of 107 STEMI patients underwent PCI with BVS implantation. The mean age of patients was 52.5±6.1 (range 27–66) years, 77.6% were males. The primary endpoints of the study were the device success defined as BVS implantation in the culprit lesion without intraprocedural complications and the rate of major adverse cardiac events (MACE) during follow-up.

Results: Among 3028 patients eligible for the current analysis, 932 patients (31%) who underwent IVUS-guided PCI. Compared with the angiography-guided PCI, the IVUS-guided PCI was associated with significantly lower incidences of TVR (22% versus 27%, log-rank P<0.001) and definite stent thrombosis (ST) (1.2% versus 3.1%, log-rank P=0.003). The cumulative incidence of all-cause death, heart failure, recurrent MI, and MACE (death, heart failure, recurrent MI, target vessel revascularization) were not significantly different between the 2 groups. After adjusting for confounders, however, there were no significant differences between the 2 groups in the risk for TVR (adjusted hazard ratio [HR]: 1.14, 95% confidence interval [CI]: 0.86–1.51, P=0.36), definite ST (adjusted HR: 0.58, 95% CI: 0.19–1.72, P=0.33), and all-cause death (adjusted HR: 0.82, 95% CI: 0.57–1.19, P=0.31).

Conclusion: IVUS-guided PCI was not associated with a lower risk for TVR as well as ST in STEMI patients who underwent primary PCI.

Acknowledgement/Funding: the Health, Labour and Welfare Ministry in Japan and the Pharmaceuticals and Medical Devices Agency in Japan

P2494 | BEDSIDE

Bioresorbable vascular scaffolds for ST-segment elevation myocardial infarction treatment

A.V. Khrigun, M.V. Malevanny, Y. Kulkovskikh. Regional vascular center, Rostov-on-Don, Russian Federation

Purpose: Everolimus-eluting bioresorbable vascular scaffolds (BVS) have been shown to be safe and effective for stable coronary artery disease treatment. The current data on the use of BVS in ST-segment elevation myocardial infarction are very limited. Short-term and mid-term outcomes of PCI with bioresorbable vascular scaffolds in STEMI were evaluated.

Methods: The prospective single-center registry was initiated to evaluate feasibility and performance of everolimus-eluting bioresorbable vascular scaffolds in STEMI setting. From 1 October 2013 to 31 December 2014 a total of 107 STEMI patients underwent PCI with BVS implantation. The mean age of patients was 52.5±6.1 (range 27–66) years, 77.6% were males. The primary endpoints of the study were the device success defined as BVS implantation in the culprit lesion without intraprocedural complications and the rate of major adverse cardiac events (MACE) during follow-up.

Results: Among 3028 patients eligible for the current analysis, 932 patients (31%) who underwent IVUS-guided PCI. Compared with the angiography-guided PCI, the IVUS-guided PCI was associated with significantly lower incidences of TVR (22% versus 27%, log-rank P<0.001) and definite stent thrombosis (ST) (1.2% versus 3.1%, log-rank P=0.003). The cumulative incidence of all-cause death, heart failure, recurrent MI, and MACE (death, heart failure, recurrent MI, target vessel revascularization) were not significantly different between the 2 groups. After adjusting for confounders, however, there were no significant differences between the 2 groups in the risk for TVR (adjusted hazard ratio [HR]: 1.14, 95% confidence interval [CI]: 0.86–1.51, P=0.36), definite ST (adjusted HR: 0.58, 95% CI: 0.19–1.72, P=0.33), and all-cause death (adjusted HR: 0.82, 95% CI: 0.57–1.19, P=0.31).

Conclusion: IVUS-guided PCI was not associated with a lower risk for TVR as well as ST in STEMI patients who underwent primary PCI.

Acknowledgement/Funding: the Health, Labour and Welfare Ministry in Japan and the Pharmaceuticals and Medical Devices Agency in Japan

P2495 | BENCH

Abnormal oscillations of circadian gene expression in peripheral blood mononuclear cells among acute myocardial infarct patients as a possible cause for increased thrombosis risk

C. Liang, Q.X. Jiang, F. Wu, Z.Q. He, Z.G. Huang, J.Y. Zhang, Z.G. Wu. Changzheng Hospital of Second Military Medical University, cardiology; Shanghai, China, People's Republic of

Background: Close relationship between circadian rhythm disruption and high risk of acute myocardial infarction occurrence is becoming increasingly evident; however, the exact role of circadian genes in modulating thrombosis remains still elusive.

Purpose: To explore the relationship of circadian rhythm disruption and ST-segment elevation myocardial infarction (STEMI).

Methods: An observatory study was implemented among 12 STEMI patients and 12 age-matched healthy volunteers. After the hospitalization, the enrollers were drawn peripheral venous blood samples to separate peripheral blood mononuclear cells starting from 2.00 a.m. every 4 hours for 24 hours. Expression of circadian genes including Clock, ROF1 and γ, Rev-erba and β, Bmal 1 and 1α, Per 1, 2, and 3, Cry 1 and 2, and thrombosis associated genes such as IL-2, S1PR 1, PAI-1, -1→-2, -1→-3, TGF-α and β, and thrombomodulin-1 and -2 (TM-1 and -2) were assessed by qPCR.

Results: Among the investigated circadian genes, Clock was found to show significant rhythmic. And compared with that of healthy volunteers, gene expression pattern of Clock exhibited rhythmicity among almost 9 (75%) STEMI patients, which accompanied an unbalanced mRNA expression of thrombosis-related PAI-1 and TM-1. Furthermore, Clock protein was shown to directly bind to the E-box of the promoters of PAI-1 and TM-1 genes by chromatin immunoprecipitation analysis, which might imply Clock gene participate in the modulation of related gene expression, and eventually increase acute thrombosis risk in clinic.

Conclusion: Our data uncovered the potential modulatory effects of Clock in the balance between thrombosis-associated PAI-1 and TM-1 in peripheral blood mononuclear cells in patients with STEMI, which might be caused by abnormal oscillation of Clock mRNA expression and needed to explore in a larger prospective-based clinic study.

Acknowledgement/Funding: The study was supported by National Natural Science Foundation of China (81130065, 81072981, 30971101, 31171130, 81473445, 81400336 and 30900528).

P2496 | BEDSIDE

Long term prognosis in transradial primary PCI versus femoral approach in elderly patients (>80 years old)

S. Gestal Romani, B. Cid Alvarez, B. Alvarez Alzate, R. Ocana Sanchez, D. Lopez Otero, N. Bouzas Cruz, A. Lopez Lopez, M. Castinie Busto, R. Trillo Nouche, J.R. Gonzalez Juanatey. University Hospital of Santiago de Compostela, Cardiology; Santiago de Compostela, Spain

Purpose: Transradial approach (TRA) in elderly patients with STEMI have not been used previously because technical and anatomical difficulties owing to delay on reperfusion therapy using these access. Our propose on this study is to evaluate the prognosis influence between radial versus femoral approach in a contemporory cohort of patients aged > 80 years admitted to our hospital with STEMI undergoing primary percutaneous coronary intervention (PPCI).

Methods: We analyzed the data and clinical outcomes of 1121 consecutive patients undergoing PPCI between January 2008 and April 2014. End-points at the end of follow-up [median 588 days (235–1281 days)] include all-cause mortality and MACE (death, heart failure, recurrent MI, target vessel revascularization).

Results: From a total of 1121 patients the 15% (169) were older than 80 years. TRA was used in 135 (39%) elderly patients. There were no statistically significant differences between TRA and transfemoral approach (TFA) in regard to hypertension, diabetes or location of AMI. TFA group had a significant higher percentage of patients with Killip ≥ 2 at hospital admission (53% TRF vs 30% TFA p=0.008).

Conclusion: Our data uncovered the potential modulatory effects of Clock in the balance between thrombosis-associated PAI-1 and TM-1 in peripheral blood mononuclear cells in patients with STEMI, which might be caused by abnormal oscillation of Clock mRNA expression and needed to explore in a larger prospective-based clinic study.
P2498 | BEDSIDE

**Shock index, as a predictor of myocardial injury in patients with ST-segment elevation myocardial infarction: a cardiac magnetic resonance imaging study**


**Background:** Little is known about the prognostic value of shock index in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).

**Purpose:** We aimed to investigate the association of shock index with myocardial injury assessed by cardiac magnetic resonance imaging (CMRI) in patients with STEMI undergoing primary PCI.

**Methods:** We analyzed CMRI data from 306 consecutive patients treated with primary PCI for STEMI. They were divided into two groups based on initial shock index: shock index $\geq 0.7$ (n=218) and shock index $< 0.7$ (n=218). Myocardial infarct size, area at risk (AAR) and hemorrhagic infarct area were compared between two groups.

**Results:** In baseline characteristics, shock index $\geq 0.7$ group had lower left ventricular ejection fraction (p=0.01) and greater level of NT-proBNP (p=0.01) than shock index $< 0.7$ group. Higher Killip classification and diabetes were more prevalent in shock index $\geq 0.7$ group than shock index $< 0.7$ group (p=0.01 and p=0.02, respectively). All angiographic and procedural characteristics were not significantly different between two groups. In CMRI analysis, shock index $\geq 0.7$ group had larger infarct size (p=0.01) and AAR (p=0.03), and greater number of hemorrhagic infarct area (p=0.02) than shock index $< 0.7$ group. In multivariate analysis, shock index $\geq 0.7$ was independently associated with large myocardial infarction (odds ratio: 3.34, 95% confidence interval: 1.76 to 6.36; p<0.01).

**Conclusions:** Initial shock index may be a reliable predictor for myocardial injury in STEMI patients undergoing primary PCI.

**P2499 | BEDSIDE**

**Abnormal chest pain and long-term mortality in patients with ST-elevation myocardial infarction (STEMI)**

L. Björck1, S. Nielsen1, T. Jernberg2, W.K. Kok1, T. Sandstrom1, A. Rosengren1, L.-G. Håkansson1, P. Norén1, P. Dehlin2, S. Li2, E. Eerenberg2, A. Beek1, N. Van Roeyen1, 1Uppsala University, Uppsala, Sweden; 2Academic Medical Center of Amsterdam, Amsterdam, Netherlands

**Background:** Chest pain is the predominant symptom in patients with ST-elevation Myocardial Infarction (STEMI), particularly in younger patients and in men. Lack of chest pain in STEMI has been associated with higher in-hospital mortality. However, whether the poorer outcome is sustained throughout the first year after onset has not be investigated.

**Purpose:** To investigate the relation between presence of chest pain and prognosis in patients with a first STEMI.

**Methods:** We used data from the quality of care register the Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA). Out of a total of 107, 903 men and women 37,707 (25,257 men and 12,450 women) admitted to coronary care units presented with STEMI between 1996 and 2010.

**Results:** Of all patients with STEMI 92.2% presented with chest pain (men 93.4%, women 89.7%). Absence of chest pain was found in 4.4% and 6.6% of men and women $<65$ years, respectively and in 8.7% and 11.6% of men and women $\geq65$ years.

In younger patients without chest pain the absolute risk in 1-year mortality was markedly higher (men 16.5% and women 20.4%) compared to those presenting with chest pain (men 3.5% and women 4.0%). In older patients ($>65$ years) without chest pain the absolute risk in 1-year mortality was more evident: 36.5% and 39.0% in men and women without chest pain compared to 14.9% men and 19.9% in women with chest pain. The relative risk in those without chest pain was higher in younger men (Hazard ratio (HR) 5.07, 95% CI: 4.04–6.38) and women (HR 5.66, 95% CI: 4.04–7.93) than in older patients (men: HR 2.80, 95% CI: 2.52–3.12; and women: HR 2.31, 95% CI: 2.08–2.58).

**Conclusions:** Lack of chest pain in patients with STEMI is associated with higher 1-year mortality in both men and women, especially in older ages. Younger men and women without chest pain had notably higher relative risk of 1-year mortality.

**P2497 | BEDSIDE**

**Development of invasively measured coronary flow reserve before and after reperfusion for acute myocardial infarction: results from an experimental porcine model and the human situation**

G.A. De Waard1, M.R. Holland1, P.F. Teunissen1, M. Jansen1, L.F. Robbers1, E. Enserink2, A. Beek1, N. Van Roeyen1, 1VU University Medical Center, Cardiology, Amsterdam, Netherlands; 2Academic Medical Center of Amsterdam, Amsterdam, Netherlands

**Introduction:** An impaired coronary flow reserve (CFR) directly after primary PCI for treatment of acute myocardial infarction (AMI), is related to a worse clinical outcome. In a combined porcine and patient study we investigated the relationship of CFR, as well as the individual baseline and hyperemic flow components of CFR, with infarct size.

**Methods:** Intra-coronary Doppler flow velocity measurements were obtained both before and directly after 90 minute balloon occlusion, with subsequent reperfusion of the circumflex coronary artery in an AMI porcine model (n=11) and also directly after successful PCI in humans (n=40). Stable patients free from angiographic coronary artery disease served as a control group. CFR was defined as the ratio between hyperemic and basal average peak velocity (h-APV and b-APV). CFR was correlated to histological infarct size as percentage of left ventricle (IS%LV) in pigs and IS%LV as defined by cardiac magnetic resonance imaging in humans.

**Results:** CFR was significantly correlated to IS%LV in both pigs (r=−0.61; p=0.047) and humans (r=−0.48; p=0.001). In pigs, CFR decreased after AMI (2.4 SD 0.9 vs. 1.5 SD 0.4; p=0.04 for pre and post AMI respectively) and this finding was consistent for the human situation (2.7 (95% CI, 2.5 to 3.0) vs. 1.8 (95% CI, 1.6 to 2.1 for control vs. AMI patients). Both components of CFR contributed to its reduction after reperfusion (in pigs, b-APV increased by 8 and h-APV decreased by 6 cm/s, while in humans, b-APV increased by 6 and h-APV decreased by 4 cm/s).

**Conclusion:** A decrease in CFR is observed in patients as well as in porcine model of reperfused AMI and is related to a larger infarct size. Both the resting and hyperemic components contribute to the reduced CFR. Finally, the porcine model used provides an adequate haemodynamic representation of the human situation.

**STEMI V**

**P2498 | BEDSIDE**

**Total bilirubin on admission predicts in-hospital clinical outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention**

T.-H. Yang, H.-C. Shin, Y.-M. Lee, H.-Y. Jin, J.-S. Seo, J.-S. Jang, D.-K. Kim, D.-S. Kim. Inje University Busan Paik Hospital, Department of Internal Medicine, Division of Cardiology, Busan, Korea, Republic of Korea

**Background:** The serum total bilirubin (TB) level has been inversely related with coronary artery disease served as a control group. CFR was defined as the ratio between hyperemic and basal average peak velocity (h-APV and b-APV). CFR was correlated to histological infarct size as percentage of left ventricle (IS%LV) in pigs and IS%LV as defined by cardiac magnetic resonance imaging in humans.

**Purpose:** We sought to evaluate the availability of admission TB level to predict clinical outcomes in patients with STEMI who underwent primary PCI with DES.

**Methods:** We analyzed 1,111 consecutive STEMI patients treated with primary PCI. The patients was divided into high TB group (n=816) and low TB group (n=218). Myocardial infarct size, area at risk (AAR) and hemorrhagic infarct area were compared between two groups.

**Results:** The high TB group was associated with a significantly higher rate of in-hospital mortality but whether the poorer outcome is sustained throughout the first year has not been investigated.

**Conclusion:** Total bilirubin on admission predicts in-hospital clinical outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention.

**P2497 | BEDSIDE**

**Total bilirubin on admission predicts in-hospital clinical outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention**

T.-H. Yang, H.-C. Shin, Y.-M. Lee, H.-Y. Jin, J.-S. Seo, J.-S. Jang, D.-K. Kim, D.-S. Kim. Inje University Busan Paik Hospital, Department of Internal Medicine, Division of Cardiology, Busan, Korea, Republic of Korea

**Background:** The serum total bilirubin (TB) level has been inversely related with coronary artery disease served as a control group. CFR was defined as the ratio between hyperemic and basal average peak velocity (h-APV and b-APV). CFR was correlated to histological infarct size as percentage of left ventricle (IS%LV) in pigs and IS%LV as defined by cardiac magnetic resonance imaging in humans.

**Purpose:** We sought to evaluate the availability of admission TB level to predict clinical outcomes in patients with STEMI who underwent primary PCI with DES.

**Methods:** We analyzed 1,111 consecutive STEMI patients treated with primary PCI. The patients was divided into high TB group (n=816) and low TB group (n=218) according to the optimal cut-off value (0.79 mg/dl). We evaluated the incidence of major adverse cardiac events (MACE), a composite of cardiac death, non-fatal MI, and definite/probable stent thrombosis during hospitalization and at 12-month follow-up.

**Results:** The high TB group was associated with a significantly higher rate of in-hospital MACE (14.2% vs. 4.2%, p<0.001) and in-hospital cardiac death (13.9% vs. 3.9%, p<0.001) compared to the low TB group. However, these differences

**Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475 by guest on 07 February 2019**
were not found after hospital discharge. In the multivariate model, high TB was an independent predictor of in-hospital mortality (HR 2.69 [1.67–4.34], p=0.010) and in-hospital cardiac death (HR 2.72 [1.64–4.44], p=0.012) after adjusting for age, gender, left ventricular ejection fraction, Killip class, creatinine clearance, and other factors included in the TIMI risk score for STEMI. There was significant difference in the logistic regression test between two p values (p=0.176).

Conclusion: An increasing admission TB level was a useful and powerful marker to predict in-hospital MACE and cardiac death in patients with STEMI undergoing primary PCI with DES.

P2499 | BEDSIDE
Acute improvement of vascular function and oxidative stress by remote ischemic-conditioning in patients with acute myocardial infarction
I. Ikonomidou, E. Ilidromitis, M. Varoudi, I. Andreoudou, G. Pavlidis, N. Liarakos, L. Palaiodimos, A. Zoga, H. Triantafyllidis, J. Lekakis. University of Athens Medical School, Attikon Hospital, 2nd Department of Cardiology, Athens, Greece

Background: Remote ischemic conditioning has been shown to reduce myocardial damage in patients with acute myocardial infarction (AMI). However, the effects of remote post-conditioning on vascular oxidative stress are not fully defined.

Methods: We examined 60 patients with ST elevation AMI and 30 healthy controls with similar age sex and atherosclerotic risk factor profile. We employed the following remote ischemic conditioning protocol: baseline assessment of vascular function (T0), 1st brachial cuff inflation of both arms at 200mmHg for 5 min, cuff deflation and vascular assessment at 5 min (T1) after 1st cuff deflation, 2nd cuff inflation for 5 min after 10 min of the 1st cuff deflation, and vascular assessment at 5 min after 2nd cuff deflation (T2). We measured a) the brachial artery reactive hyperemia index (AI) in mmHg, b) systolic blood pressure (cSBP) by Compilor b) perfusion boundary region (PBR-micrometers) of the sublingual arterial microvessels (ranged from 5–25 micrometers) using Sidview, Darkfield imaging (Microscan, Glycocheck). Increased PBR is considered an accurate non-invasive index of reduced endothelial glycocalyx thickness c) malondialdehyde plasma levels (MDA) as marker of oxidative stress.

Results: AMI patients had higher PWV, cSBP, AI, and PBR and MDA than healthy controls (p < 0.05). cSBP, Al, and PWV increased after 1st cuff inflation compared to baseline but return to baseline values after 2nd cuff inflation in AMI patients (cSBP: 119±19 vs. 121±21 vs. 118±21mmHg, AI: 8±21 vs. 13±23 vs. 9±21%; PWV: 116±24 vs. 117±12 vs. 115±20 micrometers) of the sublingual arterial microvessels (ranged from 5–25 micrometers) using Sidview, Darkfield imaging (Microscan, Glycocheck). Increased PBR was considered an accurate non-invasive index of reduced endothelial glycocalyx thickness c) malondialdehyde plasma levels (MDA) as marker of oxidative stress.

Conclusion: Remote ischemic conditioning confers acute short-term improvement of vascular function instead of further deterioration. Thus, remote ischemic conditioning confers acute short-term improvement of vascular function and endothelial glycocalyx, likely through reduction of oxidative stress.

P2500 | BEDSIDE
ProACS score: an early and simple score for risk stratification of patients with acute coronary syndromes
A.T. Timoteo, S. Aguilar Rosa, M. Alonso Vogeira, R. Cruz Ferreira on behalf of Portuguese Registry on Acute Coronary Syndromes. Hospital Santa Marta, CHLC, Lisbon, Portugal

Background: Although there are several scores for risk stratification of patients with acute coronary syndromes (ACS), the effective implementation in clinical practice is not ideal. One of the barriers for adequate implementation is the result of some complexity of the available risk scores. Our objective was to develop a simple score for risk stratification of hospital mortality in a population for early use in the first medical contact with the patient, with simple variables.

Methods: The score was developed from a nationwide ACS registry. The development and internal validation cohort was obtained from the first 31829 patients, randomly separated (60% and 40%, respectively). The external validation cohort was selected from the last 8586 patients included in the registry. This cohort is significantly different from the other cohorts in terms of basal characteristics, treatment and mortality, which allowed us to validate the score in a contemporaneous population. For the score development, we used multivariate logistic regression analysis to select four variables with the highest predictive potential. Age, systolic blood pressure (SBP), Killip class on admission and ST elevation myocardial infarction were the selected variables. Continuous variables were categorized by ROC curve analysis and area under curve (AUC). To each parameter, a score was given based in the regression coefficient of each variables in the logistic regression model: 1 point for SBP ≤ 116 bpm, Killip class 2 or 3 and ST-segment elevation myocardial infarction, 2 points for age ≥ 72 years and 3 points for Killip class 4. The primary end-point was all-cause in-hospital mortality.

Results: The new score has a good discriminative ability in the development cohort (AUC 0.796, 95% CI 0.782–0.810), and similar in the validation cohort (AUC 0.785, 95% CI 0.767–0.803, p=0.333). In the external validation cohort, there were no differences in the discrimination of the new score for the other myocardial infarction class (AUC 0.815, 95% CI 0.793–0.837), with an adequate calibration (Hosmer-Lemeshow, p=0.233). GRACE risk score has an AUC of 0.888 (95% CI 0.865–0.910) in the external validation cohort.
Conclusions: ProACS risk score allows an easy and simple risk stratification for hospital mortality at the first medical contact of patients with ACS. It has also an excellent predictive ability in a contemporaneous population of patients with ACS, although slightly inferior to GRACE risk score. Its simplicity can improve implementation of these methods of risk stratification in clinical practice.

P2503 | BEDSIDE
Chronic pre-treatment of statin is associated with low incidence of mechanical complications after acute myocardial infarction
R. Shutter1, M. Hara2, M. Nishino1, T. Yoshimura1, N. Makino1, Y. Egami1, J. Tanouchi1, Y. Sakata1, Y. Sakata1, I. Komuro1, 1Osaka Rosai Hospital, Sakai, Osaka, Japan; 2Osaka University, Department of Cardiovascular Medicine, Suita, Osaka, Japan; 3Tohoku University, Department of Cardiovascular Medicine, Sendai, Japan; 4The University of Tokyo, Department of Cardiovascular Medicine, Tokyo, Japan

Background: Recently, mortality of patients who suffered from acute myocardial infarction (AMI) have improved by various medical technology including coronary reperfusion therapy, cardioprotective medications and preventative medicine. However, some patients died due to mechanical complication including ventricular septal perforation, papillary muscle rupture and cardiac rupture which can occur after AMI. Thus, it is important to clarify the predictive factors of above-mentioned mechanical complications after AMI in clinical settings.

Purpose: In this study, we investigated the predictive factors of mechanical complications after AMI.

Methods: Study population was 3,427 consecutive patients with AMI from 2000 to 2010. Multivariate-adjusted hazard ratios (adjusted HR) and 95% confidence interval (95% CI) were estimated by multivariate analyses with above-mentioned mechanical complications as dependent variable and age, the incidence of male gender, history of old myocardial infarction (OMI), ST elevated myocardial infarction (STEMI), diabetes mellitus, dyslipidemia, hypertension, smoking, chronic pre-treatment before admission including statins, angiotensin-converting enzyme (ACEI), renin-angiotensin receptor blockers (ARB), β-blockers (Beta), calcium channel blockers (CCB), loop diuretics, spironolactone, and antplatelet as independent variables.

Results: Multivariate analyses showed only chronic pre-treatment of statin significantly reduced the incidence of mechanical complication (adjusted HR: 0.20, 95% CI: 0.03–0.76, p=0.039) (table).

Conclusion: Chronic pre-treatment of statin before onset of AMI is associated with low incidence of mechanical complications after AMI.

P2504 | BEDSIDE
Long-term prognostic significance of complete revascularisation at the acute stage of myocardial infarction. The FAST-MI 2005 registry

Purpose: To assess whether early discharge of low-risk patients after successful PCI treatment of ST-segment elevation myocardial infarction (STEMI) is safe in terms of 12-month clinical follow-up.

Aim: To assess whether early discharge of low-risk patients with STEMI successfully treated by PCI is safe in terms of 12-month clinical follow-up.

Methods: We used the PL-ACS database (for baseline characteristics of STEMI patients with and without polyhedrocytes in ICT did not differ significantly in terms of patient's age, gender, cardiovascular risk factors, pre-hospital antplatelet and antithrombotic treatment did not influence the presence of polyhedocytes in ICT. The median PRI was lower in patients with <50% of fields of view covered by polyhedocytes on ICT surface (40 vs. 70%, P<0.014) or in the interior portion (62 vs. 75%, P<0.056) as compared with arteries of >3.5 mm. Time of ischemia of >5h was associated with a trend to more frequent thrombi rich in polyhedocytes in the interior core (>3.5 mm, thrombi rich in polyhedocytes were detected more frequently both on ICT surface (6/24 vs. 2/56, P<0.005) or in the interior portion (6/24 vs. 5/56, P<0.056) as compared with arteries of >3.5 mm. Time of ischemia of >5h was associated with a trend to more frequent thrombi rich in polyhedocytes in the interior core (8/37 vs. 3/43, P<0.058) as compared with time of ischemia of >5h. Patients with and without polyhedocytes in ICT did not differ significantly in terms of the frequency of final epicardial TIMI-3 flow (82.4 vs. 74.6%, P=0.13), complete TMPG-2/3 myocardial perfusion (75.0 vs. 72.6%, P=0.085) and distal embolization (18.8 vs. 16.1%, P=0.81). Both groups had similar enzymatic injury as measured by the area under the curve of CK-MB release (7.8±5.4 vs. 7.8±5.7±5.4 IU/L/h, P=0.99).

Conclusions: Our findings suggest that polyhedocytes in ICT are formed preferentially in patients with lower PRI, narrow infarct-related artery and in late presentation of STEMI, however their presence is not associated with a higher reperfusion injury.

P2505 | BEDSIDE
Determinants and clinical relevance of polyhedocyte content in intracoronary thrombus formed during acute myocardial infarction
J. Zalewski, M. Zabczyk, J. Nesser, A. Undas, Jagiellonian University - John Paul II Hospital, Krakow, Poland

Background: Recently it has been demonstrated that clot contraction is associated with fibrin exposure on its surface and erythrocyte compression in the interior core of the tightly-packed arrays of polyhedocytes, detectable in the intracoronary thrombus (ICT) of ST-segment elevation myocardial infarction (STEMI) patients.

Purpose: We sought to investigate determinants and clinical relevance of polyhedocyte content in ICT.

Methods: We assessed the content of fibrin, platelets and erythrocytes including polyhedocytes by scanning electron microscopy on the surface and inside ICT aspirated from 80 STEMI patients within 12 hours since chest pain onset. Platelet reactivity index (PRI) and ADP-induced platelet aggregation were evaluated on admission. The effectiveness of reperfusion was assessed by TIMI and TMPG scales and by enzymatic injury.

Results: All patients received aspirin and 45 (56.3%) 600 mg of clopidogrel, 80 (60–125) min prior to aspiration. Polyhedocytes were found in 18 (20%) thrombi. They covered >50% of fields of view covered by polyhedocytes on ICT surface (40 vs. 70%, P<0.014) or in the interior portion (62 vs. 75%, P<0.056) as compared with arteries of >3.5 mm. Time of ischemia of >5h was associated with a trend to more frequent thrombi rich in polyhedocytes in the interior core (8/37 vs. 3/43, P<0.058) as compared with time of ischemia of >5h. Patients with and without polyhedocytes in ICT did not differ significantly in terms of
pts from year 2009) linked to the database from the only health insurer in Poland (NFZ) for follow-up data on cardiovascular events up to 1 year following the index MI. STEMI patients of low-risk at discharge were defined as: age < 75 years, successful PCI of infarct related artery (final TIMI flow grade 3), not significant 3-vessel disease, LVEF > 45%, and with no life-threatening arrhythmias. Patients discharged early (up to 72 hours) were compared to those discharged after 72 hours of hospitalization (late discharge).

Results: A total of 3609 STEMI pts were analyzed. There were 542 (15%) early discharges. Mean age was similar in both groups (58 years). Patients discharged early were more frequently females (32% vs. 27%, p=0.013) and with hypercholesterolemia (48% vs. 41%, p=0.0037). The frequency of diabetes mellitus was similar in both groups (16% vs. 17%). During 12 months after discharge early discharged patients were more frequently hospitalized due to stable angina and had more frequently coronary angiography and PCI performer (table). The 30-day mortality was low in both groups (0.4%) with similar 12-month mortality (2%).

P2507 | SPOTLIGHT

Short-term exposure to fine particulate air pollution and risk of ST elevation myocardial infarction, ventricular arrhythmias and mortality


Background: Although numerous population-level studies indicate that air pollution (AP) is linked to adverse cardiovascular outcomes, this relationship has poorly been explored specifically for ST elevation acute myocardial infarction (STEMI). Purpose: To assess the short-term effect of AP on STEMI incidence and on the early occurrence of ventricular arrhythmias and mortality. Methods: The period under study was from 2010 to 2011 in an urban metropolitan area (reference population of 3.5 million). Daily STEMI rate, mortality in first aid and associated ventricular arrhythmias were prospectively obtained in a STEMI reperfusion network database. The corresponding daily levels of particulate matter (PM) 10, PM 2.5, Benzene, Cadmium, Nickel, Lead, SO2, NO2, CO, and ozone as well as the atmospheric variables temperature, air pressure, rain precipitation and relative humidity were recorded 1 to 7 days (lag 1 to 7) before the event (obtained from local and regional environmental authorities). The magnitude of association was estimated using a time-series design. Models were adjusted for atmospheric variables.

Results: After taking into account potential confounding by other pollutants and meteorological conditions, we found consistent evidence that an increase of 10 μg/m3 in the PM 10 levels (lag 2), lead (lag 1) and NO (lag 4) was associated with an increase of 1.03% (95% CI: 1.00 to 1.07%), 1.02% (1.00 to 1.04%) and 1.01% (1.00 to 1.02%), respectively, in the number of hospital admissions for STEMI. An increase in 10 μg/m3 in PM 2.5 was associated (lag 4) with STEMI mortality and (lag 3) with STEMI ventricular arrhythmias, with relative risks of 1.3330 (1.0031 to 1.7409) and 1.665 (1.0183 to 2.3922) and attributable risk percents of 24.98% (0.01 to 42.2%) and 14.20% (1.20 to 24.77%), respectively.

Conclusions: Short term exposure in increasing daily levels of PM 10, lead and NO is associated with increased daily STEMI admissions. Short-term exposure in increasing levels of PM 2.5 is associated with higher STEMI mortality and increased ventricular arrhythmias.

Acknowledgement/Funding: Governmental grant: Generalitat de Catalunya. Department of Health

P2509 | BEDSIDE

Survival advantage of overweight and obesity in patients with acute myocardial infarction

D.Y. Nah1, J.W. Chung1, J.H. Baee2, J.H. Kim3, Y.S. Kim2, M.M. Lee2, Y.J. Kim2, Dongguk University College of Medicine Gyeongju Hospital, Gyeongju, Korea, Republic of; 2Dongguk University Ilsan Hospital, Goyang, Korea, Republic of; 3Yeonnam University Hospital, Daegu, Korea, Republic of

Background: There are some conflicting and limited data regarding clinical outcomes in obese patients with acute myocardial infarction (AMI). The aim of this study to evaluate the relationship between body mass index (BMI) and mortality in Korean patients with AMI.

Methods: A total of 11,483 patients with AMI in Korean AMI registry. The number of male patients was 8,256 (71.9%). We categorized the patients according to BMI degree: lean (<18.5 kg/m2, n=429), normal (18.5–22.9 kg/m2, n=2,954), overweight (23–24.9 kg/m2, n=3,113) and obesity (≥25 kg/m2, n=3,987). Obesity was defined 25 kg/m2 or higher according to the criteria of Korean society for the study of obesity.

Results: Overweight and obesity AMI group were younger than normal and lean AMI group. Lean AMI group was older and more women than other BMI groups (p=0.001). AMI patients with obesity was an independent prognostic predictor of cardiac death on one month and one year after AMI. AMI patients with overweight also was an independent prognostic predictor of cardiac death on one year after AMI.

Conclusion: There appears to be an “obesity paradox” in patients with AMI such that overweight and obesity AMI patients are associated with lower mortality at one month and one year after AMI.

P2509 | BEDSIDE

Using landiolol during primary percutaneous coronary intervention attenuates myocardial reperfusion injury in patients with ST-segment elevation acute myocardial infarction

M. Kiyokuni1, T.M. Mitsuhashi2, T.S. Sugano1, T.I. Ishigami1, T.I. Ishikawa1, T.E. Endo2, K.K. Kimura 1, S.U. Umemura 1

Introduction: Landiolol is the beta 1 selective receptor blocker and its half-life elimination is 4 minutes. The safety and efficacy of landiolol started before coronary reperfusion in patients with ST-segment elevation acute myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI) remains unclear. We assessed the hypothesis that early use of landiolol reduces myocardial injury without increasing adverse events for STEMI patients performed pPCI.

Methods: Between October 2010 and September 2014, 220 consecutive patients with STEMI performed pPCI were recruited. Patients with heart rate ≥50, Killip class ≥2, old myocardial infarction and 2 or 3 degree of AV-block on admission were excluded. Thus 115 patients were enrolled. 60 patients were non-landiolol group with conventional treatment admitted from October 2010 to September 2012, 55 patients were landiolol group admitted from October 2012 to September 2014. After the admission, landiolol was started before pPCI intravenously with 3 μg/kg/min and stopped within 12 hours after pPCI when oral beta-blockers were administered. ST-segment resolution (STR) was defined as more than 70% resolution of sum of ST-segment elevation at the J point between emergency room and when finished pPCI.

Results: Time form admission to starting landiolol was 35±23 min in landiolol group. Age, sex, coronary risk factors, culprit lesion, SYNTAX score (19±10 vs 22±10, p<0.013), reperfusion time and peak creatine kinase did not differ between landiolol and non-landiolol group (all NS). The rate of non-sustained ventricular tachycardia (27 vs 50%, p<0.013), worsening heart failure (0 vs 8%, p=0.029), shock (15 vs 31%, p=0.030) within 12 hours after the admission. After a short time of finishing pPCI, systolic blood pressure did not differ between the two groups (117±21 vs 124±24mmHg, p=0.09), heart rate was lower (66±11 vs 77±14/min, p<0.01) and the rate of STR was higher (61 vs 42%, p=0.023) in landiolol group.
P2510 | BEDSIDE
Acute coronary syndrome in elderly - what is the place for invasive strategy?
S. Aguiar Rosa, A.T. Timoteo, M. Abnoso Nogueira, R. Cruz Ferreira on behalf of ProACS registry investigators. Hospital de Santa Marta, Cardiology, Lisbon, Portugal

Background: The elderly, due to co-morbidities, are less likely to undergo an invasive strategy for acute coronary syndrome (ACS).

Objective: The aim is to characterize elderly population admitted with an ACS, determine the predictors for an invasive strategy and evaluate the revascularization treatment benefit in outcome.

Methods: Retrospective analysis of ACS patients (P) with 80 years, admitted between 2010 and 2014, in a national ACS registry. P were divided according to therapy: intervened (GI) and non-intervened (GII). We evaluated clinical, electro and echocardiographic characteristics and determined predictors for an invasive approach – percutaneous coronary intervention (PCI) or coronary bypass graft (CABG) – and compared the 1 year follow up.

Results: From 11113P admitted with ACS, 2014 (18.1%) had ≥80 years; 51.9%male, mean age 84.5±4.6 years. 1025P (50.9%) were included in GI (94.8% PCI, 4.4% CABG, 0.7% PCI+CABG) and 986 (49.0%) in GII; 3P were excluded due to insufficient data. GI had less previous ACS (19.0% vs. 27.8%; p<0.001), previous CABG (4.2% vs 7.6%; p=0.001) and valvular disease (5.0% vs 10.5%; p<0.001). In GI, 49.3% had ST segment elevation myocardial infarction (STEMI) (vs 19.2% in GII; p=0.001). GI had higher ejection fraction (EF) (EF<50% GI: 46.2% vs GI 51.4%; p=0.026). In GI, 96% received dual antiplatelet therapy (vs 77.6% in GII; p<0.001). During hospitalization, GI had less heart failures (HF) (29.3% vs 35.8%; p<0.002), more atrioventricular block (6.5% vs 4.2%; p=0.018), cardiac arrest (3.5% vs 1.9%; p=0.026). Predictors for an invasive strategy were STEMI (OR 4.97; p<0.001), previous PCI (OR 2.02; p=0.001), sinus rhythm (OR 1.56; p=0.002), and hemoglobin at admission (OR 1.10; p=0.003). Predictor of no intervention were women (OR 0.68; p=0.002), previous ACS (OR 0.67; p=0.013), previous CABG (OR 0.60; p=0.035), HF (OR 0.48; p=0.018), stroke (OR 0.58; p=0.002), demen- tia (OR 0.28; p=0.001), heart rate (OR 0.99; p=0.003) and EF<50% (OR 0.68; p=0.01). Hospital mortality was inferior in GI (8.3% vs 13.6%; p<0.001). In STEMI (OR 2.21; p=0.01), dementia (OR 2.15; p=0.021), intratopsia (OR 11.05; p<0.001) and EF<50% (OR 2.86; p=0.001) predictors of mortality and systolic blood pressure (OR 0.99; p=0.037) and angiotensin converting enzyme inhibitor (OR 0.48; p=0.002) of survival. In propensity score analysis, 1 year followed up showed a better survival in GI (88.9% vs 79.6%; p<0.001).

Conclusion: In elderly patients with ACS, an invasive strategy confers short and long-term survival advantage. The predictors for invasive intervention are STEMI, previous PCI, sinus rhythm and haemoglobin at admission.

P2511 | BEDSIDE

M. Kishi on behalf of Tokyo CCU Network Committee. NTT Medical Center Japan, Tokyo, Japan

Background: Anemia has been previously reported as a predictor of short-term mortality in patients with acute myocardial infarction (AMI). However, few data is available in Japanese patients with AMI.

Methods and results: We evaluated 30-day mortality in Japanese AMI patients using Tokyo CCU Network Database 2009–2012 (n=10783) and classified these patients into 3 groups those were non-anemia group whose serum hemoglobin (Hb) concentration ≥12.0 g/dl on admission, mild anemia group (12.0>Hb≥10.0 g/dl) and severe anemia group (10.0>Hb). The result of Cox-regression analysis showed that even mild anemia was a predictor of short-term mortality. Kaplan-Meier analysis revealed gradual increase in mortality during 3 groups.

Conclusions: The present study showed that anemia was associated with short-term mortality in Japanese patients with AMI.

P2512 | BEDSIDE
The diagnostic value of intracoronary pressure-velocity loops during primary intervention in ST-segment elevation myocardial infarction to predict subsequent development of microvascular injury.

G.A. De Waard1, P.F. Teunissen1, M.R. Hollander1, E. Echavarria-Pinto2, J. Escaned2, S. Aguiar Rosa, A.T. Timoteo, M. Afonso Nogueira, R. Cruz Ferreira on behalf of the Amsterdam Medical Centre, Amsterdam, Netherlands: 2Hospital Clinic San Carlos, Cardiology, Madrid, Spain

Background: The occurrence of cardiac magnetic resonance imaging defined microvascular injury (MVI) after angiographically successful primary percutaneous coronary intervention (PCI) for ST-segment elevation myocardial infarction (STEMI) portends worse long-term outcome. Identification of patients at risk for MVI at the time of primary percutaneous coronary intervention (PCI) might be relevant, we investigated whether intracoronary pressure-velocity-loops obtained during PCI can predict subsequent MVI.

Methods: In 28 patients, simultaneous Doppler flow velocity and distal pressure measurements were obtained directly following primary PCI. From the pressure-velocity-loops, the instantaneous hyperemic diastolic velocity-pressure slope (HVDS) and zero flow pressure (PZF) were calculated. IHVDS is defined as the slope of the distal pressure-flow-velocity relationship during mid-to-end diastole under hyperemia (mid-late diastolic conductance), and PZF as the closing coronary pressure, extrapolated from the pressure-flow-velocity relationship, largely determined by extraversus compression of the myocardial capillaries. 5 to 7 days following intervention, cardiac magnetic resonance imaging using late gadolinium enhancement was performed to assess the presence and extent of MVI, to which IHVDS and PZF were related.

Results: PZF was significantly higher in patients with MVI in comparison to patients without MVI (45.68±13.16 vs. 32.01±14.98 mmHg, p=0.015). In patients with extensive MVI, defined as more than 2.0 cm² MVI, PZF was and 48.54±13.72 vs. 34.01±13.67 mmHg, p=0.009 for extensive MVI. The area-under-the-receiver-operator-curve for PZF to predict MVI was 0.75 (95% CI 0.55–0.89, p=0.01) and 0.77 (95% CI 0.58–0.91, p=0.01) for extensive MVI. No relationship was found between IHVDS and PZF (r=0.29, p=0.13). IHVDS did not discriminate between patients with or without the development of MVI (1.47 (1.0R:0.82–2.69) vs. 1.39 (0.9R:0.25–5.55) mmHg cm⁻¹ s⁻¹ respectively, p=0.77)

Conclusions: PZF, but not IHVDS, was related to the presence and extent of MVI. This finding suggests a role for PZF in risk stratification for patients at risk of developing myocardial microvascular injury, which may imply different reperfusion strategies for STEMI. It is conceivable that in patients with MVI, elevated interstitial pressure gradients may be the driving force of transmural perfusion.

P2513 | BEDSIDE
Patient’s delay in seeking care do not affect one-year post-discharge mortality in STEMI treated with primary coronary angioplasty.

D.T. Placzkiewicz, M. Puzniak, A. Kleinrok. The Pope John Paul IInd Hospital, Zamosc, Poland

Background: Minimizing total ischemic time is associated with improved outcome in ST-segment elevation myocardial infarction (STEMI). There are some goals listed in guidelines. Patient delay (symptom onset - first medical contact (FMC)) should be as short as possible, system delay (FMC - wire passage into the culprit artery) should be ≤90 min, and hospital delay (presentation in the emergency department (ED) - wire passage) should be ≤60 min. However other kinds of delays, potentially useful in daily practice, can be defined.

Purpose: To evaluate more kinds of delays than were defined in European guidelines, and to find threshold limits in which further reduction does not impact one-year post-discharge mortality in STEMI.

Methods: This was a retrospective, observational, single-centre study. Data of all STEMI patients who were admitted to our coronary care unit between October 2005 and September 2013 were examined. 875 consecutive patients, who met criteria for the invasive treatment strategy after EGCG teletension from the field, and then underwent successful pPCI were included. All in-hospital deaths were excluded from the analysis. Evaluation of all delays was made possible by medical records. Where possible, threshold limits in which further reduction did not impact on 1-year mortality were then determined.

Conclusions: In low risk patients with STEMI, using landiolol during pPCI may attenuate myocardial reperfusion injury and reduce adverse events.

Multivariate analysis showed that landiolol use was an independent predictor of STR (OR=2.51, p<0.001). Landiolol use was also predictive of subsequent development of microvascular injury (MVVI) in patients with STEMI (OR=2.51, p=0.045).

Conclusion: In low risk patients with STEMI, using landiolol during pPCI may attenuate myocardial reperfusion injury and reduce adverse events.
post-discharge mortality were found. Pearson chi-square test was used to evaluate differences in one-year mortality between patients with longer and shorter delay. Statistical significance was considered for \( p < 0.05 \).

**Results:** Results are presented in table. Any kind of delay, which included patient's decision time, did not affect one-year post-discharge mortality.

**Conclusion:** All analyzed system-dependent delays affected one-year post-discharge mortality in STEMI. Any patient-dependent delay did not affect one-year mortality.

P2514 | BEDSIDE
The relationship between post procedural ST-segment resolution and long term clinical events in patients who underwent primary percutaneous coronary intervention

E. Turkyilmaz 1, A. Kalayoğlu 1, V. Oduncu 1, O. Özeren 1, C.Y. Karabay 1, A. Aktun 1, A. Bitüken 1, N. Teftik 1, C. Kirma 1, Kartal Kosuyolu Heart Education and Research Hospital, Department of Cardiology, Istanbul, Turkey; 2 Bafra sheer University, Istanbul, Turkey

**Aim:** In this study, we aimed to investigate the relationship between ST segment resolution (STR) obtained in the post-procedural 6 minute and long term (median follow-up, 59 months) cardiovascular events in patients with STEMI group and TTC patients elevation myocardial infarction (STEMI), treated with primary percutaneous coronary intervention (p-PCI).

**Study protocol:** The study population consisted of 3090 patients (792 females, mean age 57.1) treated with p-PCI for STEMI, who admitted within first 12 hours of chest pain between January 2006-January 2010 and post-procedural STRs were evaluated with ECG. The patients were divided into complete (>70%, n=1979), incomplete (30–70%, n=856) and no-resolution (≤30%, n=255) groups according to post-procedural ST segment resolution percentage.

**Results:** In the logistic regression analysis previous statin use [odds ratio (OR) 0.72, 95% confidence interval (CI), 0.51–0.89, p < 0.001], pre-procedural troponin level ([OR], 0.61, 95% CI 0.46–0.85, p < 0.001), baseline anemia (OR 2.04, 95% CI 1.43–3.11, p < 0.001), baseline SYNTAX score -18 (OR 1.58, 95% CI 1.15–2.87, p < 0.001), TIMI thrombus score: 4 (OR 2.94, 95% CI 1.54–4.87, p < 0.001), pain-to-balloon time <4 hr (OR 1.82, 95% CI 1.29–2.56, p < 0.001) and neutrophil to lymphocyte ratio >5 (OR 1.82, 95% CI 1.34–3.03, p < 0.001) were identified as independent predictors of no-STR. In hospital death (11.8% vs 7.5% vs 1.3%) and heart failure (35.5% vs 25.8% vs 10.5% respectively).

**Conclusion:** Pts with TTC had a lower incidence of serious complications compared to STEMI group. Moreover, in-hospital mortality was also lower in TTC group. We observed that prognosis is more favourable in pts with TTC.

P2516 | BEDSIDE
Prognostic value of hs-TnT based on cardiac magnetic resonance imaging based infarct characteristics following reperfused acute myocardial infarction

TL. Nguyen 1, J. Phan 1, J. Xiong 2, L. Hee 3, C. Juergens 1, R. Rajaratnam 1, H. Dimitro 1, J. French 1, D. Richards 2, L. Thomas 1, Liverpool Hospital, Department of Cardiology, Liverpool, Australia; 2 University of New South Wales, Sydney, Australia

**Background:** Cardiac magnetic resonance imaging (CMRI) is the current standard noninvasive imaging modality in determining infarct scar size, with high reproducibility and accurate characterisation of myocardial injury following acute myocardial infarction (AMI). Infarct scar characteristics by contrast enhanced CMRI provides independent and incrementally prognostic value in addition to left ventricular ejection fraction. High-sensitivity Troponin T (hs-TnT) levels correlate well with infarct size and have prognostic importance.

**Objectives:** Our study aims were to 1) evaluate the prognostic significance of hs-TnT compared to known prognostic CMRI infarct markers, following AMI; and 2) determine the optimal hs-TnT time point to predict major adverse cardiovascular endpoints (MACE).

**Methods:** 199 consecutive patients with first presentation ST-segment elevation myocardial infarction were prospectively recruited. Serial hs-TnT measurements were performed to determine peak, admission, 24 hour, 48 hour and 72 hour levels following AMI. Infarct scar characteristics (scar size, gray zone scar, area at risk size, and microvascular obstruction (MVO)) were evaluated by late gadolinium enhancement CMRI at a median of 4 days post AMI. The primary endpoint of MACE included death, recurrent AMI, acute exacerbation or readmission for heart failure, stroke and sustained ventricular arrhythmias.

**Results:** With a median follow-up of 60.2 months, 33 patients had a primary endpoint event. Kaplan Meier survival curves showed that 48 and 72 hour hs-TnT levels were the only time points to significantly predict MACE (by Log rank analysis, chi square = 4.33, p=0.037, chi square = 5.99, p=0.014 respectively). All hs-TnT showed significant association with MACE, by univariate analysis. Multivariate analysis, incorporating clinical and MRI variables (infarct scar core and gray zone size; MVO; and area at risk), with a single time point hs-TnT level (applied one at a time) to each model was performed. Peak, 48 hour and 72 hour hs-TnT were independent predictors of MACE (chi square = 4.79, HR=1.09, p=0.029; chi square = 6.84, HR=1.19, p=0.009; and chi square = 9.98, HR=1.31, p=0.002 respectively).

**Conclusions:** Sampling of 48 and 72 hour hs-TnT levels were the optimal time points for prediction of adverse cardiovascular events post AMI. Measurement of hs-TnT levels are a simple and inexpensive method to assess prognosis, and provide early means of identifying high risk patients following AMI.

P2517 | BEDSIDE
Primary angioplasty in acute myocardial infarction due to occluded, unprotected left main coronary artery


**Introduction:** Acute myocardial infarction (AMI) due to unprotected left main coronary artery (ULM) occlusion is a rare condition with a high mortality. Several series reported the results of primary percutaneous coronary intervention (P-PCI) in AMI involving ULM; however, no series have been published so far often than pts with STEMI. There weren’t differences in time from onset of symptoms to the hospital admission in both groups.

**Results:** Echocardiography was performed during 24h from admission to the hospital. Ejection fraction (EF) was lower in pts with TTC in comparison to pts with STEMI (41.9% vs 45.4%, p < 0.05). However, pts with STEMI had lower rates in hospital complications. They had less often cardiogenic shock, heart failure, atrial fibrillation, left ventricle rupture, ventricular septal defect (table 1). There weren’t differences in the incidence of left ventricle thrombus formation as well as in sustained ventricular tachycardia or ventricular fibrillation rates. In-hospital mortality was higher in STEMI group.

**Conclusion:** Pts with TTC had a lower incidence of serious complications compared to STEMI group. Moreover, in-hospital mortality was also lower in TTC group. We observed that prognosis is more favourable in pts with TTC.
on the outcomes of complete, unprotected ULM thrombotic occlusion as culprit vessel.

**Methods:** We reviewed the database from a university hospital including 30000+ PCI over the last 10 years. We selected patients with P-PCI on ULM and we reviewed angiographies to confirm vessel occlusion (TIMI 0). Follow up data was gathered from medical history and phone interviews. The figures mean absolute numbers (percentage) or median (interquartile range). Comparisons were done with non-parametric tests, and results were considered statistically significant if p < 0.05.

**Results:** 21 patients met the requirements for analysis. 17 (81%) male, median age 64 (53–72) years, most patients (19, 90%) had at least one cardiovascular risk factor. 15 (71%) were admitted as ST-elevation acute coronary syndrome (STEACS) while the remaining 6 (29%) had NSTEACS with an specific EKG. 11 (52%) were in cardiogenic shock and 5 (24%) required cardiopulmonary resuscitation prior to P-PCI. Intracoronary balloon counterpulsation (IABP) was started in 14 (67%) cases either before or during the intervention: its use was not significantly dependent on presence of cardiogenic shock (p = 0.18). 10 (48%) died in the cath lab or within the first 12 hours. Mortality was higher among those admitted in cardiogenic shock (73% vs. 20%, p = 0.03) or when P-PCI was unsuccessful (86% vs. 29%, p = 0.02). On the other side, we found no statistically significant differences in survival with regard to age (57 vs. 70 years, p = 0.20), EKG on admission (STEACS 17% vs. STEACS 60% p = 0.15) or presence of collaterals from RCA (57% vs. 50%, p = 1).

11 patients remaining alive were followed up for 6.8 (5.2–7.7) years: there was a CABG, 3 diagnostic and a therapeutic PCI in 4 individuals. Another patient required a left ventricle assist device (LVAD). Two died in this group: one due to cardiogenic shock 24 hours after the event, and the one with LVAD due to septic shock a week later. All the survivors but one (suffering from severe lung disease) were in NYHA class I or II at follow-up.

**Conclusion:** Clinical presentation and P-PCI are paramount in AMI due to ULM occlusion. Therefore, successful resuscitation are the most important factors associated with survival. Besides, long-term prognosis is excellent because the patient stands 12 hours after P-PCI.

### P2519 | BEDSIDE

**Impact of new-onset atrial fibrillation on 30-day and one-year mortality in STEMI patients undergoing primary PCI**


**Background:** Atrial fibrillation (AF) has been associated with adverse outcomes in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).

**Purpose:** The aim of this study was to assess the impact of new-onset AF on short- and long-term mortality in STEMI patients following primary PCI.

**Methods:** We examined records of 2108 consecutive patients from a primary PCI registry of a high-volume catheterization laboratory. Patients classified as having preexisting AF (n = 39) were excluded from the analysis. Kaplan Meier cumulative mortality curves were compared with the log rank test. Cox regression model was created to assess the mortality risk for patients with new-onset AF.

**Results:** New-onset AF was present in 7.4% of patients (n = 154). Overall mortality rates at 30-day and one-year follow-up were 6.2% and 11.2%, respectively. Patients with new-onset AF had significantly higher mortality rates at both 30 days (19.5% vs 5.1%, p < 0.001) and one year (30.5% vs 9.7%, p < 0.001). Log-rank test showed significant difference in cumulative mortality curves in patients with new-onset AF, as compared to patients without AF (p < 0.001, Figure). Unadjusted Cox regression revealed a four-fold increased risk of 30-day mortality (HR 4.05, 95% CI 2.60–4.93, p < 0.001) and one-year mortality (HR 2.17, 95% CI 1.55–3.03, p < 0.001).

**Conclusion:** New-onset atrial fibrillation in STEMI patients undergoing primary PCI is independently associated with significant increase in risk of both 30-day and one-year mortality.

### P2520 | BEDSIDE

**Can syntax score predict angiographically visible distal embolization during primary percutaneous coronary intervention?**

I. Biyik1, I.F. Akturk2, D. Ozurtk2, C. Sarkamis2, O. Celik2, F. Uzuz2, A.A. Yalcin2, G. Yildiz2, A. Ayaz2, M.K. Erol2. 1 Usak State Hospital, Department of Cardiology, Usak, Turkey; 2 Mehmet Akif Eryosy Thoracic and Cardiovascular Surgery Training and Research Hospital, Department of Cardiology, Istanbul, Turkey

**Background:** Primary percutaneous coronary intervention (PPCI) is the most effective and validated treatment strategy of ST segment elevation myocardial infarction (STEMI). Nevertheless, normal myocardial perfusion cannot always be achieved at the end of the procedure in a significant number of patients with STEMI.

**Purpose:** The aim of this study was to investigate angiographic and procedural predictors of angiographically visible distal embolization (AVDE) during PPCI and the assessment of mid and long term mortality.

**Materials and methods:** The study enrolled 954 STEMI patients admitted for primary PCI as a part of STEMI guidelines. With the aim of assessing the impact of AVDE on short- and long-term mortality, STEMI patients were divided into two groups according to AVDE presence: STEMI I/ STEMI II (No AVDE) and STEMI VI / STEMI VII (AVDE). The study population was divided into 2 groups: AVDE positive and AVDE negative. The primary endpoint was the assessment of short and long-term mortality.

**Results:** The prevalence of AVDE was 42 (4.4%) out of the 954 STEMI patients. The average age of the studied patients was 64 (53–72) years, 769 (80.6%) were male and 185 (19.4%) were female. The prevalence of diabetes mellitus (DM) was 137 (14.3%) while 226 (23.6%) had chronic kidney disease (CKD) and 166 (17.3%) had previous myocardial infarction (MI).

**Conclusion:** In the STEMI VI/ STEMI VII group, the prevalence of AVDE was significantly higher compared to STEMI I/ STEMI II group (42.1% vs 5.4%, p < 0.001). Logistic regression analysis revealed that a presence of AHF of II-IV classes by Killip increased the chances of CIN (OR: 2.47, 95% CI: 1.05–5.85, p = 0.04). Log-rank test showed significant difference in cumulative mortality curves in patients with and without CIN, a significantly greater frequency of DM (28.85% vs 15.37%, p = 0.004) and CKD (55.7% vs 41.34%, p = 0.03) and occurrence of AF (32.69% vs 17.91%, p = 0.008). None of the patients developed acute renal failure.

**Conclusion:** Syntax score was not associated with AVDE during primary PCI. However, AVDE was significantly associated with CKD, DM, AHF and previous MI. Furthermore, AVDE was found to be associated with short and long-term mortality.
and clinically apparent AHF (II-IV class by Killip) were independent predictors of CIN development which in its turn increased the frequency of adverse outcomes in hospital period in STEMI patients.

P2521 | BEDSIDE
All-cause in-hospital death analysis of patients with acute myocardial infarction from China acute myocardial infarction registry (CAMI)

L. Song, Y.J. Yang, J.G. Yang, X.J. Gao, W. Li, H.Y. Xu on behalf of CAMI Registry. Fu Wai Hospital, Beijing, China, People’s Republic of China

Background: Patients with AMI have a high in-hospital mortality rate, even in this era of PCI. The objective of this study was to determine the in-hospital death causes and mortality factors for mortality through this prospective, nationwide, multicenter, observational registry in the real world of Chinese. Methods: From January 1, 2013 to March 31, 2014, total 15445 consecutive patients from CAMI registry (NCT01784691) with or without ST-segment elevation myocardial infarction (STEMI or NSTEMI) who admitted within 7 days of acute ischemic symptoms with a primary clinical diagnosis of AMI were included (108 hospitals in 31 provinces, Mainland of China).

Results: Of 15445 patients, 73.9% (11411) was male, 73.4% (11331) was STEMI and 26.6% (4114) was NSTEMI. Of those STEMI patients, 52.8% (5988) had received emergency revascularization and 79.9% (4786) of them was primary PCI; of those NSTEMI patients had a much lower percentage (8.6%, 357). Total in-hospital mortality rate was 6.58% (1017/15445), female patients (10.26%), age >75 (14.04%), hypertension (7.06%), diabetes (7.78%), never smoking (8.90%), chronic kidney history (9.89%), chronic renal insufficiency (12.05%), chronic proliferative pulmonary diseases (12.54%), ST elevation (6.81%), anterior wall involved (7.75%), heart failure (15.77%), cardiac arrest (33.16%) or cardiac shock (36.44%) when admission, and patients not received emergency revascularization (99.76%). Overall, 32.2% death occurred in the same day of AMI and 77.3% less than a week. 37.2% (378) death cases had no certain cause, but for those who had, cardiogenic shock accounted for 42.3% of death cause, and the other four main causes were sudden cardiac death (29.3%), multiple organ dysfunction syndrome (11.1%), mechanical complications (10.0%) and pulmonary infection (2.2%). Using multiple logistic regression model, mechanical complications (OR 72.59, 95% CI 32.75–160.89, p < 0.0001), heart failure when admission (OR 5.23, 95% CI 4.24–6.44, p < 0.0001), and age >75 (OR 3.07, 95% CI 2.41–3.94, p < 0.0001) were the three leading independent predictors for in-hospital death. Conclusions: Among unselected AMI patients in China, the in-hospital mortality (6.58%) was still high, cardiogenic shock contributed to nearly half the cause of death. Mechanical complications, heart failure when admission and age >75 were the three leading independent predictors for in-hospital death.

P2522 | BEDSIDE
Residual thrombin potential predicts cardiovascular death in acute coronary syndrome patients after stent implantation

M. Attanasio1, R. Marcucci1, A.M. Gori1, R. Paniccia1, R. Priori1, S. Valerio1, D. Batiz1, A. Barchielli1, R. Abbate1, G.F. Gensini1,1 University of Florence, Dpt Experimental and Clinical Medicine, Florence; 2 Careggi University Hospital (AOUIC), Florence; 3 ASIF Tuscany Region, Epidemiology Unit, Florence, Italy

Background: Thrombin generation is a central step of the coagulation system involved in the thrombotic role of platelets clotting, to fibrinolysis, platelet activation, and inflammation. Scarce data evaluating the association between thrombin generation and the risk of cardiovascular death in acute coronary syndrome (ACS) patients is available, especially in the era of PCI and stenting with the use of dual antiplatelet treatment. Purpose: Aim of our study was to evaluate the possible association between the entity of thrombin generation and cardiovascular death in ACS patients undergoing PCI and stenting. Methods: In the frame of the Acute Myocardial Infarction (AMI)-Florence 2 study, we investigated thrombin generation in 294 ACS patients undergoing PCI with stent implantation. Venous samples were obtained within 24 hours from PCI. Thrombin generation was assessed using the calibrated automated thrombogram (CAT), and was expressed as endogeneous thrombin potential (ETP), peak, and velocity index. Results: At two years of follow-up, 57 out of 294 patients (19.4%) died from cardiovascular causes. Higher values of ETP [1115.9 (705–14411) vs 940.2 (666.0–1253.1) p < 0.049], peak [176.1 (80.5–259.4) vs 107.3 (59.9–181.1) p < 0.002] and velocity index [10.96 (9.02–12.78) vs 22.5 (25.26–58.6) p < 0.001] were detected in patients in death during follow up compared to alive patients. At the multivariate model adjusted for the Global Registry of Acute Coronary Events (GRACE) risk score, the association between thrombin generation and cardiovascular death remained significant for peak [OR (95% CI): 2.34 (1.09–5.04), p = 0.030] and velocity index [OR (95% CI): 2.16 (1.10–4.63) p = 0.048]. This result was confirmed even after adjustment for high on-treatment platelet reactivity. Conclusions: We found that thrombin generation is significantly higher in patients with cardiovascular death in ACS and is an independent predictor of cardiovascular death thus it may be useful in improving risk stratification for ACS patients. Moreover, this association maintains its significance also in a model adjusted for high on-treatment platelet reactivity.
P2525 | BEDSIDE
Relationship between infarct artery location, acute total coronary occlusion and mortality in STEMI and NSTEMI patients
J. Karwowski1, M. Gierlotka², L. Polonski², M. Gasior², M. Beckowski¹, I. Kowalki¹, H. Szwed³ on behalf of Institute of Cardiology, 2nd Department of Coronary Artery Disease, Warsaw, Poland; Silesian Center for Heart Diseases, 3rd Department of Cardiology. 1Institute of Cardiology, 2nd Department of Coronary Artery Disease, Warsaw, Poland; 2Medical University of Silesia, Silesian Center for Heart Diseases, 3rd Department of Cardiology, Zabrze, Poland

Purpose: We compared angiographic findings and mortality in patients with non-ST-segment elevation myocardial infarction (NSTEMI) versus ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous revascularization.

Methods: We analyzed 4581 STEMI pts and 2487 NSTEMI pts enrolled in the Polish Registry of Acute Coronary Syndromes who underwent an invasive strategy with percutaneous coronary intervention (PCI). Pts were divided in 2 groups according to preprocedural culprit vessel TIMI flow: TIMI flow 0 – acute total coronary occlusion (TO) and TIMI flow 1–3 – non-TO.

Results: Total coronary occlusion had 2949 (64.37%) STEMI pts and 660 (26.5%) NSTEMI pts. The most common totally occluded infarct related artery (IRA) in STEMI group was RCA 49.37% (LAD 37.84%, LCX 12.78%) whereas in NSTEMI group had a significantly higher proportion of LAD 45.5% (RCA 32.3%, LCX 22.2%). In NSTEMI pts both RCA TO and LAD TO had higher mortality during all 36-mth follow up but only in STEMI group, mortality in NSTEMI group was comparable between TO and no TO. LCX pts with TO had higher in-hospital mortality both STEMI and NSTEMI group, without differences in further follow up. There were not differences in mortality between RCA TO and no TO pts between both STEMI and NSTEMI groups.

Conclusions: An acute total coronary occlusion had 64.37% STEMI pts and 26.5% NSTEMI pts. The RCA was present among a half STEMI pts with total occlusion as well as the LCX among NSTEMI pts with total occlusion. Total occlusion had impact on mortality LAD related STEMI pts during all 36-mth follow up and had impact on only in-hospital mortality LCX-related MI pts, both STEMI and NSTEMI.

P2526 | BEDSIDE
Do women with ST segment elevation myocardial infarction submitted to primary angioplasty have a worse prognosis than men?

Introduction: There are some studies suggesting that women have higher mortality than men after ST segment elevation myocardial infarction (STEMI). The main goal of this study was to determine gender dependent differences in prognosis after a STEMI among patients submitted to primary angioplasty.

Methods: A retrospective, descriptive and correlational study was performed, involving 1230 patients with ACS (667 TO and 563 non-ST elevation ACS) from 1 October 2009 to 30 September 2010. The patient demographic, clinical and therapeutic data were collected at admission. A telephone 1 year follow-up was performed. SPSS 20.0 was used to calculate univariate and multivariate statistical analysis for 1 year mortality.

Results: We found 752 patients with STEMI submitted to primary angioplasty. 160 (21.3%) were female and had: higher mean age (66.3 vs 61.4, p<0.00), higher prevalence of arterial hypertension (p<0.00) and of diabetes mellitus (p=0.01 and less frequently smokers (p=0.00). Women had less previous history of acute coronary syndromes (p<0.05) and percutaneous revascularization (p<0.05).

Women had higher time between the first symptoms and first electrocardiogram (2.4 vs 1.9h, p=0.03) and consequently to revascularization therapy (4.5 vs 3.7 h, p=0.01). They presented more often in Killip-Kimball class different than 1 (p=0.03), longer hospitalization (4.5 vs 3.7 dias, p=0.00) and higher 30 day mortality rate (6.2 vs 2.9%, p=0.04).

Hospital complications and one year mortality rate were similar in both gender.

Conclusion: Female patients with STEMI submitted to primary angioplasty have longer hospital admission times and a higher mortality at 30 days than men. These differences can be explained in part because their older age, but more importantly because of their delay in diagnosis and consequently in the reperfusion delay when compared with men.

P2527 | BEDSIDE
Factors influencing the patient delay in STEMI
A. Kleinrook, M. Puzniak, D. Placzkiewicz, T. Jastrzębski. Regional Hospital Pope John Paul II, Cardiology, Zamosc, Poland

Background: Many papers showed that patient delay defined as time from the start of chest pain to call for help is difficult to modify.

Purpose: The aim of the study is identifying factors influencing the patient delay in STEMI.

Methods: Retrospective analysis of 954 STEMI patients admitted to the Cardiology Department after teletransmission of ECG and teleconsultation with cardiologist in the period of 07.10.2005 - 05.01.2014. Data were obtained from the Emergency Medical Service protocols and hospital records. The influence of age, gender, place of residence, living with family or alone, smoking, presence of hypertension, hypercholesterolemia, diabetes, obesity, overweight, history of CAD (myocardial infarction, interventional treatment) on the patient’s delay was determined.

Results: The factors prolonging the patient delay are: female sex (avg. + 33 min., + 15.8%, p=0.008), living in rural areas (avg. + 32 min., + 15.9%, p=0.0097), not smoking in the period preceding the hospitalization (avg. + 7 min., + 29.5%, p=0.0375). Other factors as age, living with family or alone, presence of hypertension, diabetes, hypercholesterolemia, obesity, overweight had no influence on patient delay. Interesting also the history of CAD had no influence on the point of the educational process during previous hospitalization and out-patient care.

Conclusions: Female sex, living in rural areas and not smoking are the factors increasing the patient delay time.

P2528 | BEDSIDE
Diabetes Mellitus type 2 is an important risk factor for sudden cardiac arrest in patients with STEMI
P. Tracinski, M. Jaskowski, L. Figiel, J.D. Kasprzak. Medical University of Lodz; Bieganski Hospital, Chair and Department of Cardiology, Lodz, Poland

Background and introduction: Sudden cardiac arrest (SCA) is the most serious complication of ST elevation myocardial infarction (STEMI). The negative impact of Diabetes Mellitus type 2 (T2DM) on the development of cardiovascular diseases is well known and documented. However, we lack in conclusive data about frequency of SCA in diabetic patients with STEMI.

Purpose: We aimed to assess the impact of T2DM on the incidence of SCA in patients with STEMI.

Methods: We divided 450 consecutive patients (266 men, 184 women, age: arithmetic mean 64.9 years, median 63 years, 214 smokers [47.6%]) with confirmed STEMI as the LCX among without T2DM and evaluated the incidence of prehospital SCA. Then, we performed comparative analysis between those groups.

Results: We observed 137 (30.5%) cases of T2DM (we provided 15 diagnoses during the in-patient stay, according to Polish Diabetes Association). Ventricular fibrillation or ventricular tachycardia without a pulse (VF/VT) accounted as the dominant mechanism of SCA in both groups (with and w/o T2DM).

We recorded only one case of asystole, in a patient with T2DM. Among patients with T2DM sudden cardiac arrest occurred 9 times (6.6%), whereas among patients without T2DM – 4 times (1.2%). We evaluated hazard ratio (HR) of SCA associated with T2DM at 5.08 (Fisher’s Exact Test, p<0.01).

Conclusions: In our study group SCA as a complication of ST elevation myocardial infarction appeared 5 times more frequently in patients with Diabetes Mellitus type 2 than without T2DM (6.6% vs 1.4%); HR=5.08, p<0.01.

P2529 | BEDSIDE
Kidney lesion in ST-elevation myocardial infarction- how to evaluate it?

Introduction: Chronic Kidney Disease (CKD) and acute kidney lesion are frequent co-morbidities in patients admitted for ST-elevation myocardial infarction (STEMI) and are associated with a worse outcome. There are several equations to correctly identify patients with kidney lesion through glomerular filtration rate (GFR), but it is still not consensual which one is the most appropriate in the setting of STEMI.

Purpose: We aimed to compare which of the 3 more commonly used formulas - Cockcroft-Gault [CG], Modification of Diet in Renal Disease [MDRD] and Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] - is more effective in predicting worse outcomes at 1-year follow up in STEMI.

Methods: Prospective study of 543 patients admitted for STEMI [age 63.80±12.79; 74.0% men; 23.9% diabetics; 55.1% hypertensive] in our cardiac intensive care unit, between October 2009 and September 2014. GFR estimated...
from CG, MDRD and CKD-EPI were compared in terms of mortality risk prediction and primary composite endpoint (cardiovascular death, non-fatal myocardial infarction or stroke) during hospitalization.

**Results:** The prevalence of GFR ≥60 ml/min/1.73m² was 42.2% using the CG, 46.3% with MDRD and 41.9% with CKD-EPI. All formulas had a good discriminatory power in the primary composite endpoint with CG proving to be the best formula by ROC curve analyses [AUC (CG): 0.726 vs AUC (MDRD): 0.689 vs AUC (CKD-EPI): 0.706]. All formulas were also good predicting in-hospital total mortality with CG to evidencing the best results [AUC (CG): 0.755 vs AUC (MDRD): 0.738 vs AUC (CKD-EPI): 0.748].

**Conclusion:** All formulas proved to be effective in predicting adverse outcomes during hospitalization. The CG formula is more accurate than MDRD and CKD-EPI.

---

**P2530 | BEDSIDE**

Infarct size in staged versus immediate complete revascularisation for multivessel disease: a randomised, controlled trial

**Methods:** In the prospective CVLPRIT-CMR study, in-hospital CR was staged in 30 patients and immediate in 60 patients. Acute and follow-up CMR were performed 24–96 hours and 9 months post CR, respectively. The primary CMR endpoint was in acute CMR and clinical endpoint was combined 12-month MACE (MI, heart failure, mortality, revascularisation).

**Results:** Staged and immediate CR patients were well matched. The number of infarcts and IS was higher, and MIS and LVEF were lower at staged CR. At follow-up CMR, prevalence and extent of reversible ischaemia and MACE incidence were similar (Table 1).

<table>
<thead>
<tr>
<th>Immediate complete CR (n=60)</th>
<th>Staged complete CR (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>62.8±11.7</td>
</tr>
<tr>
<td>Male infarct (n, %)</td>
<td>52/60 (86.7)</td>
</tr>
<tr>
<td>Anterior infarct (n, %)</td>
<td>21/60 (35.0)</td>
</tr>
<tr>
<td>Symptom–PCI time (min)</td>
<td>179 (127–305)</td>
</tr>
<tr>
<td>Time to acute CMR (d)</td>
<td>2.3 (1.7–3.2)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%) on acute CMR scan</td>
<td>47±2.9</td>
</tr>
<tr>
<td>Total infarct size (% left ventricular mass) on acute CMR scan</td>
<td>11.3 (5.4–17.4)</td>
</tr>
<tr>
<td>Myocardial salvage index (%) on acute CMR</td>
<td>61±22 (0.7–100)</td>
</tr>
<tr>
<td>Presence of aneurysm (d)</td>
<td>9/10 (90.0%)</td>
</tr>
<tr>
<td>LV ejection fraction (%) on follow-up CMR</td>
<td>51±9.6</td>
</tr>
<tr>
<td>Total IS (% left ventricular mass) or follow-up CR</td>
<td>5.7±3.0 (2.3–10.0)</td>
</tr>
<tr>
<td>Presence of ischaemia (n, %) on follow-up CMR</td>
<td>10/49 (20.4%)</td>
</tr>
<tr>
<td>Global ischaemia burden (% left ventricular mass) on follow-up CMR</td>
<td>12.8±10.9</td>
</tr>
<tr>
<td>Major adverse cardiovascular events (n, %)</td>
<td>4/60 (6.7)</td>
</tr>
</tbody>
</table>

**Conclusions:** This is the first CMR study comparing revascularisation for multivessel disease at PPCLI. Staged in-hospital CR was associated with increased irreversible injury, which may impact on long-term outcome.

---

**P2531 | BEDSIDE**

Transradial vs. Transfemoral Coronary Intervention for ST Elevation Myocardial Infarction

**Objectives:** We have compared the impact of access strategy change on early and two-year outcomes after primary percutaneous coronary intervention using trans-radial access (TRA) versus intervention by transfemoral access (TFA).

**Background:** Adoption of TRA was recently proposed as potentially beneficial strategy to improve outcomes of PPCI for STEMI patients.

**Methods:** We have studied 1808 consecutive patients who underwent TFA (n=646) and TRA (n=1162) intervention for STEMI at our institution between 2007 and 2010. This was an all-comers study regardless patient acute presentation of STEMI. We have compared the cardiac mortality and the MACE rates (composite of death, stroke, re MI and TVR) after two years of follow up.

**Results:** The majority of deaths occurred as early events in the first 30 days from STEMI. The major difference in early mortality rates was in favor of TRA strategy (5.2% vs 60 deaths) comparing TFA strategy (10.5% or 68 deaths) (OR 0.46; 95% CI [0.32–0.66], p<0.001). TRA was also associated with significant 30 days MACE rate reduction (7.3% vs. 12.5%, HR 0.55; 95% CI [0.39–0.76], p<0.001). Following the first year of follow up additional 1.7% and 1.0% of deaths occurred in both groups respectively. At two years follow up there were 93 deaths (8.3%) with lower 30 days mortality rate in TRA group comparing to 90 deaths (13.9%) in TFA group (OR 0.60; 95% CI [0.47–0.89], p<0.001). The difference obtained in the first 30 days between the two accesses strategies have sustained with similar trends for mortality rates in the following two years. Two year MACE rates were in favor of TRA strategy (14.6% Vs 22.1%; 95% CI [0.30–0.76], p<0.001).

**Conclusions:** We can conclude that transradial access strategy for primary coronary intervention is associated with significant early and two years MACE rate reduction comparing to default transfemoral access strategy for primary interventions in STEMI patients. TRA was associated with sustained mortality benefit after two years.

---

**P2532 | BEDSIDE**

Diagnostic accuracy of focused cardiac ultrasound performed by emergency physicians for the assessment of ascending aorta dilation and aneurysm

**Methods:** This was a prospective single-centre cohort study of a convenience sample of patients that underwent CTA in the Emergency Department for suspected aortic pathology. FOCUS was performed before CTA and the maximum ascending aorta diameter evaluated in parasternal long-axis view. Aorta diameter ≤40 mm was considered normal. Measurements were recorded in all patients with aorta diameter ≥40 mm. Diagnostic accuracy of FOCUS for detection of aortic dilation (diameter ≥40mm) and aneurysm (diameter ≥45mm) were calculated considering CTA as reference standard. In a subgroup of patients, a second EP-sonographer performed FOCUS to evaluate interobserver agreement for the diagnosis of ascending aorta dilation.

**Results:** 140 patients were enrolled in the study. Ascending aorta dilation and aneurysm were detected at FOCUS in 50 (35.7%) and in 27 (17.8%) patients respectively. Sensitivity and specificity of FOCUS were 78.6% (95% CI 65.6–87.8%) and 99.2% (95% CI 98.6–99.6%) respectively for ascending aorta dilation, and 64.7% (95% CI 46.5–80.2) and 95.3% (95% CI 89.3–98.4) respectively for ascending aorta aneurysm. Inter-observer agreement of FoCUS was κ=0.82.

**Conclusions:** FoCUS performed by EP is specific for ascending aorta dilation and aneurysm when compared to CTA and appears as a reproducible technique.

**Acknowledgement/Funding:** ADVISED study group
medially before right atrial opacification of microbubbles by agitated intravenous saline.

Results: Compared with at rest (15 patients, 7.0% of the patients), IVCC maneuver obtained higher detection rate of PFO (47 patients, 22.0%. P <0.001) which was not inferior to TEE maneuver (33 patients, 15.4%. P=0.006 vs at rest, P=0.08 vs IVCC maneuver). Conclusions: IVCC maneuver is feasible and effective provocation testing to detect PFO, which is not inferior to TEE maneuver. Especially when TEE maneuver cannot be performed under sedation, IVCC maneuver could be an alternative diagnostic method to detect PFO using TEE.

P2534 | BEDSIDE
Tissue Doppler imaging of pulmonary arteries - a novel technique for detecting pulmonary hypertension?
S. Oztürk1, M. Yılmaztepe1, F. Özkayalı1, M. Aktoz2, B. Geyik1, G. Etküktü2, H.Y. Gurlertop1, 2Trakya University, Cardiovascular Medicine, Edirne, Turkey; 2Trakya University, Public Health, Edirne, Turkey
Purpose: It is difficult to measure pulmonary artery pressure in cases without tricuspid insufficiency. In this study our aim is to determine whether tissue Doppler imaging of pulmonary arterial wall can be used for measuring pulmonary artery pressure.
Methods: 60 patients with pulmonary hypertension (50±11 years), and age and sex matched 120 subjects without pulmonary hypertension (50±12 years), were enrolled in the study. Complete echocardiographic examination was performed to all subjects, pulsed wave Doppler derived main pulmonary artery wall longitudinal velocities were obtained from parasternal short axis view and right pulmonary arterial wall circumferential velocities were obtained from suprasternal view. Waveform analysis of these recordings revealed early systolic peak velocity (ESV) and late systolic peak velocity. Main pulmonary artery early and late velocities were measured. Calculation formulas, 84.9 − [193 x ESV − 0.21 x TIBSP] and 58.6 − [137.8 x ESV – 0.29 x TIBSP], time intervals between systolic peaks (TIBSP) and early systolic peak acceleration times (ESA) were measured.
Results: Comparison of these values between two groups revealed significant difference in all parameters except right pulmonary arterial wall late systolic flow acceleration times (p<0.05) (Table 1). Using regression analysis, we were able create the formulas, 84.9 – [193 x ESV – 0.21 x TIBSP] and 58.6 – [137.8 x ESV – 0.29 x TIBSP] + 0.42 x ESA), to calculate systolic pulmonary artery pressure from the tissue Doppler derived measurements of main and right pulmonary arterial walls, respectively.

Table 1. Results
<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n=120)</th>
<th>Patients (n=60)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVPESV (cm/s)</td>
<td>15±4</td>
<td>10±2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MPESV (cm/s)</td>
<td>4±1</td>
<td>3±1</td>
<td>0.01</td>
</tr>
<tr>
<td>MPESA (cm/s)</td>
<td>66±20</td>
<td>52±15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MPTIBSP (ms)</td>
<td>141±30</td>
<td>111±24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RPESV (cm/s)</td>
<td>8±2</td>
<td>6±2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RPSLSP (cm/s)</td>
<td>3±1</td>
<td>8±3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RPESA (cm/s)</td>
<td>34±9</td>
<td>38±12</td>
<td>0.01</td>
</tr>
<tr>
<td>RPPTTIBSP (ms)</td>
<td>110±35</td>
<td>82±23</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: It is possible to perform tissue Doppler study on main and right pulmonary arteries and this might be an alternative for calculating pulmonary artery pressure.

P2535 | BEDSIDE
A novel echocardiographic method for assessing arterial stiffness in obstructive sleep apnea syndrome
Background: Obstructive sleep apnea syndrome (OSAS) is a condition characterized by repetitive episodes of complete or partial obstruction of the upper airway during sleep. The important role of OSAS in the initiation and progression of arterial stiffness has been reported in recent studies. It has been reported that color M-mode-derived propagation velocity measured along the origin of the descending thoracic aorta (aortic propagation velocity, or AVP) is associated with atherothrombus.
Purpose: The aim of this study was to determine whether the AVP (Figure 1) was an echocardiographic marker for arterial stiffness in OSAS.
Methods: The study population included 116 patients with OSAS and 90 age and gender-matched healthy subjects. Aortofemoral pulse wave velocity (PWV), carotid intima-media thickness (CIMT), brachial artery flow-mediated dilatation (FMD), and AVP were measured to assess arterial stiffness.
Results: AVP (45.8±16.1 vs. 60.7±13.6, p<0.001) and FMD (8.7±3.3 vs. 14.6±4.6, p<0.001) were found to be significantly decreased in patients with OSAS compared to controls. PWV (10.3±2.2 vs. 8.5±2.0, p<0.001) and CIMT (0.83±0.14 vs. 0.66±0.15, p<0.001) were increased in the OSAS group compared to controls. AVP was significantly positively correlated with FMD (r=0.564, p<0.001). However, it was found to be significantly inversely related to PWV (r=−0.580, p<0.001) and CIMT (r=−0.251, p<0.001).

Conclusion: AVP was found as a novel echocardiographic parameter for measuring arterial stiffness in OSAS. Moreover, it was found to be related to parameters of arterial stiffness such as PWV, CIMT, and FMD. AVP measurement may be a useful and practical method for assessing arterial stiffness, which is associated with cardiovascular risk factors in OSAS.
conventional continuity equation to evaluate aortic valve area (AVA) is cumbersome, because 5 to 10 cycles are required to ensure accuracy of results. Double-envelope (DE) is obtained by a single continuous-wave Doppler envelope with double density velocity profiles; the inner envelope represents flow across the left ventricular outflow tract (LVOT) and outer envelope represents flow across the aortic valve orifice.

The aim of this study to evaluate the usefulness of AVA measurement calculated in single-beat DE technique in patients with AS and AF.

Methods: Thirty-one AS patients (76.6±7.4 years old) with AF were examined by transesophageal echocardiography. The conventional AVA (PW/CW technique) was calculated from non-simultaneously measured LVOT flow and AVO flow in randomly picked up 8 cardiac cycles, respectively. The AVA (DE technique) was calculated from the inner and outer envelopes simultaneously recorded. A single-beat AVA was calculated from simultaneously recorded inner and outer envelopes (by DE technique) when the preceding RR interval/pre-preceding RR interval = 1.

Results: DE profiles were successfully obtained in all patients, and mean AVA (PW/CW technique) was 1.12±0.23 cm². AVA by Single-beat DE technique showed good correlation with that by PW/CW technique (r=0.87), and the mean bias in the AVA measurements between by PW/CW technique and by DE technique was 0.067 cm² (Figure).

Feasibility of DE technique in AS & AF

Conclusions: AVA in patients with AS and AF obtained by Single-beat DE technique was feasible and in good agreement with that by PW/CW technique. We suggest that DE technique should be considered to estimate the subtle temporal change of AVA in patient with AS and AF more simply and accurately.

P2539 | BEDSIDE
Quantification of valve dimensions by transesophageal 3D echocardiography in patients with functional and degenerative mitral regurgitation

Background: Aim of the study was to quantify valve dimensions based on 3D transesophageal echocardiography in patients with functional (FMR) and degenerative mitral regurgitation (DMR).

Methods: Sixty patients (age range 52–82 years, 35 men) with various conditions (ischemic 47%, congenital 17%, cardiomyopathy 20%, other 16%), scheduled for clinically indicated echo and CMR study ≤48h apart, were prospectively enrolled. LV 4- and 6-beat full volume datasets (41±9 vps) were acquired using Vivid E9 scanner (GE) and analyzed with 4D LV Analysis 3.1 software. Datasets with suboptimal image quality were not excluded. Semi-automated (i.e. after tracking, endocardial boundaries were corrected in both end-systole and end-diastole) vs automatic selection was tested in 15 datasets and measurements were compared with CMR.

Results: There was a wide range of LV end-diastolic volumes (EDV 92–381 ml), ejection fractions (EF 16–76%) and image quality (optimal = 2/3 datasets). As expected, the automated method was faster than semi-automated one (1 vs 5 min), and both were much faster than CMR (25 min). When compared with CMR, the automated method showed more underestimation of LV EDV (20±22 vs 5±13 ml), stroke volume (21±19 vs ±11 ml), and EF (7.7±9.2 vs 2.7±4.2%) than the semi-automated approach (p<0.001 for all). Using manual corrections in all 60 pts, LV volumes were still smaller than by CMR (15±350 vs 171±581 ml, p<0.0001), but EF was similar (54±11% vs 53±12% p=0.118). Semi-automated 3DE algorithm provided LV measurements with excellent correlations and agreement (bias±SD) with CMR (r=0.97 and ±9 ml for EDV; r=0.92 and 9±4 ml for ES; r=0.94±9.4% and 5±1% for EF; p<0.0001 for both). Therefore, we sought to examine LV layer torsion in patients with FMR the degree of MR mainly depends on tenting volume, whereas in DMR VCA correlated with annular area (r=0.42, p<0.001). In the group with FMR VCA correlated with tenting volume (r=0.35, p<0.001), whereas in patients with DMR VCA correlated with annular area (r=0.42, p<0.001).

Conclusion: Change of dimensions in FMR includes a more round shaped and flattened MA accompanied by an increase of tenting volume and posterior leaflet enlargement. Enlargement of annular and leaflet area are the predominant characteristics of FMR patients compared to normal valves. In patients with DMR the degree of MR mainly depends on tenting volume, whereas in DMR annular area is related to regurgitation severity.

P2540 | BEDSIDE
Assessment of left ventricular layer torsion in hypertensive patients using novel one-beat three-dimensional speckle tracking echocardiography with high volume rates
M. Ishiguro1, M. Kawasaki2, R. Tanaka1, M. Nagaya1, S. Minotoguchi2, H. Miwa1, H. Sato1, T. Noda1, S. Watanabe1, S. Minatoguchi2. 1Gifu Preclinical General Medical Center, Department of Cardiology, Gifu, Japan; 2Gifu University Graduate School of Medicine, Department of Cardiology, Gifu, Japan

Purpose: The left ventricle (LV) is composed of 3 myocardial layers and twist and torsion play an important role in squeezing the blood out of the heart. However, LV layer torsion has not yet been examined by echocardiography because until recently magnetic resonance imaging has been only noninvasive technique to evaluate LV layer torsion. Therefore, there is a need to use speckle tracking echocardiography (3D-STE) and the relation between layer torsion and systolic function in patients with hypertension (HTN) by novel one-beat 3-dimensional speckle tracking echocardiography (3D-STE).

Methods: Eighty one subjects (23 controls (age 60±12), 37 patients with HTN (age 69±12) and 21 patients with hypertensive heart failure (HHF) (age 75±18)) were enrolled to characterize layer torsion (endocardium, midwall and epicardium) by the 3D-STE with volume rates of 60–80vps. Twist was defined as
the maximum difference in rotation angle between the base and apex (unit is °). Torsion was defined as LV twist/long axis length (unit is °/cm). Time to peak torsion was earliest at epicardial layer in HHF and latest at endocardial layer in HTN (80±14°/systole and 99±5°/systole, respectively, p < 0.05).

Conclusion: This study demonstrated that the amplitude of LV peak torsion assessed by 3D-STE was greater in endocardium and followed by midwall and epicardium and that it was greater in HTN and smaller in HHF. The difference in LV torsion among the layers seemed to be a mechanism of LV systolic function.

P2541 | BEDSIDE
Impact of vendor-independent versus vendor-specific software packages on left ventricular volume measurements performed on 3D echo data sets obtained from different vendors

A. Cecchetti1, D. Muraru1, D. Ermacora1, G. Romeo1, A. Maddalozzo1, S. Onciul2, U. Cucchini1, S. Iliceto1, L.P. Badano1, Padova, Cardiology, Padua, Italy; 2 University of Medicine and Pharmacy Carol Horten, N)

Background: AVE/AECVI guidelines recommend three-dimensional echocardiography (3DE) to measure left ventricular (LV) volumes and ejection fraction (EF) in echolab with experience with this technique. However, in multivendor echocals the need to learn to use different software algorithms may limit the application of 3DE in the clinical routine. We sought to assess intervendor differences of LV volume measurements obtained by novel vendor-independent (VI) and vendor-specific (VS) 3DE algorithms for LV quantification, from 3D data sets obtained by two different 3D echo systems in the same patient.

Methods: 44 patients (age range 18–82 years, 29 men, ischemic 30%, congenital 7%, valvular 25%, cardiomyopathy 27%, and other cardiac diseases 16%) were enrolled. LV full volume data sets were acquired using Vivid 9E (GE Vingmed, Horten, N) and iE33 (Philips Medical System, Andover, MA) scanners during the same echo session. A single researcher analyzed the 3D data sets with VS software packages in row, one week apart from one vendor to the other. Then he performed a second set of measurements with 4D LV Analysis 3.1 software (Tom tec) in each data set of the same patients.

Results: Patients had a wide range of LV end-diastolic volumes (EDV 85–293 ml) and ejection fractions (EF18–79%). Differences between LV volumes obtained from Vivid 9E and iE33 data sets were smaller using VI than VS software packages (EDV VI 24±11 ml vs. 15±12 ml; p = 0.046) and end-systolic volumes (6±7 ml vs. 8±9 ml; p = 0.269). There was a lower intervendor variability of EF ages both for EDV (10±11 ml vs. 15±12 ml; p = 0.046) and end-systolic volumes from Vivid E9 and iE33 data sets were smaller using VI than VS software packages on left ventricular volume measurements performed on 3D echo data sets obtained from different vendors.

Conclusion: This study demonstrated that the amplitude of LV peak torsion assessed by 3D-STE was greater in endocardium and followed by midwall and epicardium and that it was greater in HTN and smaller in HHF. The difference in LV torsion among the layers seemed to be a mechanism of LV systolic function.

NEW INSIGHTS INTO VALVULAR HEART DISEASE

P2542 | BENCH
Automatic quantification of aortic regurgitation using 3D full volume color Doppler echocardiography: a validation study with cardiac magnetic resonance imaging

J.H. Choi1, G.R. Hong2, H.J. Chang2, I.J. Cho2, C.Y. Shim2, J.W. Ha2, N. Chung2 on behalf of Severance Cardiovascular Hospital, 1 Hallym University Hangang Sacred Heart Hospital, Cardiology, Seoul, Korea, Republic of; 2 Yonsei University Severance Cardiovascular Hospital, Cardiology, Seoul, Korea, Republic of

Aims: The aim of this study is to explore the ability of 3D full volume color Doppler echocardiography (FVCDE) to quantify aortic regurgitation (AR).

Patients and methods: This is a prospective study. Children with a moderate degree of AR were enrolled. AR volume was measured by 1) two-dimensional-CDE (2D-CDE), using the proximal isovelocity surface area (PISA) and 2) real-time 3D-FVCDE with 3) phase-contrast cardiac magnetic resonance imaging (PC-CMR)

P2543 | BEDSIDE
Dynamics of mitral valve annulus in patients with mitral regurgitation due to fibro-elastic deficiency or barlow’s disease


Leiden University Medical Center, Cardiology, Leiden, Netherlands

Background: The dynamics of the mitral valve annulus in organic mitral regurgitation (MR) may differ significantly between the various etiologies. The present study aimed to characterize the dynamics of the mitral annulus in patients with MR due to Barlow disease (BD) or fibro-elastic deficiency (FD) using 3-dimensional (3D) modeling.

Methods: 49 patients with moderate to severe organic MR (29 male, age 63±20 years, 23 FD and 26 BD) were evaluated. Mitral annular geometry was assessed with 3D transesophageal echocardiography. The 3D geometry of the mitral annulus was measured with dedicated software at begin-systole and end-systole. Parameters reflecting the saddle shape geometry of the mitral annulus (annulus height, nonplanar angle and the annular height to commissural width ratio (AH-WCR)) were measured along the systole. MR graded according to current guidelines and classified into holosystolic or late systolic.

Results: Patients with BD showed significantly larger annulus height, more acute nonplanar angle and higher AH-WCR than patients with FD at the beginning of the systole reflecting more preserved saddle shape of the mitral annulus (Table). At end-systole, the mitral annulus became more flattened in both groups of patients. However, patients with BD have a significantly more dynamic annulus as reflected by larger changes in annulus height, nonplanar angle and AH-WCR. Furthermore, 7 patients had late systolic MR, all of them with BD, suggesting more enhanced movement and flattening of the mitral annulus during late systole compared with BD.

3D dynamics of the mitral annulus

<table>
<thead>
<tr>
<th>Variables</th>
<th>FED (n=23)</th>
<th>BD (n=26)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonplanar angle, °</td>
<td>Begin-systole</td>
<td>147.0±15.1</td>
<td>137.8±7.8</td>
</tr>
<tr>
<td>End-systole</td>
<td>158.9±12.8</td>
<td>154.1±12.9</td>
<td>0.113</td>
</tr>
<tr>
<td>Annulus height, cm</td>
<td>Begin-systole</td>
<td>0.91±0.28</td>
<td>1.18±0.18</td>
</tr>
<tr>
<td>End-systole</td>
<td>0.75±0.17</td>
<td>0.62±0.19</td>
<td>0.002</td>
</tr>
<tr>
<td>AH-WCR, %</td>
<td>Begin-systole</td>
<td>22.6±6.8</td>
<td>25.9±3.9</td>
</tr>
<tr>
<td>End-systole</td>
<td>15.7±4.1</td>
<td>17.0±4.5</td>
<td>0.294</td>
</tr>
</tbody>
</table>

Conclusions: BD is associated with more pronounced changes in mitral valve annulus geometry along the systole compared with FD suggesting an important role in the pathophysiology of organic MR. Stabilization of the mitral annulus with a ring may thus be crucial step in the mitral valve repair process of patients with BD.
as the reference method. Automated AR quantification using 3D-FVCDE was feasible in 30 of the 32 patients. 2D-PISA underestimated the AR volume compared to 3D-FVCDE and PC-CMR (38.6±9.9 mL by 2D-PISA; 49.5±10.2 mL by 3D-FVCDE; 52.3±12.6 mL by PC-CMR). The AR volume assessed by 3D-FVCDE showed a better correlation and agreement with PC-CMR (k=0.93, p<0.001, 2SD: 9.9±11.7 mL vs 9.6±12.1 mL). When used to classify AR severity, 3D-FVCDE agreed better with PC-CMR (k=0.94) than did 2D-PISA (k=0.53). In patients with eccentric jets, only 30% were correctly graded by 2D-PISA. Conversely, almost all patients with eccentric jets (86.7%) were correctly graded by 3D-FVCDE. In patients with multiple jets, only 3 out of 10 were correctly graded by 2D-PISA, while 3D-FVCDE correctly graded 9 out of 10 of these patients.

Table 1. TA size relation with RA and RV volumes

<table>
<thead>
<tr>
<th>TA geometry parameters</th>
<th>RV end-diastolic volume (mL)</th>
<th>RA volume (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface area (cm²)</td>
<td>0.634</td>
<td>0.692</td>
</tr>
<tr>
<td>Perimeter (cm)</td>
<td>0.598</td>
<td>0.686</td>
</tr>
<tr>
<td>Long axis (cm)</td>
<td>0.542</td>
<td>0.745</td>
</tr>
<tr>
<td>Short axis (cm)</td>
<td>0.556</td>
<td>0.607</td>
</tr>
</tbody>
</table>

Values represent Pearson’s r coefficients (p<0.001 for all).

Conclusion: In patients with FTR, TA is enlarged and its geometry is influenced by RV and RA remodeling. The close relationship between RA size and TA geometry is a finding that may explain the onset of FTR in patients with normal RV volumes and dilated RA.

P2546 | BEDSIDE Determinants of normal tricuspid annulus area in healthy volunteers: a three-dimensional echocardiographic study

C. Jenei1, D. Muraru2, K. Addetia3, F. Veronesi4, G. Cavalli2, F. Aruta2, S. Illet2, R.M. Lang4, L.P. Badano2. 1 University of Bologna, Department of Cardiology and Cardiac Surgery, Bologna, Italy; 2 University of Padova, Department of Cardiac, Thoracic and Vascular Sciences, Padua, Italy; 3 University of Chicago, Chicago, United States of America; 4 University of Bologna, Department of Electrical, Electronic and Information Engineering, Bologna, Italy

Background: The tricuspid annulus (TA) size and function have a pivotal role in determining the need for associated tricuspid annuloplasty in patients undergoing cardiac surgery for left-sided valve diseases. Due to the lack of dedicated software packages, the non-planar TA area and its physiological determinants in normal subjects need to be clarified.

Methods: Multi-beat three-dimensional (3D) data sets of the right ventricle (RV), right atrium (RA) and tricuspid valve were acquired from the apical approach using GE Vivid E9 scanner in 79 healthy volunteers (45±13 years, range 20–74 years; 34 men). TA 3D area was measured using custom made software. The user identifies the mid-systolic (MS) reference frame, on which the TA is manually delineated by placing several points on multiple rotated planes. The software then reconstructs the 3D TA model and automatically tracks it throughout the cardiac cycle. RV and RA volumes were measured using 4D RV Function™ and LA Function™ software packages.

Results: Temporal resolution of 3D datasets was 34±6 vps (range 24–57). TA area decreased from 4.9±0.75 cm² to 4.3±0.51 cm² during systole, and increased to reach its maximal value in late diastole (6.06±0.78 cm²). Maximal TA area correlated with end-diastolic RV (r=0.57, p<0.0001) and RA (r=0.34, p=0.01) volumes, and with RA end-systolic volume (r=0.49, p<0.0001). TA areas correlated with body surface area (BSA, r=0.59 at onset systole, r=0.75 at MS, r=0.75 at end-systole, r=0.59 at early diastole, r=0.69 at late diastole, p<0.0001), but not with age. Maximal TA areas were larger in men than in women (11.8±1.5 cm² vs. 9.9±1.5 cm²; p<0.0001), although this difference disappeared after BSA indexation (6.1±0.6 cm² vs 6.0±0.9 cm²; p=0.56). Using multivariable linear regression analysis, BSA remained the only determinant of maximal TA 3D area (R²=0.48).

Conclusions: Normal TA is a highly dynamic structure that reaches its maximal dimension in late diastole. Although gender, body size, RV and RA volumes influence TA size, BSA is the only independent determinant of maximal TA 3D area in healthy subjects.

P2547 | BEDSIDE Accuracy in aortic annulus measurements: New automatic quantitative 3D method vs manual 3D transesophageal echocardiography using multidetector computed tomography as reference

A. García Martín, C. Lazaro Rivera, C. Fernandez Goñin Loban, L. Salido Tahoces, J.L. Moya Mur, A. Gonzalez Gomez, I. Aquila, L.M. Rincon Diaz, J.J. Jimenez Nacher, J.J. Zamorano Gomez. University Hospital Ramon y Cajal, Department of Cardiology, Madrid, Spain

Introduction: Non-invasive imaging modalities play an important role in preprocedural evaluation of transcatheter aortic valve replacement (TAVR) candidates. Accurate measurements of aortic annulus (AA) are essential. 3D transesophageal echocardiography (TEE) has overcome limitations of 2D TEE but measurements are still operator dependent due to wide variability and time consuming. This special- ized TEE reconstruction tool has recently been introduced, which allows automatic analysis of the aortic root from 3D TEE images. The purpose of this study was to validate this model with 3D manual analysis and with measurements obtained by multidetector computed tomography (MDCT).

Methods: 31 patients (83,9 (69–92) years, 63,9% females) undergoing TAVR in our center where included. The diameter and area of the aortic annulus (AA) were manually measured by 3D TEE. Afterwards, the images were analyzed using the new software. All measurements were performed by two independent observers. Ten patients were also evaluated by MDCT, considered it the gold standard.

Results: We found good correlation and interobserver variability between the automated and manual measurements of the AA diameter (Intraclass correlation coefficient (ICC): 0.731 (0.626–0.862); r: 0.742, p<0.01) and AA area ((ICC): 0.723 (0.495–0.85), r: 0.723, p<0.01). Correlation with MDCT was higher with the new automatic software (table 1).

Conclusions: The new automated 3D echocardiography software is accurate in
Table 1. Correlation and interobserver variability between the automated and manual measurements of the AA with MDCCT

<table>
<thead>
<tr>
<th></th>
<th>r</th>
<th>p</th>
<th>ICC 95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual assessment vs MDCCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA diameter</td>
<td>0.830</td>
<td>0.003</td>
<td>0.779</td>
<td>0.333–0.940</td>
</tr>
<tr>
<td>AA area</td>
<td>0.670</td>
<td>0.034</td>
<td>0.624</td>
<td>0.036–0.891</td>
</tr>
<tr>
<td>Automatic assessment vs MDCCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA diameter</td>
<td>0.901</td>
<td>0.000</td>
<td>0.941</td>
<td>0.761–0.985</td>
</tr>
<tr>
<td>AA area</td>
<td>0.744</td>
<td>0.014</td>
<td>0.853</td>
<td>0.409–0.964</td>
</tr>
</tbody>
</table>

P2548 | BEDSIDE

Color Flow Quantification: a new method to assess mitral regurgitation severity

C. Vieira1, F. Islas2, J.A. De Agustín2, G. Feltes2, J.J. Gomez De Diego2, P. Marcos-Alberca2, C. Almería2, J.L. Rodríguez2, M.A. Garcia Fernandez2, L. Perez De Isla2, Hospital de Braga, Braga, Portugal; 2Hospital Clínico San Carlos, Cardiovascular Institute, Madrid, Spain

Introduction: Mitral regurgitation (MR) is a frequent finding and the assessment of its severity is still difficult, as in patients with more than one regurgitation jet.

Purpose: Assess if 3D color flow method allows accurate quantification of MR.

The two-dimensional (2D) methods have important limitations. Single-beat, real-time three-dimensional (3D) color Doppler imaging allows direct measurement of proximal isovelocity surface area (PISA) and it has been validated. 3D Color Flow is a new tool that measures the flow that passes through cardiac valves.

Population and methods: Prospective study, including consecutive patients with more than mild chronic MR. Effective regurgitant orifice area (EROA) and regurgitant volume were assessed by transthoracic 2D PISA and volumetric methods, 3D PISA method and by 3D color flow method using Siemens SC 2000 technology. The EROA 3D PISA was used as reference method.

Results: 33 consecutive patients were included (males: 63.6%; mean age: 68±15 years). Table below shows the most important results. When using the EROA 3D PISA as reference method, the best linear correlation and agreement was seen with EROA 3D color flow method. The intraserver and interserver agreement for 3D PISA measurements were good, with intraclass correlation coefficients of 0.97 and 0.83 respectively; for 3D color flow, these agreements were also good, with intraclass correlation coefficients of 0.94 and 0.95 respectively.

Table 1. Inter-methods agreement analysis using 3D PISA EROA as gold standard

<table>
<thead>
<tr>
<th>Method</th>
<th>r</th>
<th>ICC 95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>EROA 3D PISA, EROA 2D volumes</td>
<td>0.32</td>
<td>0.10</td>
<td>0.24–0.013–0.35</td>
</tr>
<tr>
<td>EROA 3D PISA, EROA 2D PISA</td>
<td>0.753</td>
<td>0.567</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EROA 3D PISA, EROA 3D color flow</td>
<td>0.98</td>
<td>0.95</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

r, linear correlation coefficient of Pearson; ICC, intraclass correlation coefficient; CI, confidence interval.

Conclusion: 3D color flow is a simple and accurate method to assess MR severity. Its implementation can be an important help in the clinical decision making of these patients.

P2549 | BEDSIDE

Three-dimensional dynamic assessment of tricuspid annulus in patients with functional tricuspid regurgitation in rheumatoid left heart valve disease

P. Mahia, M.T. Nogales-Romo, F. Islas, A. De Agustín, J.J. Gomez De Diego, C. Almería, J.L. Rodrigo, M.A. Garcia-Fernandez, C. Macaya, L. Perez De Isla, Hospital Clínico San Carlos, Madrid, Spain

Background: Anatomical changes that take place in the tricuspid annulus (TA) morphology play a fundamental role in the mechanism of the functional tricuspid regurgitation (FTR). Little is known about the architectural changes in TA diameters during the cardiac cycle.

Objectives: To explore the potentiality of 3D transthoracic eco (3DTE) in the evaluation of TA dynamic changes in relation to the severity of FTR in patients with left side rheumatic valvular disease.

Methods: 3DTE was performed in 50 patients (Age: 69±9, 82% women) with rheumatic left side disease an FTR. FTR was graded in two groups: Severe (N: 14) or non-severe (N: 26). Two orthogonal planes corresponding to the anatomical antero-posterior (APD), septo-lateral (SLD), long intercommisural (LID) and Area (A) of TA were analysed by end-systole and end-diastole to calculate the mean fractional shortening (FS) for each parameter.

Results: APD 3DTE diameters differed significantly among the two groups. Despite the increase in the size of the TA in the presence of severe TR, FS showed no significant differences between groups (Table 1).

Conclusions: We provide new 3DTE parameters related to TA morphology in presence of FTR in this subgroup of patients. FTR severity seems to be associ-
changes and functional abnormalities. LA size is often used as a surrogate marker of LA function in clinical practice. However, whether functional abnormalities also occur in patients with CKD who have normal LA size is unknown.

**Purpose:** The aim of this study was to explore LA strain using speckle-tracking echocardiography in CKD patients with preserved left ventricular ejection fraction (LVEF) and normal LA size.

**Methods:** LA strain was studied by speckle-tracking echocardiography in 30 patients with CKD (eGFR <60 ml/min/1.73 m²) with LA volume indexes <28 ml/m² and 95 control subjects. Global atrial longitudinal strain was measured by averaging all atrial segments. Reservoir (S-LAs), conduit (S-LAe), and contractile (S-LAa) phase strain were obtained. The ratio of E/Ea to LA strain was used as an index of LA stiffness.

**Results:** S-LAs and S-LAe were significantly decreased in the CKD group compared with that in the control group (S-LAs: 18.2±4.7 vs. 23.5±7.0, p<0.005; S-LAe: 8.5±2.7 vs. 11.7±5.8, p=0.0001). LA stiffness was significant correlation with eGFR (Figure).

**Conclusion:** LA function and stiffness are significantly impaired in CKD patients with preserved LVEF and normal LA size. LA myocardial fibrosis and myopathy may play a role in the LA functional and stiffness abnormalities in CKD patients with preserved LVEF and normal LA size.

---

**P2552 | BEDSIDE**

**Prognostic value of right atrial function and dimensions in patients with pulmonary hypertension**


**Introduction:** Clinical assessment is essential when evaluating patients with suspected pulmonary hypertension (PH), however, echocardiography is a key screening tool in the diagnostic algorithm. Right ventricular dysfunction has been associated with adverse outcomes but few studies have focused on the structure and function of the right atrium (RA).

**Objectives:** To determine the prognostic value of RA dimensional and functional parameters in patients with PH.

**Methods:** Prospective study of patient (pts) with PH undergoing clinical and echocardiographic evaluation, focusing on RA dimensions and deformation analysis. Association with the composite endpoint death or hospitalization for cardiac causes was tested using the Kaplan-Meier analysis and Cox multivariate regression analysis. Prognostic accuracy was evaluated by the area under the receiver operator curve (ROC).

**Results:** Seventy-seven pts (75% female; 55±16 years; 68% with group 1 PH) were included. At baseline atrial dimensions were: diastolic area - 24±13.1 cm²; systolic area - 19.3±11.1 cm²; 4C view longitudinal diameter - 56±12.9 mm. During a median follow-up period of 25 months, 9 patients died and 29 were admitted for cardiac causes. The composite endpoint occurred in 39% of pts (N=30) and the risk increased for higher RA sizes and lower atrial systolic deformation. The risk of events increased 6% per each cm² of increased RA area (HR: 1.06; 95% CI 1.03–1.10; p=0.001). Longitudinal systolic strain of all septal segments and that of lateral apical segment were strong prognostic predictors. The risk of events increased 7% for each 1% reduction of atrial deformation (HR: 1.07; 95% CI 1.02–1.13; P=0.003). Midseptal segment longitudinal systolic strain was the strongest prognostic predictor at multivariate Cox regression analysis (including all RA echocardiographic parameters) (HR: 1.10; 95% CI 1.02 to 1.18; P=0.012).

**Conclusions:** RA deformation and dimensional indexes showed prognostic value in PH pts and should be considered for routine echocardiographic assessment.

---

**P2554 | BEDSIDE**

**Left atrial mechanics after successful surgical ablation of atrial fibrillation during valvular heart disease surgery**

N. Lorenzo, I. Mendez, G.F. Martinis, M. Tabo, R. Montes De Oca, S. Badia, G. Reyes, F. Alfonso, R. Aguilar, University Hospital La Princesa, Madrid, Spain

**Background and purpose:** Left atrial (LA) mechanics after surgical ablation (SA) of AF in valvular heart disease (VHD) is not fully known. This study aimed to explore LA mechanics and to identify predictors of recurrence.

**Methods:** 44 patients who maintained sinus rhythm (SR) 3 months after SA during VHD surgery (82% mitral) were studied. Strain (S) and Strain Rate (SR) parameters (Fig. 1.1) were obtained in apical 4-, 3- and 2-chamber views, using speckle tracking echocardiography. Simultaneously, 30 volunteers were studied with the same protocol.

**Results:** 1,886 LA segments were analysed (70% of total LA segments). LA was severely dilated in the post-surgery group and, myocardial properties of LA did not recover after surgery (Fig. 1.2, A-B) when compared with normal values (Fig.

**Conclusion:** Using TTE, the baseline echographic features of the ACP are representative of an easily obtained and reproducible 8-like shaped image proving the proper device position. TTE seems reliable to view peri-device leaks but it needs to be confirmed in larger series. The utility of TEE instead of TTE in the routine follow-up of these devices remains to be approved.
Table 1. LA volume and S and SR parameters

<table>
<thead>
<tr>
<th>Procedure</th>
<th>LA volume (mL)</th>
<th>S (mm)</th>
<th>SR (% of LA volume)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AutoLVQ</td>
<td>57.5±3</td>
<td>31.6±0.3</td>
<td>13.1±0.3</td>
</tr>
<tr>
<td>QLAB</td>
<td>57.5±3</td>
<td>31.6±0.3</td>
<td>13.1±0.3</td>
</tr>
<tr>
<td>Linear regression</td>
<td>r² = 0.84</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Left atrial volume determined by AutoLVQ and QLAB software show a good correlation (r² = 0.84) with linear regression. Future studies are required to confirm the clinical value of this non-invasive method.

---

P2558 | BEDSIDE

The application of a novel three-dimensional transesophageal echocardiographic technique for the assessment of left atrial appendage anatomy in transcatheter LAA closure


Purpose: To assess the clinical value of two dimensional (2D) and three dimensional transesophageal echocardiography (3D-TEE) for the left atrial appendage (LAA) closure by a precise evaluation and measurement of the anatomic morphology of the LAA.

Methods: Nineteen patients with non-valvular atrial fibrillation (AF) patients who received a transcatheter LAA closure were enrolled in the study. For 2D-TEE, the transesophageal images of the LAA ostium were used to measure the maximal and minimal dimensions. For 3D-TEE, the LA volume and S and SR parameters were measured.

Results: Among the nineteen patients, the LA volume determined by 2D-TEE was significantly different from that determined by 3D-TEE (p=0.006). In the twenty device closure patients assessed by RT3DE, there were seven single-lobe cases and eight double-lobe cases, and the remaining five patients were identified as multi-lobe, which led to the selection of eighteen regular and two special devices. With monitoring of the TEE and X-ray, the LA closure procedures using the LAMbreTM device were successful for all twenty patients. The housing domain for the surgical LTAA closure was determined using 2D-TEE and 3D-TEE, and fluoroscopy was analyzed to determine each individual modality feasibility for the assessment of the LAA ostium domain for the conclusion.

Conclusions: Compared with routine 2D-TEE, RT3DE-TEE allows for a more precise assessment of left atrial appendage morphology and device delivery in LAA closure procedures.

---

P2557 | BEDSIDE

Left atrial global longitudinal strain, a new and early cardiotoxicity marker?

L. Perez De Isla, J. Moreno, F. Moreno, J.A. Garcia Saenz, M. Clavero, G. Serrano, F. Islas, P.M. Alberca, J.A. De Agustin, J.J. Gomez De Diego, Hospital Clinic San Carlos, Madrid, Spain

Purpose: The knowledge of breast cancer biology has identified therapeutic targets to develop specific agents beyond classic chemotherapy. While these drugs are very active, their cardiotoxicity profile is a concern. Left ventricular global longitudinal strain (LVGLS) has been shown to be a marker of cardiac toxicity, however, the clinical value of left atrial longitudinal strain (LAGLS) is less clear.

Methods: A pilot, non-interventional, observational, prospective study in newly diagnosed breast cancer patients to receive potential antitumoral cardiac agents (doxorubicin or trastuzumab) was designed. A complete echocardiogram, including a 3D wall motion tracking analysis to assess LVGLS and LAGLS were performed before and after the first dose of anticancer drug.

Results: Thirty four breast cancer patients were enrolled. Mean age was 50.97±14.0 years. LVGLS did not significantly changed after the first cancer drug dose. Nevertheless, LAGLS did. Furthermore, the LA indexed volume increased after the first dose.

Conclusions: LAGLS may result a sensitive parameter to detect the cardiotoxic effect following the first dose of cancer agent in breast cancer patients. Our hypothesis that LAGLS earlier than LVGLS could be a marker of cardiotoxicity should be confirmed in a validation cohort.

---

P2558 | BEDSIDE

Measurement of maximal and minimal left and right atrial volumes: comparison of different semi-automatic algorithms of real-time 3D echocardiography


Purpose: Real-time full-volume 3D echocardiography (RT3DE) allows rapid and non-invasive measurement of left (LA) and right atrial (RA) volume without making geometric assumptions. Recently software with semiautomatic endocardial and epicardial contouring algorithms has become available, which considerably speeds up the procedure. Our aim was to compare LA and RA volumes determined by semi-automatic contour detection algorithms from different commercial providers.

Methods: 50 patients were studied by RT3DE. Maximal and minimal atrial volumes were measured using five different software (AutoLVQ vs. QLAB vs. 3D-STE). These volumes were compared with atrial volumes determined by the 3D-STE software using also a semiautomatic border detection method.

Results: Linear regression showed for both LA and RA a good correlation between atrial volumes determined by AutoLVQ and QLAB (r² = 0.80 vs. 0.87 respectively, p < 0.001). Bland-Altman analysis of AutoLVQ versus QLAB maximal atrial volume determination showed narrow 95% limits of agreement (-9.1 to 13.1 ml for LA volume and -8.9 to 13 ml for RA volume) with a minimal bias of
2 + 5.7 ml and 2.1 + 5.6 ml respectively by the AutoLVQ method. Correlation was slightly less well for minimal volumes (LA r²=0.69 and RA r²=0.65, p < 0.001); however agreement was comparable to maximal volumes (LA –5.8 to 8.6 ml and RA –8.1 to 10.2 ml, minimal bias of 1.4±3.7 ml and 1.05±4.7 ml respectively by AutoLVQ). Feasibility with both algorithms was slightly less for determination of RA volumes (n=48 vs. n=50 for the LA), especially for minimal volumes (n=42 vs. n=49 for the LA). LA and RA maximal and minimal volumes by AutoLVQ and QLAB

<table>
<thead>
<tr>
<th></th>
<th>Mean ± 3D (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left atrium (LA)</strong></td>
<td></td>
</tr>
<tr>
<td>LA AutoLVQ maximal volume (ml)</td>
<td>40.6±13.6 (14–70)</td>
</tr>
<tr>
<td>LA QLAB maximal volume (ml)</td>
<td>36.6±13.8 (13–79.4)</td>
</tr>
<tr>
<td>LA AutoLVQ minimal volume (ml)</td>
<td>16.4±6 (6–33)</td>
</tr>
<tr>
<td>LA QLAB minimal volume (ml)</td>
<td>15.6±6.3 (4.3–36.3)</td>
</tr>
<tr>
<td><strong>Right atrium (RA)</strong></td>
<td></td>
</tr>
<tr>
<td>RA AutoLVQ maximal volume (ml)</td>
<td>37.4±15.2 (11–79)</td>
</tr>
<tr>
<td>RA QLAB maximal volume (ml)</td>
<td>35.3±14.8 (10.8–78.1)</td>
</tr>
<tr>
<td>RA AutoLVQ minimal volume (ml)</td>
<td>17.4±7.5 (3–36)</td>
</tr>
<tr>
<td>RA QLAB minimal volume (ml)</td>
<td>16.4±7.3 (5–31.3)</td>
</tr>
</tbody>
</table>

Results: The QLAB 9.1 semiautomatic border detection method shows good correlation and agreement for left and right atrial volume determination compared to the semiautomatic 4D LAQ software. Correlation was slightly less well for minimal volumes; however agreement was comparable to maximal volumes. The results indicate that values of left and right atrial volumes obtained by either algorithm can be compared, for example during follow-up examinations.

Conclusions: The QLAB 9.1 semiautomatic border detection method shows good correlation and agreement for left and right atrial volume determination compared to the semiautomatic 4D LAQ software. Correlation was slightly less well for minimal volumes; however agreement was comparable to maximal volumes. The results indicate that values of left and right atrial volumes obtained by either algorithm can be compared, for example during follow-up examinations.
CI changes (+0.66). Area under the curve optimal cutoffs for predicting reduced CI was 16.89% (sensitivity: 90% - specificity 54%).

Conclusions: RA 2D STE is superior to conventional 2D parameters in indentifying early RA functional remodelling and hemodynamic deterioration in patients with PH and may have a very important clinical impact as prognostic tool.

P2562 | BEDSIDE
Carotid plaque neovascularization is independently associated with atheromatous South Asians vs Europeans: A possible mechanism underlying the greater cardiovascular disease burden in South Asians
B.N. Shah 1, N.S. Chahal 2, A. Anantharam 3, J.S. Kooner 4, R. Senior 3.

Background: South Asians (people of Indian, Pakistani & Bangladeshi origin) living in the UK have a ~ 50% higher risk of cardiovascular disease (CVD) death compared with native European whites. The mechanisms underlying their excess mortality are unclear. The burden of subclinical atherosclerosis detected in the carotid arteries is an established prognostic marker for major CVD events. However, our group has shown that there were 17 significant differences in intima-media thickness, plaque prevalence or plaque echogenicity between asymptomatic South Asian and European populations. We therefore hypothesized that a difference in plaque vulnerability may account for the observed increased risk in South Asians. Plaque neovascularization (IPN) is a surrogate marker of plaque vulnerability. Contrast enhanced ultrasound (CEUS) of the carotid arteries allows accurate determination of the presence or absence of IPN.

Methods: Individuals from the London Life Sciences Population (LDDPOP) study, a community study comparing Northern European and South Asian populations, that had plaques detected during initial carotid imaging were invited back for B-mode and CEUS carotid scanning. Long and short axis ECG-gated cine-loops were acquired of both carotid arteries. CEUS imaging was performed using an intravenous infusion of Sonovue contrast. Plaques were interrogated in detail with careful angulation of the transducer to maximize the opportunity for detection of neovessels. Presence of IPN was graded semi-quantitatively as absent (Grade 0), limited to the adventitia/plaque base (Grade 1) or extensive and/or extending into the plaque body (Grade 2). Logistic regression was used to identify independent predictors of the presence of IPN.

Results: A total of 175 patients underwent B-mode and CEUS carotid ultrasonography. Mean age was 64.7±8.9yrs and 140 (80%) were male. There were 96 Northern European subjects (55%) and 79 South Asian subjects (45%), in whom 197 and 170 plaques were identified respectively. On a per-patient basis, IPN was detected in 56/79 (71%) Asian subjects and 55/96 (57%) European subjects. After adjustment for clinical variables, South Asian ethnicity was the only independent predictor of presence of IPN (Odds Ratio 2.8, 95% CI 1.36–5.92, p=0.006).

Conclusions: This is the first study to document that IPN is independently associated with South Asian ethnic origin. As a marker of plaque vulnerability, this finding may in part account for higher CVD risk observed in South Asians. Larger studies are required to confirm these preliminary findings.

Acknowledgement/Funding: N/A

P2563 | BEDSIDE
Echolucent carotid plaque is useful for assessment of residual risk in patients with myocardial infarction on statin therapy

Background: Ultrasound assessment of either intima-media thickness (IMT) or plaque echolucrency of the carotid artery provides prognostic information on coro-nary events. Although lipid-lowering treatment using statin therapy reduced car-diovascular events, residual risk still remains after achieving LDL-C goals in patients with coronary artery disease. This study examined the hypothesis that IMT and plaque echolucreency of the carotid artery may remain useful for prediction of cardiovascular events in patients with history of myocardial infarction (MI) after achieve-ment of LDL-C goal on statin therapy.

Methods: Ultrasound assessment of carotid IMT and plaque echolucreency with integrated backscatter (IBS) analysis was performed in 192 patients with history of MI, carotid plaques (IMT > 1.1 mm) and LDL-C levels <100mg/dl on statin ther-apy. As the greatest axial thickness in carotid arteries was the target for measurement of maximum IMT (maxIMT) and echolucreency (lower IBS reflecting echolucreency). All patients were prospectively followed up until the occurrence of one of the following coronary events: cardiac death, non-fatal myocardial infarction, or unstable angina pectoris requiring unplanned revascularization.

Results: During a mean follow-up of 32±18 months, 17 coronary events occurred (cardiac death in 2 patients, myocardial infarction in 4, unstable angina in 11). On multivariate Cox proportional hazards analysis, plaque echolucreency (lower IBS value) was an independent predictor of coronary death, non-fatal MI and unstable angina pectoris (p<0.05), whereas maxIMT was not (HR: 0.44 and 0.96, 95% CI 0.24 – 0.82 and 0.76–1.23, p<0.01, respectively). The addition of plaque echolucreency to traditional risk factors improved net reclassification improvement (NRI) and integrated discrimination improvement (NRI: 0.59; p<0.05; and IDI: 0.075; p<0.05), while addition of maxIMT did not (NRI: –0.03; p=0.63, and IDI: 0.01; p=0.57).

Conclusions: Plaque echolucreency but not maxIMT was an independent predictor of recurrent coronary events. Moreover, the addition of IBS of the carotid artery to traditional risks had additive value for prediction of coronary events. Thus, measurement of plaque echolucreency of the carotid artery was used for assessment of residual coronary risk in patients with history of MI after LDL-C goal attainment on statin therapy.

P2564 | SPOTLIGHT
Right ventricular function: the neglected issue in systemic hypertension
I. Eweada, A.E. Mostafa, O. Awad, P. Demian. Ain Shams University, Cardiology, Cairo, Egypt

Background: The right ventricle (RV) is neglected in clinical practice. The aim of this study is to analyse impact of systemic hypertension (HTN) on RV function by tissue doppler echocardiography.

Patients and methods: Sixty hypertensive consecutive patients referred to echo lab (study group) and thirty healthy individuals (control group) were included in this study during the period from January to June 2014. Hypertensive patients were classified into two groups (stage I and stages II) according to JNC 7. All subjects underwent echocardiography with use of GE Medical Vivid 7. RV global systolic function was assessed as tricuspid annular plane systolic excursion (TAPSE). The RV global filling measurement was determined as E and A waves and E/A wave velocity decrease (E/A') as well as peak systolic and diastolic isovolumetric relaxation time (ms). The longitudinal tricuspid annular velocities were recorded from lateral right ventricular site using PW-DTI. Three major velocities were taken into account: the peak systolic velocity (S) and two other velocities (E and A).

Results: The study included 90 patients (54 males, 60%) with a mean age of 48.57±6.82. TAPSE measurements did not show any significant differences between the 3 groups (control, stage I HTN and stage II HTN) patients. Doppler data obtained at the mitral annulus in the 3 studied groups showed statistically significant results regarding E (p<0.001), E/A (p<0.001), DT (p<0.001), IVRT (p<0.001). When we compared acquired DTI measurements at the RV tricuspid annulus in the control, stage I HTN vs. Stage II HTN we found statistically signifcant differences regarding E' (p<0.001), S (14.97±8.91 vs. 12.37±0.72 vs. 10.63±1.07 cm/sec respectively; p<0.001) while E’ measurements were (16.93±17.14 vs. 14.07±6.44 vs. 12.17±0.75; p<0.001) and A’ measurements were (16.73±12.3 vs. 17.47±1.07 vs. 17.5±1.17 cm/sec respectively; p=0.018). Similarly significant values were found in bi- Hoc analysis between the 3 groups with LSD test.

Conclusion: This study revealed that HTN, and severity of HTN as well, significantly affects the systolic and diastolic function of the right ventricle by pulsed wave and tissue doppler echocardiography. Tissue Doppler echocardiography is a useful tool in detecting right ventricular systolic dysfunction even with normal TAPSE measurements.

P2565 | BEDSIDE
3-year outcomes after test with measuring coronary artery flow velocity reserve at the peak of exercise
A. Zagatina, N. Zhuravskaya. Cardiocenter Medika, Saint Petersburg, Russian Federation

Assessment of coronary flow is used only during pharmacological tests. Never-theless, supine bicycle tests have allowed the application of coro-nary flow assessments during exercise.

The aim of the study was to define the outcomes of the consecutive cohort in three years period after coronary artery flow velocity analysis during exercise tests.

Methods: There is a single center prospective cohort study of 242 consecutive patients who underwent a bicycle exercise echocardiography with the analysis of coronary artery flow velocity in left anterior coronary artery (LAD) in November 2011—February 2012. Coronary flow velocities were measured before and at the peak of exercise at the medium segment of the LAD. In addition, the coronary flow velocity reserve (CFVR) and the differences between the peak and rest velocities (ΔV) were calculated. Two hundred and thirteen patients had well visualized coronary flow in LAD during exercise. One hundred and seventy-eight patients were accessible for follow-up analysis (55.4±9.9 years, 116 men). Cardiovascular death, nonfatal myocardial infarction, revascularization or cardiac arrest with cardiopulmonary resuscitation were defined as major adverse cardiac events (MACE). The period after stress test was 3±0.1 years.

Results: There were 46 patients with MACE. One cardiovascular death, 2 non-fatal myocardial infarctions, 1 cardiac arrest occurred, and 44 revascularizations were performed. The group with MACE vs. the rest patients had a lower velocity in LAD at the peak of exercise (59±27 vs. 70±26 cm/s, p<0.04), ΔV (18±22 vs. 37±26 cm/s, p<0.0002), and CFVR (1.5±0.7 vs. 2.1±0.7, p<0.00001). The group with the most severe MACE – death, myocardial infarction, and coronary artery bypass grafting also had a lower velocity in LAD at the peak of exercise (47±12 vs. 57±16 cm/s, p<0.01). ΔV was decreased in the group with independent coronary E/e’ ratio (p<0.05) and (p<0.001) to other patients. Among the group with CFVR: 2.0, 0% had myocardial infarction, death or coronary artery bypass grafting, and 1.7% patients had coronary artery stenting in others non-LAD arteries.
Conclusion: The analysis of coronary flow in LAD during exercise can be used as a predictor of 3-year outcomes.

P2566 | BEDSIDE
Resting myocardial deformation by 2D speckle tracking echocardiography predicts left ventricular functional improvement 12 months after myocardial infarction
E. Szymczyk, P. Lipiec, B. Michalski, K. Szymczyk, J.D. Kasprzak. Medical University of Lodz, Lodz, Poland

The aim of this study was to assess if the quantitative resting assessment of local myocardial function by 2D speckle tracking echocardiography may be helpful for the prediction of left ventricular (LV) functional improvement 12 months after myocardial infarction (MI) treated with primary percutaneous intervention (pPCI).

Methods and materials: The study group comprised 96 patients (69 male, mean age 58±10 years) with first STEMI treated with successful pPCI. 7-12 days after STEMI, all patients underwent resting echocardiography. Subsequently, acquired images were analyzed off-line using 2D speckle tracking algorithm. Measurements included global peak systolic longitudinal and transverse strain (SLS and STS) – maximal value before aortic valve closure, global peak longitudinal and transverse strain (PLS and PTS) – including possible post-systolic contraction, global systolic longitudinal and transverse strain rate (SLSR and STSR) at baseline. After 12 months each patient underwent control resting echocardiography. LV functional improvement was defined as an absolute increase of LV ejection fraction >5% while LV remodeling was defined as an increase of LV enddiastolic volume ≥15%.

Results: LV functional improvement and remodeling was observed in 28 (29.2%) and 30 (31.3%) patients, accordingly. Biochemical (CKMB mass, troponin T, CRP, lipids), standard echocardiographic (LV enddiastolic and end systolic volume and diameter, ejection fraction, and 2D speckle tracking (global SLS, STS, PLS, PTS, SLRS, STSR) parameters were included in the analysis. Statistical multivariate analysis revealed that baseline values of CKMB mass (p<0.02, OR=0.99, CI 0.990–0.999) and global SLSR (p=0.005, OR=0.006, CI 0.0002–0.006) were predictive for LV functional improvement, while baseline values of LV enddiastolic volume (p=0.02, OR=0.97, CI 0.952–0.995) and global PTS (p=0.02, OR=1.06, CI 1.008–1.106) were predictors of LV remodeling 12 months after MI.

Conclusions: Measurement of resting global SLSR applied early post STEMI as well as maximal value of CKMB mass are predictive for LV functional improvement, while global PTS and LV enddiastolic volume can be helpful in the prediction of LV remodeling 12 months after MI.

P2567 | BEDSIDE
Prognostic value of transthoracic coronary flow reserve in medically treated patients with remaining non-culprit stenosis of intermediate severity after primary percutaneous intervention

Background: Current guidelines recommend culprit lesion treatment with primary PCI in the setting of ST-elevation myocardial infarction (STEMI), while deferred revascularization of non-culprit coronary artery stenosis of intermediate severity after primary PCI in the setting of non-culprit coronary artery stenosis of intermediate severity after primary PCI. Therefore, we aimed to assess if transthoracic coronary flow reserve (CFR) could predict long-term event-free survival in patients with remaining non-culprit stenosis of intermediate severity after primary PCI.

Methods: We enrolled 194 patients, 58±10 years of age, with remaining intermediate coronary artery stenosis (visual assessment 50–70%) on non-infarct related artery (LAD or RCA). All patients were followed for 32±15 months. CFR was defined as the ratio between maximal velocity of diastolic coronary blood flow during maximal hyperemic state and resting coronary blood flow. CFR values ≤2 were considered abnormal. We compared CFR in study patients with non-culprit stenosis of intermediate severity after primary PCI to the control group and we also compared CFR between patients with remaining non-culprit stenosis of intermediate severity after primary PCI to the control group.

Results: LV functional improvement and remodeling was observed in 28 (29.2%) and 30 (31.3%) patients, accordingly. Biochemical (CKMB mass, troponin T, CRP, lipids), standard echocardiographic (LV enddiastolic and end systolic volume and diameter, ejection fraction, and 2D speckle tracking (global SLS, STS, PLS, PTS, SLRS, STSR) parameters were included in the analysis. Statistical multivariate analysis revealed that baseline values of CKMB mass (p<0.02, OR=0.99, CI 0.990–0.999) and global SLSR (p=0.005, OR=0.006, CI 0.0002–0.006) were predictive for LV functional improvement, while baseline values of LV enddiastolic volume (p=0.02, OR=0.97, CI 0.952–0.995) and global PTS (p=0.02, OR=1.06, CI 1.008–1.106) were predictors of LV remodeling 12 months after MI.

Conclusions: Measurement of resting global SLSR applied early post STEMI as well as maximal value of CKMB mass are predictive for LV functional improvement, while global PTS and LV enddiastolic volume can be helpful in the prediction of LV remodeling 12 months after MI.

P2568 | BEDSIDE
Value of detecting severe multi-vessel coronary artery stenosis using three-dimensional speckle tracking echocardiography
Y. Mu, Y.H. Li, X.P. Gong, Z.S. Wu. First Affiliated Hospital of Jinan Medical University, Department of Echocardiography, Jinan, China, People’s Republic of China

Background: The aim of this study was to assess the value of three-dimensional (3D) speckle tracking echocardiography (STE) for the detection of non-myocardial infarction (non-MI) severe multi-vessel coronary artery stenosis (≥75%)

Methods: A total of 101 consecutive patients underwent coronary angiography (CAG), two-dimensional (2D) and three-dimensional echocardiography and three-dimensional speckle tracking echocardiography. Left ventricular (LV) global longitudinal strain (GLS), global radial strain (GRS), global circumferential strain (GCS), global area strain (GAS), and global radial strain (GRS) were quantified by 3D STE. Receiver operating characteristic curves (ROC) were computed to determine optimal strain cutoff values to predict severe multi-vessel coronary artery stenosis. Observer reliability of our study employing 3D STE was assessed by independent, blinded observers.

Results: Ninety-two patients were enrolled and divided into the following three groups according to the CAG: control group (without coronary stenosis, n=37), severe single-vessel coronary stenosis group (one vessel stenosis ≥75%, n=17) and severe multi-vessel coronary artery stenosis group (stenosis of 2 and more than 2 coronary arteries ≥50%, at least one branch coronary stenosis ≥75%, n=48). All 3D speckle-tracking echocardiographic parameters (GLS, GCS, GAS, and GRS) were significantly decreased compared with the control group (p<0.05); the 3D speckle-tracking echocardiographic parameters of the severe multi-vessel coronary artery stenosis group were more dramatically decreased (GLS: 29.5±2.19 vs. 13.35±2.89, GCS: 12.32±5.2 vs. 17.16±5.51, GAS: 18.5±5.93 vs. 26.11±5.25, GRS: 29.08±10.92 vs. 44.43±14.42, p<0.001). Similar changes were also observed for all four 3D STE parameters in the severe multi-vessel coronary artery stenosis group compared with the severe single-vessel coronary artery stenosis group, whereas only GLS and GRS had statistically significantly decreased (p<0.05). Receiver operating characteristic curve analysis demonstrated areas under the curve of 0.87 for 3D GLS, 0.75 for 3D GCS, 0.82 for 3D GAS, and 0.81 for 3D GRS. An optimal 3D GLS cut-off value of magnitude <-11% with 84.2% sensitivity and 3D GAS cut-off value of magnitude <-19% with 91.9% specificity predicted severe multi-vessel coronary artery stenosis (severe multi-vessel coronary artery stenosis by CAG). Good intra-observer and inter-observer reliabilities were seen by 3D STE.

Conclusions: Global strain by 3D STE is useful to detect severe multi-vessel coronary artery stenosis, wherein GLS and GAS are more valuable indicators.

P2569 | BEDSIDE
Three-dimensional speckle tracking echocardiography in ischemic and non-ischemic cardiomyopathy: correlation with myocardial scar imaging using cardiac magnetic resonance
M.F. Aly1, S.A. Kleijn2, R.F.M. Memken-Negroul1, L.F.R. Robbers1, A.M.B. Beek 2, O.K. Kamp 2 on behalf of The VUMC-Amsterdam group.
1. Beni-Suef University Hospital, Cardiology, Beni-Suef, Egypt; 2. VU University Medical Center, Cardiology, Amsterdam, Netherlands

Cardiac magnetic resonance (CMR) delayed contrast enhanced (DCE) is considered the clinical imaging method to identify myocardial fibrosis. The aim of this study was to correlate three-dimensional speckle tracking echocardiography (3DSTE) strain to the localization, extent and distribution of myocardial scar by CMR DCE. Furthermore, we aimed to assess the ability of 3DSTE to differentiate between patients with ischemic and patients with non-ischemic LV dysfuction.

A total of 120 consecutive patients with ischemic (n=80) and non-ischemic (n=40) LV dysfunction underwent CMR DCE for myocardial scar identification and 3DSTE for left ventricular (LV) strain.

DCE analysis revealed 157 segments with transmural enhancement, 668 segments with non-transmural enhancement, and 730 segments without enhancement. The correlations between 3DSTE global strains and either the total or the percentages enhanced LV mass were modest and for 3DSTE regional strains were poor. All 3DSTE regional strain values except for radial strain were lower in segments with compared to segments without transmural hyperenhancement. However, the sensitivity and specificity for all strains were insufficient to differentiate between segments with different percentage of scar nor to differentiate between ischemic and non-ischemic patients.

Segmental 3DSTE strain & hyperenhancement

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-enhanced (%) (A)</th>
<th>Non-transmural enhanced (%) (B)</th>
<th>Transmural enhanced (%) (C)</th>
<th>P value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVS (%)</td>
<td>0.02</td>
<td>0.001</td>
<td>-0.01</td>
<td>-0.01</td>
<td>-0.01</td>
</tr>
<tr>
<td>BVS (%)</td>
<td>0.02</td>
<td>0.001</td>
<td>-0.01</td>
<td>-0.01</td>
<td>-0.01</td>
</tr>
</tbody>
</table>

Conclusion: Functional impairment by 3DSTE strain does not correlate well with scar localization, extent and distribution by CMR DCE. Myocardial deformation is attenuated in cardiomyopathy regardless the presence or the extent of myocardial scar. 3DSTE
did not differentiate between patients with ischemic and non-ischemic LV dysfunction.

Acknowledgement/Funding: No funding

P2570 | BEDSIDE
3D myocardial strain measurement after reperfusion therapy is useful to predict future clinical events in patients with ST-segment elevation myocardial infarction

C.H. Kim, G.Y. Cho, Y.E. Yoon, J.J. Park, T.J. Yoon, I.H. Chae. Seoul National University Bundang Hospital, Cardiovascular Center, Seongnam, Korea, Republic of

Background: Three-dimensional (3D) myocardial strain has been proposed as a gauge to differentiate the prognosis of patients with myocardial infarction.

Purpose: We examined whether assessment of 3D strain after reperfusion therapy can be helpful to predict adverse clinical outcomes.

Methods: In patients with ST-segment elevation myocardial infarction (STEMI), 3D echocardiographic parameters such as global area strain (GAS) were systematically measured within 24 hours after successful reperfusion therapy. Every measurement using speckle tracking was obtained from the electrocardiographic gated 3D volume dataset with a reasonable resolution. Clinical follow-up was performed up to the time of 1 year after the index intervention, and composite outcome of all-cause death, recurrence of non-fatal myocardial infarction, stroke, and admission for aggravated heart failure or unplanned revascularization was used to measure the prognosis. Patients with atrial fibrillation, cardiogenic shock requiring mechanical support in hospital death were excluded from this study.

Results: A total of 231 patients was prospectively enrolled to this preliminary analysis and 3D echocardiographic parameters such as end-diastolic volume or ejection fraction (EF) were well correlated with two-dimensional measurements. Adverse clinical events occurred in 25 patients (10.8%), and these patients had higher 3D GAS values than those without events (−14.6±5.3 vs. −17.2±5.2, p<0.021). Higher 3D GAS score can be used to predict adverse outcomes according to the univariate binary logistic regression analysis (odds ratio (OR) 1.102, 95% confidence interval (CI) 1.013−1.197, p=0.023). Best cut-off value of 3D GAS was −17 according to the receiver operating characteristic curve analysis (area under curve = 0.639, p=0.023, sensitivity = 0.760, specificity = 0.485). And in the multivariate Cox regression analysis, 3D GAS values of −17 or higher can also independently discriminate the prognosis even after adjustment for the influence of patient’s age, 2D EF, deceleration time of mitral inflow E wave, wall motion score index, peak value of troponin I at the time of index procedure (relative risk for adverse events = 3.053, 95% CI 1.033−9.020, p=0.043).

Conclusion: 3D GAS derived from 3D myocardial imaging has a considerable clinical potential, and 3D GAS score of −17 or higher would help estimate the clinical outcomes of STEMI patients at risk.

Acknowledgement/Funding: none

P2571 | BENCH
Translational potential of cardiac regeneration: from fish & mice to men?

R.S.M. Gomes1, P. Skrobilin1, X. Yin1, A.B. Munster2, M. Chong3, H. Tomilins1, S. Langley2, A. Zampetakis1, F. Wardle1, M. Mayr1, King’s College, London, King’s British Heart Foundation Centre, London, United Kingdom; 2University of Cambridge, Faculty of Medicine, Cambridge, United Kingdom; 3Imperial College London, London, United Kingdom; 4King’s College London, Cardiovascular Development, Randall Division, London, United Kingdom

The human myocardium is incapable of regeneration; yet, the zebrafish (Danio rerio) can regenerate the damaged myocardium, and it serves as an important tool and starting point for comparative analysis. Hearts of neonatal, but not adult mice are capable of myocardial regeneration not dissimilar in manner to the zebrafish heart. Thus we performed a proteomics analysis of adult zebrafish hearts and compare the protein expression profile to hearts from neonatal and adult mice.

Using two-dimensional in-gel electrophoresis, we observed an overlap between the proteome from adult mouse and adult zebrafish hearts. Similarly, there was a degree of mismatch between the protein expression in neonatal and adult mouse hearts. Gene enrichment analysis of the selected proteins revealed overexpression of DNA synthesis-related proteins in the cardiac proteome of the adult zebrafish heart similar to neonatal and adult mouse hearts, whereas in hearts of adult mice there was a mitochondria-related predominance in protein expression. Importantly, we noted pronounced differences in the myofilament composition: the zebrafish heart has just a single ventricle and lacks many of the myofilament proteins of differentiated adult cardiomyocytes. For example, we failed to detect expression of ventricular myosin light chain isoforms both at the protein and transcript level. Moreover, troponin I was expressed as skeletal isoform rather than the cardiac isoform as in adult mice. In addition, myosin-2 (also known as cardiac myosin-2) is a cardiac-inhibiting protein. H-MPs demonstrated highly expression of cardiac myosin-2, but not neonatal mouse hearts and was barely detectable in zebrafish hearts. Nebulette, another protein linked to myocyte maturation, was also absent in zebrafish hearts.

In conclusion, our proteomics assessment of zebrafish and mammalian mammalian hearts challenges the assertions on the translational potential of cardiac regeneration in the zebrafish model. The immature myofilament composition of the fish heart may explain why adult mouse and human cardiomyocytes lack this endogenous repair mechanism.

Acknowledgement/Funding: None
lar result was obtained treating HUVECs with T2D+CLI-MPs-conditioned medium (11.8±1.04 vs 16±1.4, p<0.05 vs. HUVECs alone). These altered functions of T2D+CLI-MPs were associated with an imbalance in the cellular redox state involving altered expression of SOD-1 (0.41±0.11 vs 1.03±0.11), catalase (0.41±0.1 vs 0.97±0.02), and p66Shc (2.84±0.6 vs 0.81±0.02) and were reverted by antioxidant treatment (data are expressed as T2D+CLI vs. H, p<0.05).

**Conclusions:** T2D+CLI hampers MPs biological functions relevant to muscular repair. Reversion of T2D+CLI-MPs alterations by antioxidant treatment suggests possible therapeutic targets for attenuation of peripheral complications.

---

**P2574 | BEDSIDE**

_Determinants of accelerated vascular aging: results from the Cardiovascular Risk Factors Affecting Vascular age (GRAVE) study_


**Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece**

**Purpose:** Vascular aging is an independent indicator of cardiovascular risk. We sought to investigate whether the number of cardiovascular risk factors (RFs) determines the progression of vascular aging.

**Methods:** 142 subjects (mean age 51±10.8 years, 94 men) with no established cardiovascular disease were investigated in two examinations over a 2-year period. Subjects were classified at baseline according to their number of cardiovascular RFs (from 0 to 2 and more). The RFs were hypertension, dyslipidemia, smoking and diabetes. Subjects had at the beginning and end of the study determinations of carotid-foveal pulse wave velocity (cfPWV), aortic augmentation index corrected for heart rate (Aix75), brachial flow-mediated dilation (FMD) and carotid intima-media thickness (cIMT). Based on these measurements the annual absolute changes were calculated.

**Results:** The baseline values were statistically different between groups for FMD, Aix75 and cIMT (p<0.05), but not for cfPWV. Subjects with more RFs had a gradual higher annual progression of cfPWV (0.089 m/s/year for no RF, 0.141 m/s/year for 1 RF and 0.334 m/s/year for more than 2 RFs; p<0.009). (Figure) Subjects with more RFs did not show an association with a gradual higher annual deterioration of FMD (0.14%/year for no RF, -0.1%/year for 1 RF and -0.3%/year for more than 2 RFs; p=0.495). Annual progression of Aix75 and mean common cIMT between groups was not statistically significant. However, when only subjects <55 years where considered the progression rate was significantly higher in subjects with more RFs (1.17%/year vs. 1.52%/year vs. 3.15%/year, respectively, p=0.045).

**Conclusions:** The presence of more cardiovascular RFs is associated with accelerated progression of vascular aging in the general population.

---

**P2575 | BENCH**

_Folic acid administration has a modest anti-inflammatory effect in apoE deficient mice_


**University of Athens Medical School, 1st Cardiology Department, “Hippokration” Hospital, Athens, Greece**

**Background:** Supplementation with folic acid (FA) has been proposed as a means to suspend atherosclerosis progression in subjects at risk. Recent large randomized clinical trials failed to document a benefit of a low dose folic acid administration in the clinical outcome of patients with atherosclerosis.

**Purpose:** As inflammation precedes atherosclerosis progression we sought to investigate the effects of high dose FA administration on inflammatory status in apolipoprotein E deficient (apoE/–/–) mice fed cholesterol-rich diet, an animal model of premature atherosclerosis

**Methods:** Apo E/–/– mice were randomly assigned to four groups. The first group (n=9) was treated with regular diet (RD). The second group (n=18) was treated with RD and an aqueous solution of FA (75 mcg/kg/day). The third group (n=9) was treated with high-fat, high-cholesterol diet-western diet (WD). The fourth group (n=18) was treated with WD and FA for 6 weeks. Interleukin (IL)-6, tumor necrosis factor alpha (TNFα) and regulated on activation, normal T cell expressed and secreted cytokine (RANTES) were measured with ELISA as well established inflammatory cytokines implicated in the progression of atherosclerosis.

**Results:** At the end of study period in mice fed with RD (group 1) FA treatment (group 2) decreased IL-6 levels [8.82 (3.51–35.37) pg/ml vs. 3.06 (1.42–3.552) pg/ml, p<0.01], while there was no impact in TNFα levels [2.30 (2.05–2.80) pg/ml vs 2.10 (1.80–2.50) pg/ml, p=0.63] and in RANTES levels [12.25 (3.81–17.70) pg/ml vs. 9.80 (8.52–16.19) pg/ml, p=0.44]. In mice fed with WD (group 3), FA treatment (group 4) had no impact in IL-6 levels [4.93 (1.35–94.65) pg/ml vs. 20.25 (20.47–52) pg/ml, p=0.58], in TNFα levels [2.10 (1.70–5.89) pg/ml vs. 3.27 (1.43–8.4) pg/ml, p=0.17] and in RANTES levels [13.09 (10.43–30.42) pg/ml vs. 12.25 (5.90–29.88) pg/ml, p=0.69].

**Conclusions:** High dose folic acid administration in an atherosclerotic model of apoE deficient mice has only a modest anti-inflammatory effect and cannot reverse the additive atherosclerotic stimulus of a diet rich in cholesterol. These findings further elucidate the effects of folic acid administration in subjects with increased cardiovascular risk.

---

**P2576 | BENCH**

_Fenofibrate and vildagliptin: from blood glucose lowering to nephroprotection_

V. Bayrasheva1, E. Oikonomou2, A.Y. Babenko1, Y.V. Dimitriev1, S.G. Chefu1, I. Shakalov1, S. Ivanovs1, A. North-West Federal Medical Research Centre, Institute of Endocrinology, Saint Petersburg, Russian Federation; 2 Saint Petersburg Pavlov State Medical University, Saint Petersburg, Russian Federation; 3 National Research University of Information Technologies, Mechanics and Optics, Saint Petersburg, Russian Federation; 4 Saint Petersburg State University, Saint Petersburg, Russian Federation

**Purpose:** Prevention of diabetic nephropathy (DN) progression could lead to a decrease in concomitant cardiovascular morbidity and mortality rates. Several recent studies have demonstrated beneficial effects of biguanide metformin and DPP4-inhibitor vildagliptin on certain processes associated with reduced renal function in diabetes. Indeed, in our previous study vildagliptin attenuated routine renal dysfunction markers in insulinopenic diabetic rats. However, metformin did not improve it.

**Purpose:** To evaluate not only glomerular dysfunction marker (albuminuria), but also novel markers of proximal tubular injury (KIM-1, NGAL) in rats with non-genetic type 2 diabetic nephropathy treated with metformin and vildagliptin.

**Methods:** 3 weeks after unilateral nephrectomy, adult male Wistar rats were randomly divided into diabetic group (fed high-fat diet for 5 weeks and then successively received nicotinamide (NA, 230 mg/kg) and streptozotocin (STZ,85 mg/kg) intraperitoneally) and non-diabetic group (ND) fed with normal diet and received citrate buffer without NA and STZ. 10 weeks later, diabetic animals were divided to receive either metformin (M group) 300 mg/kg/day, or vildagliptin (V group) 8 mg/kg/day, or placebo (P group) for another 10 weeks, n=9 each.

**Results:** HbA1c in diabetic groups was considerably higher compared to ND (4.6±0.12). At the end of the experiment, vildagliptin treatment was able to considerably improve creatinine clearance (2.9±0.13 ml/min/kg), and reduce urinary albumin excretion ratio (21.9±1.4 mg/24h). Even though metformin did not attenuate routine kidney dysfunction markers such as creatinine, creatinine clearance and albuminuria (61±2.9 u ml/min/kg; 29±5.4 mg/24h respectively) compared to P group (65±3.6; 2.30±2.01; 38±8.25, P<0.05 each), urinary levels of KIM-1 (589±93.3 ng/ml) and NGAL (154±9100.6 pg/ml) in metformin-treated animals were significantly lower than those in diabetic rats without treatment: (249±191, 1.918±118.1, respectively), P<0.05 each. Moreover, renoprotection in the study groups was confirmed by histological examination and electronic microscopy.

**Conclusion:** Thus, whereas vildagliptin treatment could attenuate routine markers of kidney injury, metformin has shown tubuloprotective properties without any effects on glomerular dysfunction in type 2 diabetic rats.

**Acknowledgement/Funding:** This work was supported by the grant of the Russian foundation for basic research(project 15-04-08138).
protzoan metagenomic analysis using the RiDI™ Next Generation Sequencing (NGS) analysis system, and specific protzoan multiplex PCR probes were used to assess the presence and composition of biofilm populations.

Results: Bacteria were not detected in peripheral blood; however, 4 of 12 filters and 2 of 5 atheroma debris samples had identified bacterial populations (2 patients had atheroma debris and filter evaluated). Evidence of protzoan populations was obtained in 4 of 15 peripheral blood samples, 11 of 12 filters and 4 of 5 atheroma debris samples. Microscopy illustrated a complex composition of biofilm communities in blood, devices, and atheroma debris samples. The identified bacterial taxa in atheroma debris suggest a diverse and novel population composition. Biofilm dwelling bacteria, while present in several atheroma or filter samples, were not detectable in peripheral blood and were not universally present in atheroma or filter. Taxonomic comparisons of sequenced protozoa are consistent with a diverse array of organisms similar to poorly characterized environmental protozoa.

Conclusion: Of 15 patients, 6 patients had evidence of bacteria and 13 had evidence of protozoa in debris and all exhibited evidence of complex biofilm communities. This data suggests that biofilm forming protozoa may play a key role in atherosclerotic vascular disease.

P2579 | BENCH Microparticle-induced thrombin formation predicts severity of coronary artery calcification in patients with severe aortic valve stenosis

P. Horn1, G. Eritkét1, T. Kroep1, L. Schurgers1, T. Zeuz1, C. Heiss1, M. Kem1, R. Westenfeld1. 1 Division of Cardiology, Pulmonology, and Vascular Medicine, Medical Faculty, University of Duesseldorf, Duesseldorf, Germany; 2 Division of Radiology, Medical Faculty, University of Duesseldorf, Duesseldorf, Germany; 3 Cardiovascular Research Institute Maastricht (CARIM), Maastricht, Netherlands

Background: Thrombin, the central protease of the coagulation cascade exerts proinflammatory effects potentially involved in the progression of atherosclerosis. Recently, thrombin generation was shown to be associated with coronary artery calcification. The role of thrombosis itself as well as the formation of microparticles (MPs) from endothelial and various blood cells, including platelets.

Hypothesis: Procoagulant activity of circulating MPs mediates CAC via enhanced thrombin formation.

Methods: In a cross-sectional study of 55 consecutive patients with severe aortic valve stenosis (AS) who were referred for transcatheter aortic valve implantation (TAVI), we assessed CAC and aortic valve calcification (AVC) by 128-row computed tomography applying standard Agatston calcium scoring algorithm. Circulating MPs were assessed by flow cytometry according to the expression of established surface antigens: Endothelial (EMP) CD31+CD41+, CD14+ and CD 62E+ and platelet (PMP) CD41+. Procoagulative activity of circulating MPs was assessed using a two-step amniolytic assay for thrombin formation. Patients with CAC Score below the median (Agastston Score 974) were compared with patients with CAC Score above the median.

Results: Level of PMPs (R=0.461, p=0.001) and CDE2E+ EMPs (R=0.300, p=0.046) correlated positively with MP-induced thrombin formation. Level of PMPs (R=0.698, p<0.001), CD62E+ EMPs (R=0.439, p<0.002) and MP-induced thrombin formation (R=0.587, p<0.001) correlated positively with CAC score. In a multivariate regression analysis increased level of PMPs was an independent predictor for thrombin formation and severity of CAC. AVC Score did not correlate with CAC, thrombin formation or MP levels.

Conclusion: PMP-induced thrombin formation is associated with coronary artery calcification independent of valvular calcification creating a potential vicious cycle.
is a growing body of evidence for an immunomodulatory effect by DPP4i therapy and GLP1a supplementation. With the present study we investigated whether DPP4i and supplementation with GLP1a may improve sepsis associated vascular complications and disseminated intravascular coagulation.

**Methods:** C57BL/6j-, DPP4−/− and GLP1 receptor−/− mice were used. DPP4i (linagliptin) and GLP1a (liraglutide) were applied s.c. Sepsis was induced by lipopolysaccharide (LPS) injection. Fluorescence-based imaging technique was used to detect microvascular occlusion in lungs. Vascular function was tested by isolated perfused lungs. Aorta and heart tissue was used for Western blotting analysis. Isolated platelets were applied for aggregometry in platelet-rich plasma (PRP), cell count and quantification of oxidative stress were tested.

**Results:** In-vitro experiments revealed antiaggregatory effects of GLP1a and DPP4i in response to ADP and thrombin. In cultured monocytes, oxidative burst was not affected by GLP1a and DPP4i. However, in an in vivo model of DPP4 inhibition and GLP1a supplementation of septic animals reduced leukocyte-dependent oxidative burst and NO production, diminished the decrease in blood platelet count and microvascular occlusion of lung vessels. DPP4 knockout revealed similar effects. In GLP1 receptor−/− mice, GLP1a therapy failed to improve both normalization of platelet count and microvascular occlusion. Endothelial function was impaired in LPS-induced sepsis and improved by DPP4i, GLP1a therapy and DPP4 knockout. Endothelial function was per se impaired in GLP1 receptor−/− animals as compared to untreated wild-type mice, and this endothelial dysfunction was even more pronounced in the presence of DPP4 inhibition.

**Conclusion:** The present studies demonstrate that DPP4i and GLP1a therapy ameliorates sepsis-induced microvascular occlusion by prevention of DIC and endothelial dysfunction. These beneficial effects are likely to be mediated by inhibitory effects of GLP1 on platelet function and leukocytes.

**Acknowledgement/Funding:** BMBF 01EO1003

---

**P2582 | BENCH**

**Patients with stable and acute coronary artery disease show a different inflammatory mRNA and miRNA expression pattern in their monocyte subpopulations than healthy subjects**

A. Kratzer 1, H. Giral 1, N. Kraenkel 1, M.F. Mueller 1, R. Klingenber 2, P. Jakob 2, T.F. Luescher 2, U. Landmesser 2, J. Charite - Campus Benjamin Franklin, Cardiology, Berlin, Germany; 3 University Hospital Zurich, Cardiology, Zurich, Switzerland

**Background:** Inflammation and inflammatory cells play a vital role in tissue repair process and in defence against infectious agents, yet an unresolved inflammation can be harmful to the human organism. In recent years it became important to study inflammasomes as role players in different diseases such as arthritis or viral infections. Although there have been more than 20 inflammasomes identified in humans the most studied one has been the Nucleotide-binding domain and leucine rich repeat containing protein 3 (NLRP3). Recently, miRNAs have been also identified to play a role in regulation of inflammasomes. For example, miR-223 has been shown to negatively regulate NLRP3 and also to regulate cholesterol homeostasis.

**Methods and results:** Blood was taken from healthy male subjects, stable (CAD) or acute coronary artery disease (ACS) patients. We isolated peripheral blood mononuclear cells (PBMC) and pre-sorted them based on their CD14 expression using magnetic beads and MACS columns. With a BD Aria III the cells were sorted based on their CD14 and CD16 expression and collected in RPMI medium. We found significantly more CD14+ cells in both the CAD and ACS compared to healthy subjects. Additionally, the ACS patients showed a significantly higher amount of CD14+ cells in comparison with CAD patients. The isolated monocytes were lysed in Glazol and total RNA was isolated and reverse transcribed for miRNA (GE Healthcare) or for microRNA (EXIQON) and expression of NLRP3 and miR-223 has been evaluated using real time PCR. NLRP3 is highly expressed in classical monocytes (CD14+CD16−) but both in CAD, ACS patients as well as healthy subjects and to a much lower extent in intermediate (CD14+CD16+) and non-classical monocytes (CD14+CD16+). Its expression was significantly higher in classical monocytes from CAD and ACS patients compared with healthy subjects. Interestingly, miR-223 was significantly increased in CAD, but significantly decreased in ACS patients. We also found another miRNA that showed a similar pattern, miR-181a, which was significantly increased in P1 of CAD, but not in ACS patients.

**Conclusion:** Different inflammasomes expression patterns in different monocyte subpopulations can be found in CAD and ACS patients. Identifying changes in different RNA types of monocyte subgroups, and identifying their interactions might help to identify novel therapeutic approaches in CAD and ACS.

**Acknowledgement/Funding:** partly funded by HDL Leducq
LVGLS is supranormal in pts with dilated AscAo, despite normal LVEF and the absence of more than mild aortic regurgitation, possibly as a result of increased afterload which is due to the stiff, dilated aorta. Deformation mechanics of the LV gives us valuable insight into the pathophysiologic interaction of the left ventricle and the aorta.

P2585 | BEDSIDE
CMR assessment of arterial stiffness in patients with large vessel vasculitis
C. Wuttiachaipradit, T. Yinghongcharoen, A. Clifford, G. Hoffman, S. Flamm, M. Bolen. Cleveland Clinic Foundation, Cleveland, United States of America

Background: Large-vessel vasculitis (LVV) is often characterized by increased aortic stiffness, which is associated with cardiovascular morbidity and mortality. Measuring aortic pulse wave velocity (PWV) with cardiovascular magnetic resonance (CMR) is a noninvasive method of estimating aortic stiffness. We hypothesized that CMR derived PWV would provide prognostic information to determine the risk of major adverse cardiovascular events in patients with LVV.

Methods and results: This observational study assessed 183 patients (mean age=56.5±17.4 y) who underwent velocity-encoded CMR between 2008 and 2012, including 83 patients with Takayasu arteritis, 81 with giant cell arteritis, 11 with temporal arteritis, and 8 with other systemic disease associated with LVV. Clinical outcome was defined as a composite endpoint of major cardiovascular events including all-cause mortality, myocardial infarction, stroke or transient ischemic attack, aortic or aortic valve surgery, and heart failure hospitalization. Mean aortic PWV was 10.3±4.3 m/s; PWV was highest in patients with polymyositis and lowest in those with Takayasu arteritis. Over a mean follow-up time of 760 days (SD, 559 d), major cardiovascular events occurred in 50 patients (27.3%). In a multivariable Cox regression model, aortic PWV and diabetes mellitus were independent predictors of major cardiovascular events (odds ratio, 1.10 [95% CI, 1.01–1.18]; P=0.04; and odds ratio, 2.03 [95% CI, 1.04–3.97]; P=0.04, respectively). Patients with PWV >10 m/s had a higher incidence of cardiovascular events than those with PWV <10 m/s (log rank P=0.007).

Conclusion: CMR-derived aortic PWV is a powerful independent predictor of major cardiovascular events in patients with LVV.

P2586 | BENCH
Role of sildenafil in the recruitment of hematopoietic progenitor cells in hypoxia-induced pulmonary hypertension

1University Hospital Centre Vaudois (CHUV), Cardiovascular research, Lausanne, Switzerland; 2San Paolo Hospital, Milan, Italy; 3Cardiology Center Monzino IRCCS, Milan, Italy

Rationale: A major contributor to pulmonary hypertension (PH) is loss of endothelium-derived nitric oxide (NO). Sildenafil, phosphodiesterase-5 inhibitor approved for PH treatment, inhibits breakdown of cGMP, NO bioavailability. Since c-kit+ hematopoietic progenitor cells (BMPCs) are involved in PH pathogenesis, we investigated whether sildenafil has the therapeutic potential to improve hypoxia-induced PH modulating the recruitment of BMPCs.

Methods: Adult male Sprague-Dawley rats were exposed 2 weeks to chronic hypoxia (CH, 10% O2) or normoxia (N, 21%O2, n=12). CH rats received silde- nafl (1.4 mg/kg/day ip, n=12) or saline (n=12). Then rats were anaesthetized and cardiac output pressure (RVS) measured. Lung and RV were removed and frozen for biochemical analysis or formalin-fixed and paraffin-embedded for immunohistochemistry (α-smooth muscle actin) and immunofluorescence (c-kit and VEGF-R2). Medial wall thickness (MWT) % of pulmonary arteries (<100μm), plasma levels of stromal cell-derived factor-1 (SDF-1) and erythropoietin (EPO) were measured.

Results: CH increased RVS (46.2±6.3mmHg) and MWT (37.2±5.0%) compared to N (24.8±1.6mmHg and 24.6±0.9%, respectively). CH increased the percentage of SA-β-galactosidase (SA-β-gal) activity, a characteristic of senescence-related growth arrest. In PDL8 with increased expression of p53 and p21 and shortened telomere length in PDL44. We found that miR-216a expression is up-regulated by 64% in PDL44 (P<0.05). Next, we examined the effect of miR-216a on senescence-associated β-galactosidase (SA-β-gal) activity, a characteristic of senescence-related growth arrest. In PDL8 with stable miR-216a lentiviral transfection, we found that miR-216a overexpression increased the percentage of SA-β-gal+ positive cells by 1.8-fold compared with control at all 15 days. We also found that telomerase activity was dependent on APEX1-mediated miR-216a level, which can be corrected for miR-216a levels in HUVEC senescence. To further analyze the effect of miR-216a on endothelial functions, we tested the cell proliferation, migration, adhesion, and tube-formation abilities. The results showed that miR-216a overexpression accelerated the decline of endothelial functions at about 15 days, which led to a significant inhibition of endothelial proliferation and migration by 15% (P<0.001) and 8% (P<0.001) and increased adhesion capability of THP-1 cells to HUVECs by 1.9-folds (P<0.001).

Conclusion: Our data indicated that miR-216a can promote the premature senescence and may serve as a target in regulating endothelial dysfunction associated with atherosclerosis.
Deregulation of thioredoxin system contributes to monocyte dysfunction in diabetes mellitus: Implications for impaired arteriogenesis in type 2 diabetic patients

Department of Cardiovascular Medicine, Department of Internal Medicine III, University Hospital Jena, Jena, Germany;  
Institute of Molecular Cell Biology, Centre for Molecular Biomedicine, University Hospital Jena, Jena, Germany.

**Purpose:** Arteriogenesis is a process encompassing the growth of pre-existing collagenous blood vessels to form functional new vessels. Monocytes play a positive role in this process. Diabetes mellitus (DM) causes monocyte dysfunction. The impaired arteriogenesis seen in DM patients is linked to the reduced ability of monocytes to respond to VEGFR1 agonists. Molecular mechanisms leading to this VEGF-specific signal transduction defect in monocytes is incompletely understood.

**Methods:** Monocytes from diabetic patients (n=14) or non diabetics (n=8) and monocytes from db/db mice (n=6) or Wt littermates (n=6) were used. The expression of thioredoxin 1 and 2 (Trx1 and Trx2) and Trx-interacting protein (Trnip) were detected by using qPCR and WB. Activities of protein tyrosine phosphatase (PTP) and Trx and Trph were measured in the monocyte cell lysates. Pharmacological inhibitors were used to inhibit Trx and a Trx Mimetic Peptide (TMP) was used to study the effects of Trx. Ex vivo analysis of monocyte function from db/db mice and Wt mice was assessed by using a 4-oxo-octanoic acid chamber assay (induced by PGF-1). Hindlimb perfusion in db/db and Wt mice with unilateral hindlimb ischemia (HLI) receiving TMP or placebo was determined.

**Results:** DM led to significant downregulation of Trx1/2 and an upregulation of Trn and Trph expression in diabetic monocytes. Blockade of Trx activity in diabetic mice resulted in VEGF receptor 1 (VEGFR1) signal transduction defect. Blockade of Trx activity by pharmacological inhibitors in normoglycemic monocytes and Trx activity in diabetic mice was impaired. As a consequence, the total PTP activity was downregulated in hyperglycemia in a Trx-dependent fashion which resulted in VEGF receptor 1 (VEGFR1) signal transduction defect. Blockade of Trx activity in hyperglycemic monocytes. Improving Trx function by supplementing Trx mimetic reverse monocyte dysfunction in diabetic mice. Most importantly, hindlimb perfusion improved in db/db mice with Trx mimetic peptide treatment with Trx mimetic peptide indicating that reconstitution of monocyte function might be an important component in this recovery process. We propose functional complementation of Trx as a novel therapeutic strategy for restoring a functional arteriogenesis response in the diabetic environment.

**Conclusion:** Selective inhibition of BET bromodomains sufficiently prevented neonintimal lesion formation in vivo and thus might represent a novel therapeutic approach to prevent negative vascular remodeling.

**Acknowledgement/Funding:** German Research Foundation (Cluster of Excellence REBIRTH)

---

Inhibition of BET bromodomains attenuates smooth muscle cell proliferation and prevents neointima formation

Hannover Medical School, Hannover, Germany.

**Background:** Smooth muscle cell proliferation and migration following acute vascular injury significantly contributes to neointima formation. Recent studies showed that epigenetic regulation has a strong impact on cellular key processes like proliferation, migration or inflammatory responses. Epigenetic readers e.g. BET bromodomains are evolutionary conserved protein-interaction modules that recognize acetylated lysines and therefore play a crucial role in the transcriptional control of function-regulating gene sets.

**Purpose:** The aim of the study was to show whether epigenetic modulation contributes to altered signaling responses in activated vascular cells in vitro and impacts neointimal lesion formation in vivo.

**Methods and results:** Selective inhibition of BET bromodomains by (+)-JQ1 had a remarkable effect on important cell features in primary human SMC in vitro. Smooth muscle cell migration was significantly attenuated under (+)-JQ1 treatment (1 μM (+)-JQ1) whereas the rate of apoptosis was not affected. SMC exhibited a more contractile phenotype as determined by morphological analysis and the expression of the smooth muscle marker gene SMMHC. Moreover, BrdU incorporation assays showed significantly reduced cell proliferation rates of SMC due to BET bromodomain-inhibition. Flow cytometry-based cell cycle analysis of propidium iodide-stained cells revealed that bromodomain-inhibition lead to a G0/G1 arrest and subsequent microarray analyses affirmed a profound regulation of gene sets involved in cell cycle regulation. Specifically, FOXO1 was found to be robustly and significantly upregulated following BET bromodomain inhibition with JQ1. Conclusively, expression of FOXO1-transcribed genes was substantially enhanced. Enrichment analysis suggested that FOXO1 and HNF4A to be responsible for bromodomain-dependent transcriptions of FOXO1. In vivo femoral artery wire injury was performed in C57BL/6J mice to induce neointimal lesion formation. The local application of (+)-JQ1 (10 μM) via a self-degrading thermosensitive Pluronic F-127 resulted in a significantly attenuated neointimal lesion formation compared to vehicle treated control mice.

**Conclusion:** BET bromodomain-containing proteins are critically involved in the epigenetic regulation of cellular function and specifically in the differentiation and cell cycle regulation of SMC and therefore play a crucial role in vascular remodeling. Selective inhibition of BET bromodomains sufficiently prevented neointima formation in vivo and thus might represent a novel therapeutic approach to prevent negative vascular remodeling.

**Acknowledgement/Funding:** German Research Foundation (Cluster of Excellence REBIRTH)

---

Selective PPARa agonist, K-877 suppresses macrophage activation and experimental arterial lesion formation


**Background:** We tested the hypothesis that nuclear receptor PPARa suppresses macrophage activation and the development of arterial disease using the highly selective, novel PPARa agonist K-877.

**Methods and results:** Silencing of PPARa induced pro-inflammatory gene products TNFa and IL1b in macrophage cell line THP-1 cells, suggesting anti-inflammatory effects of PPARa. The network prediction analysis revealed a close relationship between PPARa and the coronary artery disease module (p<0.001). In mouse and human macrophage cell lines and primary macrophages, 1–10 mM of K-877 suppressed mRNA and protein levels of TNFa, NO, IL1 and IL-6, induced by IFNg or LPS. K-877 suppressed an IFNg-induced pro-inflammatory subpopulation in human primary monocytes (CD64+ cells, Figure). K-877 potentiated the effect of K-877 on pro-inflammatory gene expression (p<0.001). In vivo, K-877 reduced aortic intima and media thickness compared to vehicle-treated control mice. K-877 reduced aortic intima-media thickness in K-877 treated mice whereas a delay in the aPC-high group was observed in aPC-treated control mice. K-877 significantly reversed monocyte dysfunction in a PC-dependent fashion in vitro. K-877 rescues IFNg-induced suppression of co-repressors in macrophages.

**Conclusion:** These results indicate anti-inflammatory properties of the PPARa and the clinical benefits of its potent agonist K-877 in inflammatory vascular disease.

**Acknowledgement/Funding:** supported by a research grant from Kowa Company, Ltd. (to M.A.) and a National Heart Lung and Blood Institute grant R01HL107550 (to M.A.)
Ctr. with 13×3 collagen/muscle (n=8, p<0.05). In addition, a significantly lower perivascular monocyte infiltration revealed to the collateral arteries in the aPC-high group 0.76±1 cells/vessel vs. Ctr. 1.17±3 cells/vessel (n=4; p<0.001). On the other hand there was a significantly higher capillary density in the aPC-high group of 864±134 capillaries/mm² vs. Ctr 541±34 capillaries/mm² (n=6; P<0.01) in the lower limb. This results for an inadequate blood supply because of less collateralization within the upper limb. In clinical score, the reduced revascularization confirmed after ligature in the aPC-high group. Ctr. 1.3 vs. 3.7 aPC-high on day 7.

Our experiments of activated protein C has an inhibitory effect on arteriosclerosis. While they are more substantial (day 14; Ctr. 0.89 vs. 4.01 aPC-high) and day 21 (0.17 ctr. vs. 3.7 aPC-high (P<0.05, n=6).

In our experiments of activated protein C has an inhibitory effect on arteriosclerosis. While they are more substantial (day 14; Ctr. 0.89 vs. 4.01 aPC-high) and day 21 (0.17 ctr. vs. 3.7 aPC-high (P<0.05, n=6).
were treated with RNase and proteinase. Treated HUVECs were analyzed for LL37 expression. To investigate the uptake of LL37/RNA complexes, premarked RNA was added to cells prior to treatment and uptake was tracked. C57BL/6 mice were subjected to hind limb ischemia and subsequently treated with SWT. Treated muscles were analyzed for LL37 expression by Western blot analysis. A significant increase in LL37 expression was observed with VEGF positive cells at capillary site in earlier stage after ligation. Furthermore, we could show that the isoform expression is regulated by post transcriptional alternative splicing activity. We identified enzymes, such as Cdc2-like kinases and S RNAse bound “full length” (fl)TF and a soluble “alternatively spliced” (as)TF. Recently, side coagulation TF plays an important role in vessel wall hemostasis, angiogenesis through bone marrow cells activation, resulting in promoting neovascularization. The modulation of IL-6 might be a potential target for treatment for the patients diagnosed as arteriosclerosis obliterans.

were treated with RNase and proteinase. Treated HUVECs were analyzed for LL37 expression. To investigate the uptake of LL37/RNA complexes, premarked RNA was added to cells prior to treatment and uptake was tracked. C57BL/6 mice were subjected to hind limb ischemia and subsequently treated with SWT. Treated muscles were analyzed for LL37 expression by Western blot analysis. A significant increase in LL37 expression was observed with VEGF positive cells at capillary site in earlier stage after ligation. Furthermore, we could show that the isoform expression is regulated by post transcriptional alternative splicing activity. We identified enzymes, such as Cdc2-like kinases and S RNAse bound “full length” (fl)TF and a soluble “alternatively spliced” (as)TF. Recently, side coagulation TF plays an important role in vessel wall hemostasis, angiogenesis through bone marrow cells activation, resulting in promoting neovascularization. The modulation of IL-6 might be a potential target for treatment for the patients diagnosed as arteriosclerosis obliterans.

were treated with RNase and proteinase. Treated HUVECs were analyzed for LL37 expression. To investigate the uptake of LL37/RNA complexes, premarked RNA was added to cells prior to treatment and uptake was tracked. C57BL/6 mice were subjected to hind limb ischemia and subsequently treated with SWT. Treated muscles were analyzed for LL37 expression by Western blot analysis. A significant increase in LL37 expression was observed with VEGF positive cells at capillary site in earlier stage after ligation. Furthermore, we could show that the isoform expression is regulated by post transcriptional alternative splicing activity. We identified enzymes, such as Cdc2-like kinases and S RNAse bound “full length” (fl)TF and a soluble “alternatively spliced” (as)TF. Recently, side coagulation TF plays an important role in vessel wall hemostasis, angiogenesis through bone marrow cells activation, resulting in promoting neovascularization. The modulation of IL-6 might be a potential target for treatment for the patients diagnosed as arteriosclerosis obliterans.

were treated with RNase and proteinase. Treated HUVECs were analyzed for LL37 expression. To investigate the uptake of LL37/RNA complexes, premarked RNA was added to cells prior to treatment and uptake was tracked. C57BL/6 mice were subjected to hind limb ischemia and subsequently treated with SWT. Treated muscles were analyzed for LL37 expression by Western blot analysis. A significant increase in LL37 expression was observed with VEGF positive cells at capillary site in earlier stage after ligation. Furthermore, we could show that the isoform expression is regulated by post transcriptional alternative splicing activity. We identified enzymes, such as Cdc2-like kinases and S RNAse bound “full length” (fl)TF and a soluble “alternatively spliced” (as)TF. Recently, side coagulation TF plays an important role in vessel wall hemostasis, angiogenesis through bone marrow cells activation, resulting in promoting neovascularization. The modulation of IL-6 might be a potential target for treatment for the patients diagnosed as arteriosclerosis obliterans.

were treated with RNase and proteinase. Treated HUVECs were analyzed for LL37 expression. To investigate the uptake of LL37/RNA complexes, premarked RNA was added to cells prior to treatment and uptake was tracked. C57BL/6 mice were subjected to hind limb ischemia and subsequently treated with SWT. Treated muscles were analyzed for LL37 expression by Western blot analysis. A significant increase in LL37 expression was observed with VEGF positive cells at capillary site in earlier stage after ligation. Furthermore, we could show that the isoform expression is regulated by post transcriptional alternative splicing activity. We identified enzymes, such as Cdc2-like kinases and S RNAse bound “full length” (fl)TF and a soluble “alternatively spliced” (as)TF. Recently, side coagulation TF plays an important role in vessel wall hemostasis, angiogenesis through bone marrow cells activation, resulting in promoting neovascularization. The modulation of IL-6 might be a potential target for treatment for the patients diagnosed as arteriosclerosis obliterans.
DNA Topoisomerase I. In the current project we identified the role of microRNAs (miRNAs) as a regulator of TF isoform expression.

**Methods:** The TF isoform expression and the miRNA126 expression in human microvascular endothelial cells (HMEC-1) were detected with TaqMan and western blot before and after stimulation with 10ng/ml TNFα. To analyse the influence of miRNA126 on TF isoform expression and activity HMECs were transfected with miRNA126 and control (co) mimics and inhibitors. The TF isoform expression was detected on mRNA and protein level before and after stimulation with 10ng/ml TNFα. The TF activity was determined with a colorimetric enzyme activity assay.

**Results:** HMEC-1 cells express fTF, aSTF and miRNA126 under normal conditions. The treatment with TNFα for 2h and 6h reduced the expression of miRNA126 and induced miRNA expression of fTF and aSTF (p<0.05). The aSTF and fTF protein expression was increased 24h post stimulation with TNFα. The transfection with the miRNA126 mimic for 24h significantly reduced the fTF and aSTF protein and mRNA expression compared to the transfection with the co-mimic under inflammatory conditions (p<0.05). In contrast, the miRNA126 inhibitor resulted in a significantly enhanced mRNA and protein expression of both isoforms after stimulation with TNFα for 2h and 24h, respectively (p<0.05). In line, the TF activity was significantly decreased after transfection of HMEC-1 cells with the miRNA126 mimic. The transfection with the miRNA126 inhibitor the TF activity upregulated compared to co mimics and inhibitors, respectively (p<0.05).

**Conclusions:** Mice derived from mice expressing a subset of monocyte/macrophages.

---

**P2601 | BENCH**

**CD14+CD16+ patrolling monocytes expressing LRP5 are internalized in advanced coronary atherosclerosis**

M. Borrell-Pages, J.C. Romero, O. Juan-Babot, J. Crespo, L. Badimon. Barcelona Cardiovascular Research Center (CSIC-ICCC), IIB-Sant Pau, Hosp Sant Pau, UAB, Barcelona, Spain

**Background:** Atherosclerosis (AT) is driven by lipid infiltration and chronic inflammation. However there are no successful anti-inflammatory treatments for atherosclerosis because of the partial understanding of immunomodulation in AT. Monocytes represent a heterogeneous population with differences in phenotype, function and microvascular macrophages are believed to differentiate from monocytes recruited from circulating blood. We have recently shown that LRPs (low-density lipoprotein receptor-related protein 5), a member of the LDL family of receptors, regulates monocyte to macrophage differentiation and triggers the Wnt-signaling pathway.

**Purpose:** The aim of this study was to investigate whether macrophages observed in atherosclerotic lesions express LRP5 and whether expression is associated to a subset of monocyte/macrophages.

**Methods:** Magnetic cell sorting with CD16 monoclonal antibodies was used to separate monocytes from healthy individuals yielding highly purified populations of CD16- and CD16+ monocytes, corresponding to M1 and M2 macrophages, respectively. LRP5 expression levels were studied in the M1 or M2 macrophage subsets in human atherosclerotic plaques obtained from heart transplants operated at our hospital. Circulating monocytes from WT and LRP5−/− mice were analysed.

**Results:** We observed that LRP5 expression is significantly increased in human M2 macrophages derived from patrolling CD14+CD16+ monocytes and not derived from circulating CD14+CD16+ monocytes. Circulating monocytes from WT mice also show increased expression of LRP5 in CD115+GR1low monocytes, the mice equivalent for human patrolling monocytes. CD14+CD16+ patrolling monocytes expressing LRP5 are internalized into the deep layers of atherosclerotic plaques towards the intima-media boundaries showing increased migratory activity.

**Conclusions:** These results demonstrate that anti-inflammatory M2 macrophages found in atherosclerotic human plaques express LRPs suggesting that M2 macrophages in advanced atherosclerotic plaques trigger the anti-inflammatory, defence and repair response through LRPs signalling.

**Acknowledgement/Funding:** Plan Estatal de I+D+i 2013-2016 SAF2013-42962-R (LB) FEDER “Una manera de hacer Europa”; ISCIII RD12/0042/0072 (LB)

---

**P2602 | BENCH**

**TGFbeta signaling as modulator of endothelial-to-mesenchymal transition during chronic thromboembolic pulmonary hypertension**

M.L. Bochenek1, N.S. Rosinus1, M. Lanke2, M. Bosmann3, H. Horke4, E. Mayer5, T. Muenzel6, S. Konstantinides7, K. Schaefer7,1. University Medical Center of Mainz, Medical Clinic 2, Mainz, Germany; 2Center for Thorbosis and Hemostasis, Mainz, Germany; 3University Medical Center of Mainz, Medical Clinic 3, Mainz, Germany; 4University Medical Center of Mainz, Department of Pharmacology, Mainz, Germany; 5Kerckhoff Clinic, Bad Nauheim, Germany

**Background:** Chronic thromboembolic pulmonary hypertension (CTEPH) is a major cause of pulmonary hypertension and right heart failure. Clinical as well as experimental evidence suggests that CTEPH results from an inadequate healing response to pulmonary thromboemboli. However, the molecular mechanisms underlying the excessive thrombotic pulmonary artery remodelling are largely unknown.

**Purpose:** To investigate the role of TGFβ1 released from activated platelets, during CTEPH and to determine whether it may promote pulmonary fibrosis via endothelial-to-mesenchymal transition (EndMT).

**Methods:** Endothelial-to-mesenchymal transition (EndMT) in CTEPH and in vitro in human pulmonary arteries, including human pulmonary arteries from patients with CTEPH and their normal lung controls, and in human pulmonary arterial smooth muscle cells (HPASMCs) treated with TGFβ1 or BMP2.

**Results:** In human pulmonary arteries, including human pulmonary arteries from patients with CTEPH and their normal lung controls, and in human pulmonary arterial smooth muscle cells (HPASMCs) treated with TGFβ1 or BMP2, the TGFβ receptor (TGFβR)-dependent pathway was activated. Inhibition of TGFβRII, ALK1 and ALK5 expression in HMEC-1 cells with the miRNA126 mimic. The transfection with the miRNA126 inhibitor the TF activity upregulated compared to co mimics and inhibitors, respectively (p<0.05).

**Conclusions:** TGFβ1-induced signalling events in endothelial cells and/or myofibroblasts were found to be strongly positive for phospho-Smad2 and phospho-Smad3, indicating active TGFβ1 signaling. qPCR and immunohistochemical expression analysis suggested that activation of TGFβ1 signaling occurs primarily through TGFβ1 or BMPs (BMP2 and BMP4), whereas TGFβ3 or the TGFβ antagonist BMP7 were not detected. To study the chronic remodeling response to the venous thrombus and the role of TGFβ1, chronic, mice with platelet-specific TGFβ1 deletion (P4.Cre x TGFβ1flox/flox) and their littermate controls are subjected to subtotal Vena cava inferior (VCI) ligation followed by ultrasound and histological examination of venous thrombus formation and resolution after 8 weeks.

**Conclusions:** Our findings suggest that TGFβ1-induced signalling events in endothelial cells and myofibroblasts may enhance post-thrombotic fibrosis in CTEPH by promoting EndMT.

---

**P2603 | BENCH**

**Fish oils, eicosapentaenoic acid and docosahexaenoic acid, attenuate oxidative stress-induced DNA damage in vascular endothelial cells**

C. Sakai, M. Ishida, Y. Kihara, M. Yoshizumi, T. Ishida. Hiroshima University Graduate School of Biomedical and Health Sciences, Hiroshima, Japan

**Background:** Accumulative evidence has suggested that omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are effective in the prevention of coronary artery disease (CAD). Some progeroid syndromes caused by genetic DNA repair deficiency present the early onset of atherosclerosis, which suggests that DNA damage plays a causative role in its pathogenesis. We have previously reported the presence of DNA damage in atherosclerotic lesions.

**Purpose:** To clarify the mechanisms whereby EPA and DHA prevent CVD, we investigated the effects of EPA and DHA on DNA damage in human endothelial cells.

**Methods and results:** We examined the effect of EPA and DHA on H2O2-induced DNA damage response in human aortic endothelial cells (HAECs). HAECs were treated with EPA or DHA for 48 h prior to H2O2 (100μM) exposure for 15 min. DNA damage was detected by immunofluorescence staining as a cytologically visible “foci” using an antibody against the phosphorylated form of the histone H2AX (γH2AX). H2O2-induced γH2AX foci formation was significantly reduced in HAECs treated with EPA (30%; 30 min and 47%; 24 h incubation after the H2O2 exposure) and DHA (27% and 48%, respectively). H2O2-induced phosphorylation of ATM, a major player for the DNA damage response, was significantly reduced with EPA and DHA treatment (31% and 33%, respectively). These results suggested that EPA and DHA have protective effects on DNA damage rather than promoting DNA repair response. Thus we examined the effect of EPA and DHA on reactive oxygen species (ROS) production in HAECs. Chloromethyl-2′,7′-dichlorofluorescein diacetate (CM-H2DCFDA) measurement showed that treatment with EPA significantly reduced ROS synthesis under both basal condition and H2O2 stimulation. Western blotting analysis indicated that EPA and DHA significantly increased the expression of catalase (43% and 38%, respectively). To further investigate the anti-oxidative effect of EPA and DHA, nuclear factor erythroid 2-related factor 2 (Nrf-2), a cellular sensor for oxidative stress, was silenced using short interfering RNA in HAECs. The mRNA expressions of anti-oxidative molecules regulated by Nrf-2, such as heme oxygenase-1 and NADPH quinone oxidoreductase 1 significantly increased with EPA and DHA, and Nrf-2 silencing attenuated the increases.

**Conclusion:** Our results suggest that both EPA and DHA attenuate oxidative stress-induced DNA damage by upregulating ROS scavenging enzymes, which is, at least in part, via Nrf-2 activation, in human endothelial cells.
P2604 | BENCH
Transcription factor Runx2 promotes aortic fibrosis and stiffness in type 2 diabetes

U. Raaz1, I. N. Schellinger1, F. C. Emrich1, J. K. Hennigs1, S. Eken2, E. Chernogubova2, M. Adl1, L. Maegeldelessel1, J. M. Spin1, P. S. Tsao1.
1Stanford University Medical Center, Division of Cardiovascular Medicine, Stanford, United States of America; 2Karolinska Institute, Department of Medicine, Stockholm, Sweden

Background: Accelerated arterial stiffening is a major complication of diabetes with no specific therapy available up to date.

Purpose: The present study investigates the role of the osteogenic transcription factor Runx2 as a potential mediator and therapeutic target of aortic fibrosis and aortic stiffening in diabetes.

Methods and results: Using a murine model of type 2 diabetes (db/db mice) we identify progressive structural aortic stiffening (by pressure myography; Figure 1) that precedes the onset of arterial hypertension. At the same time, Runx2 is aberrantly upregulated in the medial layer of db/db aortae as well as in thoracic aortic samples from type 2 diabetic patients. Vascular smooth muscle-specific overexpression of Runx2 in transgenic mice increases expression of its target genes, Col1a1 and Col1a2, leading to medial fibrosis and aortic stiffening. Interestingly, increased Runx2 expression per se is not sufficient to induce aortic calcification. Using in vivo and in vitro approaches, we further demonstrate that Runx2 expression in diabetes is regulated via a redox-sensitive pathway that involves a direct interaction of NF-κB with the Runx2 promoter.

Conclusion: In conclusion this study highlights Runx2 as a previously unrecognized inducer of vascular fibrosis in the setting of diabetes, promoting arterial stiffness irrespective of calcification.

Acknowledgment/Funding: National Institutes of Health (NIH), Deutsche Forschungsgemeinschaft (DFG)

P2605 | BENCH
A DPP4 inhibitor, vildagliptin, attenuates monocyte inflammatory response through suppression of MAP kinase pathways and ameliorates CaCl2-induced vascular remodeling in mice

Y. Noda1, T. Miyoshi1, T. Yonezawa2, K. Nakamura1, H. Morita3, H. Ito1.
1Okayama University, Cardiovascular Medicine, Okayama, Japan; 2Okayama University, Department of Molecular Biology and Biochemistry, Okayama, Japan; 3Okayama University, Department of Cardiovascular Therapeutics, Okayama, Japan

Purpose: Recent studies showed that a dipeptidyl peptidase-4 (DPP4) inhibitor directly inhibits smooth muscle cell proliferation and monocyte inflammation independent of the increase in circulating glucagon-like peptide-1 level. We investigated the incretin-independent effect of a DPP4 inhibitor, vildagliptin on monocyte inflammation and vascular remodeling in murine aorta induced by CaCl2.

Methods: The effects of vildagliptin were investigated in a monocyte cell line, U937 cells. The expression of DPP4 in U937 was knocked down by specific siRNA. As a genetic tool we used DPP4 knockdown mice. As a DPP4 inhibitor we used vildagliptin alone (20nM-2μM). In addition, silencing of DPP4 in U937 cells by specific siRNA suppressed the production of interleukin-6 by lipopolysaccharide (62% reduction compared to scramble siRNA). The addition of vildagliptin to lipopolysaccharide-stimulated U937 cells was suppressed by vildagliptin alone (20nM-2μM).

Results: In vitro experiments, induction of interleukin-6 by lipopolysaccharide in U937 cells was suppressed by vildagliptin alone (20nM-2μM). In addition, silencing of DPP4 in U937 cells by specific siRNA suppressed the production of interleukin-6 by lipopolysaccharide (62% reduction compared to scramble siRNA). The addition of vildagliptin to lipopolysaccharide-stimulated U937 cells was accompanied by suppression of MAPK phosphorylation both of ERK and p38. In vivo experiments, the expression of DPP4 in abdominal aorta was strikingly increased at 6 weeks after application of CaCl2. Then, vildagliptin significantly attenuated aortic dilation (external diameters: 1.11±0.06 mm [CaCl2] vs. 0.95±0.05 mm [CaCl2-vildagliptin] vs. 0.64±0.02 mm [Saline], p=0.05, respectively). Histological analysis showed that the recruitment of macrophages into media and adventitia in CaCl2 group was significantly greater than that in vildagliptin group (3.3±2.0 cell/mm^2 vs. 1.2±3.2 cell/mm^2, p=0.03). Quantitative PCR demonstrated that the elevated expressions of MMP-2, -9 as well as interleukin-6 in vehicle aortae were significantly decreased in the vildagliptin group.

Conclusion: Vildagliptin suppressed inflammatory response through suppressing MAP kinase pathways in monocyte and may ameliorated vascular remodeling, partly independent of incretins.

MITRAL VALVE DISEASE

P2606 | BENCH
Induction of aortic valve interstitial cell transformation and calcification via angiotensin type 1 receptor (AT1R)

P. Kapusta, P. Mazur, J. Natoroka, E. Wypasek, J. Sadowski, A. Undas. Jagiellonian University Medical College, Krakow, Poland

Background and introduction: Aortic stenosis (AS) involves the transformation of valvular interstitial cells (VICs) into osteoblastic phenotype regulated by runt-related transcription factor (Runx2). Runx2 increases the expression of proteins directly associated with calcification and osteoblasts phenotype like osteopontin (SP1) and bone sialoprotein (IBSP). Recent evidence suggest that angiotensin-converting enzyme (ACE) is locally expressed in aortic valves and is upregulated in AS. Increased expression of local angiotensin II-forming system may be involved in fibrosis and calcification processes in AS.

Purpose: The objective of this study was to investigate the effect of angiotensin II forming system on VICs calcification.

Methods: Human VICs were isolated from calcified aortic leaflets and cultured in DMEM medium. Cultured VICs were stimulated with angiotensin I (AngI) or AngII (both 0.1–10 μM) alone or in combination with enalapril or ramipril (ACE inhibitors, 10 μM), or candesartan (an angiotensin type-1 receptor (AT1R) blocker antagonist, 10 μM). Expression analysis of ACE, AT1R, Runx2 SP1 and IBSP was performed by reverse transcriptase-polymerase chain reaction (RT-PCR) reaction after 8 hour of VICs stimulation. Calcification was measured using Alizarin Red S staining after 14 days of culture in osteogenic medium containing β-glycerophosphate, ascorbic acid and CaCl2.

Results: Analysis of relative gene expression revealed that both Ang and AngII stimulation increased mRNA expression of RUNX2 (3.2-fold and 4.5-fold, respectively), p<0.01. Other markers indicating osteoblastic transformation such as SP1 and IBSP were also increased 3.4-fold and 5.3-fold, respectively for Ang I and 5.6-fold and 4.9-fold, respectively for Ang II (all p<0.01). Furthermore, calcification of cultured VICs was 5.8-fold and 8.3 fold higher after Angl and AngII, respectively (p<0.01) stimulation. No changes in ACE and AT1R mRNA expression after Angl or AngII stimulation were observed. The both ACE inhibitors reduced Ang but not AngII induced stimulation of calcification process and up-regulation of calcification markers. In turn, candesartan completely blocked the effect of both Ang and AngII stimulation.

Conclusion: These results provide evidence that increased activation of angiotensin II forming system may induce transformation of valvular interstitial cells and increase calcification within aortic valve leaflets partially via AT1R.

P2607 | BEDSIDE
Low gradient severe aortic stenosis with preserved ejection fraction: reclassification of severity by fusion of Doppler and computed tomographic data

V. Kamperidis1, P. Van Rosendale1, S. Katsanos1, F. Van Der Kley2, M. Regeer1, J. Al Amri1, G. Sianos2, N. Ajmone Marsan1, V. Delgado1, J.J. Bax1. 1Leiden University Medical Center, Cardioiology, Leiden, Netherlands; 2ÅHEPA Hospital, Aristotle University, Thessaloniki, Greece

Aims: Low gradient severe aortic stenosis (AS) with preserved left ventricular ejection fraction (LVEF) may be attributed to aortic valve area index (AVAi) underestimation due to the assumption of circular left ventricular outflow tract (LVOT) with 2-dimensional echocardiography. The current study evaluated whether fusing Doppler and multi-detector computed tomography (MDCT) data to calculate AVAi may result in significant reclassification of inconsistently graded severe AS.

Methods and results: Of 191 patients with AVAi <0.6cm^2/m^2 and LVEF >50%, 88 (46% with 51% male) had low gradient and were included in the current analysis. Patients were divided into low flow (n=42) and normal flow (n=46) according to stroke volume index of 35ml/m^2. LVOT area was also measured by }

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475 by guest on 07 February 2019
planimetry on MDCT and combined with Doppler hemodynamics to obtain the fusion AVAI. The group of patients with normal flow had significantly larger AVAI and LVOT area index compared with the low flow group. Although the MDCT-derived LVOT area index was comparable between the 2 groups, the fusion AVAI was significantly larger in the normal flow group. By using the fusion AVAI, 52% (n=24) of patients with normal flow and 12% (n=5) of patients with low flow would have been classified into moderate AVA due to low gradient and AVAI >0.6cm²/m². The aortic valve calcium, sodium density and calcium index were not significantly different between the 2 low-gradient groups and between those reclassified to true moderate AVA versus those remaining severe with low gradient.

Conclusion: In patients with low gradient severe AVS with echocardiographic AVAI >0.6cm²/m² and preserved LVEF, fusion AVAI evaluation permits reclassification to true moderate AVA in 52% of the normal flow and 12% of the low flow patients.

P260 | BEDSIDE
Transcatheter mitral valve-in-ring implantation with the direct flow medical valve
A. Laba, F. Gatto, K. Brijikic, C. Oezbek, A. Colombo, J. Schoter, R. Raffaele Hospital of Milan (IRCCS), Milan, Italy; 2 SHG Kliniken Völklingen, Germany; 3 Medical Care Center Prof. Mathey, Prof. Schofer, University Cardiovascular Center, Hamburg, Germany

Background: Recurrent mitral regurgitation may occur after mitral annuloplasty and reoperation may be associated with significant morbidity and mortality in elderly patients. Recently, transcatheter mitral valve-in-ring procedures have been shown to be a feasible alternative in selected high-risk patients and associated with good short-term outcome. However, there are still numerous procedural challenges that can occur such as device malpositioning, valve stability and anchoring, paravalvular leak, and the risk of LVOT obstruction. Until now only balloon-expandable valves have been implanted with navigational assistance.

Objective: To evaluate the feasibility of transcatheter mitral valve-in-ring implantation of the Direct Flow Medical valve

Methods and results: Between April and November 2014, 3 patients underwent transcatheter valve-in-ring implantation for severe mitral regurgitation after failure of surgical ring annuloplasty. All patients were evaluated by a multidisciplinary heart team as high or extreme risk for redo-surgery and underwent MSCT and TEE evaluation prior to the procedure. Annuloplasty rings were semi-rigid in all 3 cases and valve sizing was based on MSCT measurements: 1) St. Jude Seguin 34mm, perimeter 86.1mm, 29mm DFM; 2) Edwards Physio 30mm, perimeter of 75.6mm, 27mm DFM; 3) Medtronic CG Future 26mm, perimeter 65.8mm, 25mmDFM. All cases were performed via the transapical approach with a 24fr sheath. The DFM was successfully positioned within the mitral ring in all 3 cases resulting in excellent seal, no PVL, no LVOT obstruction and a mean transprosthetic gradient of 3mmHg. However, in the 2nd case, a mild pre-existing para-ring leak became severe in keeping with acute detachment of partially dehisced mitral ring. The DFM valve was deflated and easily retrieved with a dedicated basket system within the left ventricle, resulting in acute hemodynamic stabilization of the patient who then underwent elective surgery.

Conclusions: This initial experience confirms the feasibility and possible advantages of implanting a fully resorbable and retrievable valve within a failed mitral annuloplasty ring with excellent acute hemodynamic outcomes.

P2608 | BEDSIDE
Size of mitral valve leaflet and predominant tethering of posterior leaflet determine degree of residual functional mitral regurgitation following isolated coronary artery bypass grafting
S. Yoshida, K. Toda, T. Nakamura, S. Miyagawa, Y. Yoshikawa, S. Fukushima, S. Saito, D. Yoshioh, S. Yajima, Y. Sawata. Osaka University, Department of Cardiovascular Surgery, Osaka, Japan

Background: Presence of functional mitral regurgitation (MR) is known to be associated with poor prognosis in coronary artery disease. Revascularization by coronary artery bypass grafting (CABG) has been shown to reduce degree of functional MR, although predictive factors or mechanisms of reversibility of functional MR post-CABG are not fully understood.

Purpose: To review clinical outcome following isolated CABG for patients having functional MR preoperatively and to explore predictive factors in the reversibility of functional MR post-CABG.

Methods: Of a consecutive series of 85 patients who had functional MR of mild degree preoperatively and underwent isolated CABG in our institution between 2002 and 2013, 51 patients who were echocardiographically followed-up for more than 6 months post-CABG were enrolled. Preoperative ejection fraction was less than 40% in 19 patients (37.3%) of the cohort, while 23 patients (41.5%) presented with medically intractable severe angina preoperatively.

Results: The MR degree was promptly reduced in 22 patients (43.1%) postoperatively, in association with a significantly less rate of in-hospital treatment for cardiac failure long-term, compared with the 29 patients that showed residual mild or more severe MR postoperatively (P<0.05). There was no significantly independent factor to predict postoperative change in the MR degree in the background of the cohort, including low ejection fraction, severe angina or posterior infarct preoperatively, as assessed by multivariate logistic regression analysis. Instead, preoperative length of the anterior and posterior mitral leaflets in the long-axis echocardiographic view was positively correlated with postoperative reduction in the MR degree (P=0.001), whereas the tenting height was not associated with the change of the MR degree. In addition, posteriorly directing MR jet preoperatively, which suggests unbalanced tethering of the leaflets, was another statistically significant factor to predict residual MR post-CABG (P=0.001).

Conclusions: Residual mild degree of functional MR was associated with poor clinical outcome long-term post-CABG. A specific mitral valve configuration, such as large size of the mitral leaflets or predominant tethering of the posterior leaflet, was indicated to be a predictive factor in reversibility of functional MR after isolated CABG.

P2611 | BEDSIDE
Cutoff mitral gradient and systolic pulmonary artery pressure predictive of dyspnea on Doppler stress in mitral stenosis
S. Lelahchi. Beni-Messous Hospital, Cardiology, Algiers, Algeria

Background: In mitral stenosis (MS), the American Recommendations AHA/ACC advocate percutaneous mitral commissurotomy (PMC), when in stress echo Doppler the mean gradient mitral (MGM) or the systolic pulmonary artery pressure (SPAP) predictive of dyspnea justifying the PMC were sought using the table of stress echocardiography. In no dyspneic patients, the MGM was ≥15 mmHg and SPAP ≥60 mmHg in respectively 99.1% and 66.1% of the peak of the effort, reflecting the low specificity of the tests with these values. At the peak of the effort, the optimal thresholds are 35.5 mmHg for the MGM and 75.5 mmHg for SPAP; their diagnostic indices are respectively 13 and 47 for the positive likelihood, 95% and 99% for positive predictive value, 5% and 1% for positive predictive error.

Objective: To evaluate the functional outcomes following transcatheter edge-to-edge mitral valve repair

Methods: Between 2009 and 2013, 99 consecutive patients underwent quality of life testing using the Minnesota living with heart failure questionnaire (QoL) and six minute walk test (6MWT) at baseline, one month and 6–12 months following the MC procedure.

Results: Cohort characteristics included a mean age of 77±10.2 years, female gender 39%, atrial fibrillation 58%, functional regurgitation 46%; left ventricular ejection fraction 50.3±15.9%, creatinine 119±50.1 (micromol/l), and haemoglobin 12.6±14.9 (g/dl)

At baseline patients had impaired 6MWT to and gender matched values in a general population (282.9±114.4 m vs 467.8±83.1 m, p<0.001). Following MC procedures were seen at one month for both QoL scores (48.2±21.3 vs 34.4±21.8, p<0.002) and 6MWT distance (292.8±107.7 m vs 342.7±113.9 m, p<0.001). These improvements remained apparent at 6–12 months follow-up (mean follow up 221 days IQR 114.5–409.25) (48.2±21.3 vs 31.5±21.1, p<0.002 and 292.8±117.7 vs 351.2±130.1 m, p<0.01, respectively.

There were no differences in QoL between patients with moderate and secondary mitral regurgitation (QOL secondary MR 47.4±24.5 vs 34.1±23.2, p=0.0002, QOL primary MR 43.1±16.8 vs 29.7±12.2, p=0.0008)
P2610 | BEDSIDE
Impact of atrial fibration on mitral annular morphology in severe degenerative mitral regurgitation: implication in repair strategy
C.N. Jin, K.K. Kam, J.L. Looi, X.S. Yang, J.P. Sun, A.P. Lee. Lui Che Woo Institute of Innovative Medicine, The Chinese University of Hong Kong, Hong Kong, Hong Kong SAR, People's Republic of China

Background: Atrial fibration (AF) is common in patients with degenerative mitral regurgitation (DMR) due to mitral valve prolapse, associated with atrial remodeling and worse outcome. However, the impact of AF on mitral annular morphology and implication in repair strategy remain unclear.

Purpose: To test the hypothesis that mitral annulus of DMR patients with AF has significant morphological differences from that in patients with sinus rhythm (SR).

Methods: A total of 34 subjects including 34 patients with severe DMR and AF (DMR-AF), 64 patients with severe DMR and SR (DMR-SR), and 29 normal controls were prospectively studied using real-time 3-dimensional (3D) transesophageal echocardiography. The 3D geometry of mitral valve was measured with custom software. Left atrial maximal volume was measured by 3D transthoracic echocardiography, and Left atrial peak systolic longitudinal strain by 2D speckle tracking echocardiography.

Results: Compared with DMR-SR (age=56±19y; 19 women) and normal subjects (57±15y, 12 women), DMR-AF patients were older (age=62±11y; P<0.05; 6 women). Adjusted for age, DMR-AF group had significantly reduced annular height and height-to-commissural width ratio, increased annular area, increased left atrial maximal volume and reduced left atrial systolic strain (all P<0.05) (Table). There were no differences in regurgitant volume, left ventricular volumes and ejection fraction between DMR-SR and DMR-AF groups (P>0.05).

Conclusions: In patients with severe DMR, AF is associated with more severe left atrial remodeling and dysfunction, causing more severe annular flattening and dilatation. These findings imply that restoration of annular saddle shape with annuloplasty may be more important in DMR patients complicated by AF.

P2611 | BEDSIDE
Comparison of transoesophageal and transthoracic echocardiographic measurements of mechanism and severity of mitral regurgitation in ischaemic cardiomyopathy
P.A. Grayburn1, L. She2, K. Golba3, K. Mokrzycki4, J. Drozdzt5, A. Cherniavskya6, R. Przybylski2, K. Wrobel6, H. Haddad7, G. Maurer10 on behalf of STICH Trial. 1Baylor University Medical Center, Dallas, United States of America; 2Duke Clinical Research Institute, Durham, United States of America; 3Medical University of Silesia, Katowice, Poland; 4Pomeranian Medical University, Szczecin, Poland; 5Medical University of Lodz, Lodz, Poland; 6State Research Institute of Circulation Pathology, Novosibirsk, Russia; 7Silesian Center for Heart Diseases (SCHD), Zabrze, Poland; 8John Paul II Hospital, Krakow, Poland; 9University of Ottawa Heart Institute, Ottawa, Canada; 10Medical University of Vienna, Vienna, Austria

Background and purpose: Functional mitral regurgitation (MR) often complicates ischaemic heart disease and contributes to symptoms and mortality. This report compares baseline transoesophageal (TEE) and transthoracic echocardiographic (TTE) imaging of the mechanism and severity of MR in patients with ischaemic cardiomyopathy in the STICH trial.

Methods: Independent core labs measured TEE and TTE images on STICH patients. Measurements common to both modalities included MR grade, tenting height and tenting area, and mitral annular diameter. For each parameter correlation were compared by Spearman rank coefficients. Results: There were 2136 patients in STICH who were eligible for this study. Of those, 196 had TEE measured by the core lab, all of whom also had TTE. Compared to STICH patients not in this substudy, our patients were more likely European, had lower NYHA heart failure class, larger LV end-systolic volume index and were more likely to be on a beta-blocker. Mean LVEF was 27%; MR was moderate or severe in 18% and 11%, respectively. A modest correlation (figure) was present between TEE and TTE for MR grade (n=176, r=0.50, P<0.0001). For mechanism of MR, modest correlations were present for long-axis tenting height (n=128, r=0.27, P<0.0001), tenting area (n=152, r=0.35, P<0.0001), and long-axis annular diameter (n=123, r=0.41, P<0.0001). For each measurement, there were no statistically significant differences between methods. Potential explanations for the scatter include the mean temporal delay of 6 days between TEE and TTE and different orientation of the imaging planes between TEE and TTE.

Conclusions: TEE and TTE measurements of MR mechanism and severity correlate only modestly with enough scatter in the data that they are not interchangeable.

Acknowledgement/Funding: National Institutes of Health, RO1HL72430, UO1HL69015, and UO1HL60913

P2614 | BEDSIDE
Mitralclip versus heartport mitral valve annuloplasty in very severe heart failure
T. Ondrus, J. Bartunek, M. Vanderheyden, B. Stockman, C. Mirica, M. Kotrc, F. Van Praet, M. Penicka. Cardiovascular Center Aalst, Aalst, Belgium

Background: Functional mitral regurgitation (FMR) worsens prognosis in patients with heart failure. Catheter-based Mitralclip implantation and surgical Heartport technique are minimally invasive approaches to repair FMR.

Purpose: To compare mid-term efficacy and outcomes of Mitralclip and Heartport techniques in matched patients with very severe systolic heart failure and FMR.

Methods: A total of 23 patients (Mitralclip; age 75±8 y, 72% males, LVEF 31±9%, NYHA III 91%, Euroscore II 19±14%) and 56 matched patients (Heartport; age 76±4 y, 57% males, LVEF 31±7%, NYHA III 91%, Euroscore II 13±12%) with severe systolic heart failure and significant FMR underwent implantation of Mitraclip or Heartport mitral valve annuloplasty. Median follow-up was 1.9 years (IQR 0.5–1.5 years).

Results: Incidence of life threatening periprocedural complications was similar in both groups (Mitraclip vs Heartport, 21% vs 31%; NS). There was no difference in the 30-day (5% vs 9%; NS) and total mortality (36% vs 38%; NS). We observed statistically less heart failure re-hospitalizations favoring the Mitraclip group (29% vs 56%, p=0.04). Significant symptomatic improvement and reduction of FMR grade were present in both groups (Table 1). Both techniques were associated with stabilization of LV remodeling (LVEF 0.5–1.5 years).

Conclusions: In patients with systolic heart failure and significant FMR, both Mitralclip and Heartport procedures showed comparable outcome. Patients with the highest Euroscore II (>20%) have poor prognosis regardless of treatment strategy and these patients should not undergo mitral valve repair.
the two groups (NYHA II: 48.9% vs. 49.9%, p=0.648). Patients with AF had more frequently a Wilkins score >8 (51.4% vs. 30.9%, p=0.001), a larger left atrium (41 cm² vs. 32 cm², p=0.001) and a lower transmural gradient (11.1 mm Hg vs. 16.6 mm Hg, p=0.001).

BMV was equally successful in the two groups (90.6% vs. 94%, p=0.187) but resulted in a smaller post BMV area (2 cm² vs. 2.15 cm², p=0.012) with a lower mitral valve area gain (0.9 cm² vs. 1.0 cm², p=0.015), BMV was not associated with a higher risk of complications (4.3% vs. 4.7%, p=0.844).

After a mean follow-up of 74 months, patients with AF had the same rate of restenosis (28.3% vs. 25.6%, p=0.96) but required more frequently a mitral valve replacement (16.3% vs. 7.7%, p=0.012). They also experienced higher rates of systemic embolism (3.8% vs. 0.6%, p=0.018) and had a lower rate of event free survival (freedom from death, restenosis and systemic embolism) (52.2% vs 68.8%, p=0.047).

In the group of patients in AF, predictive factors for combined adverse events including death, restenosis, systemic embolism and mitral valve replacement were: post BMV area <2cm² (OR: 2.5, 95% CI [1.2; 5.18], p=0.014), procedural complications including a mitral regurgitation and tamponade (OR: 3.95, 95% CI [1.4; 11.13], p=0.009) and NYHA II during follow up (OR: 3.46, 95% CI [2.09; 5.73], p=0.001).

Conclusion: Our data support the fact that patients with AF have worse immediate and long term outcome after BMV. Post BMV area <2cm², procedural complications and NYHA II predict adverse events during follow up.

AORTIC VALVE DISEASE

P2618 | BEDSIDE

Determinants of functional capacity in aortic stenosis patients

F. Bandera, G. Generati, M. Pellegrino, F. Carbone, V. Labate, E. Alfonzetti, M. Guazzi. IRCCS Policlinico San Donato, Heart Failure Unit, San Donato Milanese, Italy

Background: Aortic stenosis (AS) is clinically characterized by dyspnea and intolerance to exercise. Clinical interpretation of such symptoms is often difficult due to the advanced age of AS patients. We aimed at identifying cardiac determinants of exercise intolerance in AS (Aortic Vmax >3 m/s).

Methods and results: We performed cardiopulmonary exercise test (CPET) simultaneously combined with exercise echocardiography in 43 patients with AS referred for functional assessment. Severe AS were evaluated because of symptomatic limitations maximal exercise, considering the 75% of predicted VO2 consumption as a marker of preserved functional capacity. Twenty-three patients had preserved functional capacity (group A), showing higher work, maximal VO2, O2 pulse and better VE/VO2 and heart rate recovery. No differences were found in terms of rest systolic function and AS severity, while group A had higher peak heart rate (HR), higher peak cardiac power output (cardiac EF or MTG x systolic pressure) and higher peak-rest transaortic mean gradient difference (ΔMG). At multivariate analysis, only ΔMG resulted independently associated with impaired functional capacity (p=0.048; CI 1.001–1.323).

P2619

Transcatheter aortic valve implantation in patients with reduced ejection fraction and low transvalvular gradient: the rule of 40

F. Conrotto1, F. D’Ascenzo1, G. Tarantini2, P.F. Agostoni3, A. Marzocchi4, P. Presbitero1, F. Bedogni5, M. D’Amico1, F. Carbone, V. Labate, E. Alfonzetti, M. Guazzi. IRCCS Policlinico San Donato, Heart Failure Unit, San Donato Milanese, Italy

Aims: This multicenter study aimed to clarify the prognostic role of low mean trans-aortic gradient (MTG) and reduced left ventricular ejection fraction (LVEF) after transcatheter aortic valve implantation (TAVI).

Methods and results: From 2007 to 2012, 764 consecutive patients with severe symptomatic aortic valve stenosis underwent TAVI at participating hospitals. One hundred and forty patients (18.3%) had LVEF <40% and 624 (81.7%) >40% while 227 had mean transvalvular gradient (MTG) <40 mmHg while 537 ≥40 mmHg. Three-years mortality was significantly higher in patients with low EF and low MTG while was similar in patients with low EF and high MTG, high EF and low MTG and high EF and high MTG (60.1% Vs 30% Vs 30.1% Vs 29.2% respectively; p=0.001). These results were confirmed by multivariate analysis, as the combination of low EF and low MTG (both less than 40) was identified as the stronger mid-term mortality predictor (HR 2.4, CI 95% 1.4–3.9; p=0.001).

Conclusions: At least one parameter of EF or MTG (or both) predicts a good prognosis for TAVI patients at mid-term follow up, while those with both left ventricular dysfunction and low mean aortic pressure gradient are at high risk of all cause death after TAVI.

AORTIC VALVE DISEASE

P2617 | BEDSIDE

Impact of pre-operative moderate/severe functional tricuspid regurgitation in TAVI population and its post-procedural modifications

S. Miyazaki, M. Barletta, I. Rosa, C. Marinis, A. Chieffo, M. Montorfano, A. Latib, A. Margonato, A. Colombo, E. Agricola, San Raffaele Hospital of Milan (IRCCS), Milan, Italy

Background and purpose: TAVI (transcatheter aortic valve implantation) has become a widespread solution in high-risk patients (pts). Functional tricuspid regurgitation (FTR) is a frequent finding in these pts and its impact on prognosis is unclear. Moreover TR severity may improve after TAVI but it is still unknown if TAVI has an effect on TR severity changes. Aim of the study is to assess FTR prognostic meaning in TAVI population and its possible changes after this procedure.

Methods: From 2009 to 2014, 529 TAVI pts were screened. Clinical and echocardiographic baseline data were collected. Echocardiographic follow up was collected in two groups: FTR non-improvement. The presence of more than moderate FTR, even if not improving after TAVI, was associated with a higher risk of complications (4.3% vs. 4.7%, p=0.844).

Conclusions: AS patients can present functional impairment which is related to cardiac response to exercise rather than to stenosis severity. These results suggest the role of inotropic and contractile reserve supporting the routinely evaluated cardiac assessment. Limited maximal exercise, considering the 75% of predicted VO2 consumption as a marker of preserved functional capacity. Twenty-three patients had preserved functional capacity (group A), showing higher work, maximal VO2, O2 pulse and better VE/VO2 and heart rate recovery. No differences were found in terms of rest systolic function and AS severity, while group A had higher peak heart rate (HR), higher peak cardiac power output (cardiac EF or MTG x systolic pressure) and higher peak-rest transaortic mean gradient difference (ΔMG). At multivariate analysis, only ΔMG resulted independently associated with impaired functional capacity (p=0.048; CI 1.001–1.323).

P2618 | BEDSIDE

Determinants of functional capacity in aortic stenosis patients

F. Bandera, G. Generati, M. Pellegrino, F. Carbone, V. Labate, E. Alfonzetti, M. Guazzi. IRCCS Policlinico San Donato, Heart Failure Unit, San Donato Milanese, Italy

Background: Aortic stenosis (AS) is clinically characterized by dyspnea and intolerance to exercise. Clinical interpretation of such symptoms is often difficult due to the advanced age of AS patients. We aimed at identifying cardiac determinants of exercise intolerance in AS (Aortic Vmax >3 m/s).

Methods and results: We performed cardiopulmonary exercise test (CPET) simultaneously combined with exercise echocardiography in 43 patients with AS referred for functional assessment. Severe AS were evaluated because of symptomatic limitations maximal exercise, considering the 75% of predicted VO2 consumption as a marker of preserved functional capacity. Twenty-three patients had preserved functional capacity (group A), showing higher work, maximal VO2, O2 pulse and better VE/VO2 and heart rate recovery. No differences were found in terms of rest systolic function and AS severity, while group A had higher peak heart rate (HR), higher peak cardiac power output (cardiac EF or MTG x systolic pressure) and higher peak-rest transaortic mean gradient difference (ΔMG). At multivariate analysis, only ΔMG resulted independently associated with impaired functional capacity (p=0.048; CI 1.001–1.323).

Conclusions: AS patients can present functional impairment which is related to cardiac response to exercise rather than to stenosis severity. These results suggest the role of inotropic and contractile reserve supporting the routinely evaluated cardiac assessment. Limited maximal exercise, considering the 75% of predicted VO2 consumption as a marker of preserved functional capacity.

P2619

Transcatheter aortic valve implantation in patients with reduced ejection fraction and low transvalvular gradient: the rule of 40

F. Conrotto1, F. D’Ascenzo1, G. Tarantini2, P.F. Agostoni3, A. Marzocchi4, P. Presbitero1, F. Bedogni5, M. D’Amico1, F. Carbone, V. Labate, E. Alfonzetti, M. Guazzi. IRCCS Policlinico San Donato, Heart Failure Unit, San Donato Milanese, Italy

Aims: This multicenter study aimed to clarify the prognostic role of low mean trans-aortic gradient (MTG) and reduced left ventricular ejection fraction (LVEF) after transcatheter aortic valve implantation (TAVI).

Methods and results: From 2007 to 2012, 764 consecutive patients with severe symptomatic aortic valve stenosis underwent TAVI at participating hospitals. One hundred and forty patients (18.3%) had LVEF <40% and 624 (81.7%) >40% while 227 had mean transvalvular gradient (MTG) <40 mmHg while 537 ≥40 mmHg. Three-years mortality was significantly higher in patients with low EF and low MTG while was similar in patients with low EF and high MTG, high EF and low MTG and high EF and high MTG (60.1% Vs 30% Vs 30.1% Vs 29.2% respectively; p=0.001). These results were confirmed by multivariate analysis, as the combination of low EF and low MTG (both less than 40) was identified as the stronger mid-term mortality predictor (HR 2.4, CI 95% 1.4–3.9; p=0.001).

Conclusions: At least one parameter of EF or MTG (or both) predicts a good prognosis for TAVI patients at mid-term follow up, while those with both left ventricular dysfunction and low mean aortic pressure gradient are at high risk of all cause death after TAVI.
P2620 | BEDSIDE
Serial NT-pro-B-type natriuretic peptide measurements after transcatheter aortic valve replacement: diagnostic and prognostic value for mortality, cardiac decompensation and cardiac rehospitalisation
L.S.E. Gaede1, C. Liebetrut1, W.K. Kim1, J. Blumenstein1, O. Doerr2, A. Berkowitsch1, T. Walther1, G. Hamm3, H. Nerf4, H. Moellmann1, 1Kerckhoff Heart and Thorax Center, Cardiology, Bad Nauheim, Germany; 2Justus-Liebig University of Giessen, Giessen, Germany

Background: The serum level of NT-pro-B-type natriuretic peptide (NT-proBNP) is related to the severity of both valvular aortic stenosis and chronic aortic regurgitation. In this context patients with elevated preoperative NT-proBNP levels show a higher postoperative morbidity (e.g. NYHA class, heart insufficiency) and mortality after aortic valve replacement and after transcatheter aortic valve replacement (TAVR).

Purpose: The aim of the present study is to examine the serial changes and the prognostic significance of NT-proBNP in a large cohort of patients undergoing TAVR within a long-term follow-up.

Methods: Consecutive patients (n=503) undergoing TAVR were included. NT-proBNP levels were measured prior to and directly after the procedure, 4, 24, 48, and 72 hours afterwards, and 6 days afterwards. Patients were followed for 1 year. Patients who died within 10 days after TAVR or for whom a blood sample at one of the time points was missing were excluded.

Results: All patients included (n=423) had elevated NT-proBNP levels at baseline (median 2025 pg/ml [IQR 998–5146]) compared with the control value for healthy subjects (<400 pg/ml). During the serial measurements NT-proBNP levels rose until 72 hours after TAVR and decreased thereafter. NT-proBNP levels prior to TAVR were predictive of 12-month mortality (AUC 0.536; 95% CI 0.499–0.637). NT-proBNP levels 72 hours after TAVR showed an even higher correlation with mortality (AUC 0.691; 95% CI 0.628–0.7539) and for the combined endpoint of morality, cardiac decompensation and cardiac rehospitalisation (AUC 0.61; 95% CI 0.562–0.671).

Conclusion: Treatment with controlled release metoprolol for 6 months did not reverse, nor exacerbate left ventricular remodelling in patients with moderate to severe aortic regurgitation.

Acknowledgement/Funding: Grants were provided by the South-East Norway regional health authority and the Norwegian ExtraFoundation. AstraZeneca provided the study drugs.

P2621 | BEDSIDE
Bench test vs. post-procedural stent sizes
K. Miyake, K. Kadota, Y. Hyodo, S. Otsuru, D. Hasegawa, S. Habara, T. Maruo, Y. Fuku, T. Goto, K. Mitsudo, Kurashiki Central Hospital, Cardiology Department, Kurashiki, Japan

Background: In transcatheter aortic valve implantation (TAVI), the selection of an appropriate stent size is important to prevent complications; however, the currently available stent sizes are limited. In actual clinical practice, when the nominal stent size cannot bring the most appropriate stent size, a strategy of over-filling or underfilling can be taken. Estimates of the stent sizes at each inflation volume can contribute to technical success but remain unclear. In the present study, we conducted a bench test and compared them with the post-procedural stent sizes.

Methods: The 23- and 26-mm stents of SAPIEN XT for transfemoral approach were selected for the bench test. The inflation was started from 3-cc underfilling and was increased by 1 cc up to 4-cc overfilling for 23-mm stent and 2-cc overfilling for 26-mm stent. The stent size measurement was conducted with calipers and computed tomography (CT) based on the midpoint of the stent height. Also, in 24 patients after TAVI, their stent sizes were measured with CT.

Results: There were no obvious differences between caliper and CT measurements. The stent sizes in the bench test were considerably smaller than the manufacturer’s description. The post-procedural stent sizes of both 23- and 26-mm stents were even smaller than those in the bench test. In particular, the stent sizes at underfilling tended to be markedly smaller than those at the nominal inflation volumes.

Conclusion: Estimates of the stent sizes at each inflation volume, in addition to the accurate aortic annulus measurement and selection of an appropriate stent size, are crucial for technical success of TAVI. The actual sizes can be smaller than the manufacturer’s description. Particular caution should be exercised in stent placement with underfilling.

P2622 | BEDSIDE
Change in stent size at each inflation volume of SAPIEN XT: bench test vs. post-procedural stent sizes
K. Broch1, S. Urheim1, M.T. Lonnewabken2, W. Stueflotten2, R. Massey3, K. Fossaa3, E. Hopp3, S. Aakhus3, L. Gullestad1, 1University of Oslo, Rikshospitalet University Hospital, Department of Cardiology, Oslo, Norway; 2Haukeland University Hospital, Department of Cardiology, Bergen, Norway; 3Oslo University Hospital, Department of Radiology and Nuclear medicine, Oslo, Norway

Background: In transcatheter aortic valve implantation (TAVI), the selection of

Methods: The 23- and 26-mm stents of SAPIEN XT for transfemoral approach were selected for the bench test. The inflation was started from 3-cc underfilling and was increased by 1 cc up to 4-cc overfilling for 23-mm stent and 2-cc overfilling for 26-mm stent. The stent size measurement was conducted with calipers and computed tomography (CT) based on the midpoint of the stent height. Also, in 24 patients after TAVI, their stent sizes were measured with CT.

Results: There were no obvious differences between caliper and CT measurements. The stent sizes in the bench test were considerably smaller than the manufacturer’s description. The post-procedural stent sizes of both 23- and 26-mm stents were even smaller than those in the bench test. In particular, the stent sizes at underfilling tended to be markedly smaller than those at the nominal inflation volumes.

Conclusion: Estimates of the stent sizes at each inflation volume, in addition to the accurate aortic annulus measurement and selection of an appropriate stent size, are crucial for technical success of TAVI. The actual sizes can be smaller than the manufacturer’s description. Particular caution should be exercised in stent placement with underfilling.
P2624 | BEDSIDE
Rapid deployment balloon-expandable aortic valve replacement: rates of major paravalvular leak and new permanent pacemaker implantation
T. Wahlers1, G. Lauffer2, M. Borger3, M. Shrestha4, A. Kocher1, T. Walther5, F. Mohr6, C. Schmidt7, F. Duha8, A. Haverich1, University of Cologne, Cologne, Germany; 9Medical University of Vienna, Vienna, Austria; 10Columbia University Medical Center, New York, United States of America; 11Hannover Medical School, Hannover, Germany; 12Klinikum Grosshadern, Munich, Germany; 13Heart Center of Leipzig, Leipzig, Germany; 14University Hospital of Munich, Munich, Germany; 15Edwards Lifesciences LLC, Irvine, CA, United States of America

Background and introduction: Rapid deployment aortic valve replacement (RDAVR) may facilitate minimally invasive surgery and reduce potential concerns associated with TAVR such as increased rates of PVL and the need for permanent pacemaker implantation. Two different valve designs are commercially available in Europe – balloon-expandable (stainless steel) and self-expanding (nitinol). The latter has been associated with rates of major paravalvular leak between 6.7% and 19.4%, and new permanent pacemaker implantation between 7.0% and 17.0%.

Purpose: The study aim was to examine the rates of these complications in a large series of patients receiving the balloon-expandable valve.

Methods: The TRITON Trial was a prospective, multicenter, single-arm study of 287 patients with aortic stenosis who required elective aortic valve replacement with or without concomitant coronary artery bypass grafting. All subjects underwent RDAVR using a trileaflet bovine pericardial bioprosthesis (available in sizes 19, 21, 23, 25, and 27 mm) affixed to a balloon-expandable frame. The nominal balloon size was pressure needed to expand the frame in the left ventricular outflow tract and secure the valve ranged between 4.5 and 5.0 atm. Layers of low density polyester cloth enveloped the frame to promote a relatively blood-tight seal. The frame length extending below the annulus ranged between 6.6 and 8.0 mm. Patients were followed annually for 3 years. Echocardiograms were adjudicated by an independent Echo Core Laboratory.

Results: One-hundred-fifty-eight patients underwent isolated RDAVR; the surgery approach included, full sternotomy (n=77), upper hemisternotomy (n=77), and right anterior thoracotomy (n=10). Mean age was 75.7±6.8 years; female, 49.4%; NYHA III/IV, 57.1%; hypertension, 84.3%; chronic renal failure/dialysis, 18.2%; prior cardiac surgery, 15.6%; diabetes, 11.7%; and, COPD, 7.8%. Logistic EuroSCORE was 8.2±6.6%. Early (30 day) rate of all-cause mortality was 1.3%; reoperation for bleeding, 7.0%; acute kidney injury, 5.7%; major paravalvular leak, 0.6%; new permanent pacemaker implantation (total), 5.1% and valve related pacemaker implantation, 3.2%.

Conclusion: These data suggest that isolated RDAVR, using a balloon-expandable valve, can achieve rates of major paravalvular leak and new permanent pacemaker implantation that appears to be superior to a self-expanding valve. Moreover, early rates of mortality and complications are low and comparable to those seen with conventional surgical aortic valve replacement.

Acknowledgement/Funding: This study was supported by Edwards Lifesciences LLC

P2625 | BEDSIDE
Value-Based approach in re-designing the care pathway for patients with infective endocarditis
R. Dworakowski, A. Fille, J. Byrne, D. Whittaker, F. Matcham, M. Gunnings, S. Block, P. MacCarthy, O. Wendler. King’s College Hospital, London, United Kingdom

Background: Making a definitive diagnosis and decision regarding mode of treatment for infective endocarditis (IE) may be difficult. It has been proposed that a Heart team (infection specialist, cardiologist and cardiac surgeon) look after patients with IE. This has potential significant resource and financial implications with no evidence that it improves outcomes.

Objective: In this study we aim to look how a process of improving care pathway for patient with IE using value-based strategy affects outcomes and costs.

Methods: In 2012 we established multidisciplinary IE team. Between June 2010 and August 2014 there were 229 patients with IE treated in our institution. We analyzed 32 patients with confirmed IE treated between January-December 2011 (cohort 1) and 39 patients treated between July-December 2014 (cohort 2) after multidisciplinary clinical team was fully established and functional.

Results: Demographic data are shown in table 1. In hospital mortality in cohort 1 was 22% and in cohort 2 was 8% (P=0.05). Total length of stay in cohort 1 was 32 days and 37 days in cohort 2 (NS). 14% patients were discharged for outpatient antibiotic therapy compared to 0% in 2011 (P=0.05). Using activity based costing we calculated a total cost of treatment per patient. A total cost for Cohort 1 was total was £319,647GBP and 28,465GBP for surgically and medically treated patients, respectively) and for Cohort 2 was 32,048 GBP (37,061 GBP and 25,492 GBP for surgically and medically treated patients, respectively).

Conclusion: Creating IE Heart Team results in improvement in patients outcomes and is not associated with increased costs.

Acknowledgement/Funding: Kings Fund

P2626 | BEDSIDE
Ross procedure as a treatment of aortic valve endocarditis
A. Ringle1, M. Richardson1, F. Juthier2, N. Rousseau3, A. Solme1, A. Duva-Pertain1, A. Vincentelli3, D. Montaigne1, A. Charmel1. Cardiothoracic Hospital of Lille, Explorations Fonctionnelles Cardio-vasculaires, Lille, France; 2Cardiology Hospital of Lille, Cardiovascular Surgery, Lille, France

Background: Aortic root replacement with a pulmonary autograft (Ross intervention) can be performed as a treatment of aortic valve endocarditis, avoiding prosthetic valve implantation in septic context. We sought to assess long-term outcomes of Ross procedure in this indication.

Methods: From April 1992 to March 2009, Ross intervention was performed in 42 patients (Mean age 34±8 years, 86% male) suffering from an active or ancient aortic valve endocarditis. 33% patients had extensive perivalvular involvement, and surgery was urgent in 16 patients (38%). We performed a prospective clinical and echocardiographic follow-up of this population.

Results: Median follow-up was 10 years (range 4–21 years). Overall survival at 10 and 15 years was 87±5% and 81±8% respectively. Perioperative mortality was 4.7% (2 patients) and no late cardiac death was reported. Eight patients (19%) underwent repeat surgery for autograft and/or homograft dysfunction at a mean time of 9 months (3 times to 18 years). Rate of recurrent endocarditis was low (7% - 3 patients), including 1 in a context of persistent intravenous drug abuse. Clinical follow-up showed a good functional status for all patients with NYHA ≤ II, and less than 25% of patients receiving cardiovascular medication. Late echocardiographic follow-up demonstrated well functioning autograft and homograft, with only one severe aortic regurgitation, and one significant increase in pulmonary mean gradient.

Conclusion: Ross intervention in aortic valve endocarditis is an interesting alternative to prosthetic valvular replacement in a selected population, with a high rate of survival free from any cardiovascular event or medication requirement.
P2629 | BEDSIDE
Role of reversibility assessment of pulmonary vascular resistance index (PVRI) and echocardiography in management of valvular heart disease (VHD)
K.B. Khokhar, R. Devlin, R. Fisher, M.A. El-Gamel, P. Jogia on behalf of Midland VHD and Heart Failure Group. Waikato District Hospital, Cardiology, Waikato, New Zealand

Background: VHD leading to pulmonary hypertension (PHT) is an important predictor of mortality in patients following surgical intervention. Echocardiography and reversibility assessment of PVRI may be useful in identifying high risk patients resulting in better procedural outcomes.

Methods: We performed a retrospective study of 100 consecutive patients of VHD with moderate to severe PHT (systolic pulmonary artery pressure (PAP) of 50mmHg, mean PAP > 30mmHg and mean pulmonary capillary wedge pressure (PCWP) > 15mmHg), from June 2010 till June 2013. Transthoracic echocardiography (TTE) was performed in all patients pre-PVRI assessment (average 4weeks). PVRI reversibility was performed using nebulised iloprost (20microgram/ml for 10 minutes).

Results: Median age of our cohort was 77 years (range 27 to 84), (60%) male. Seventy two (72%) had severe mitral and 28 (28%) had severe aortic valve disease. PVRI reversibility was assessed in all patients (30%). Seventeen (53%) of our patients were responders and had 20% or greater decrease in PVRI. Non-responders had dilated left ventricle with reduced right ventricle TAPSE on echo with high PCWP during right heart study.

Conclusion: Reversibility assessment of PVRI is infrequently performed in patients with moderate to severe PHT secondary to VHD. Non-responders had reduced biventricular function on echocardiography. Combining echo and PVRI data in VHD patients may help in better risk stratification resulting in improved intervention outcome.

P2630 | BEDSIDE
Impact of patient blood management on the incidence of acute kidney injury in patients undergoing transcatheter aortic valve implantation
T. Tesoriero 1, A. Coppi 1, L. Salemme 2, A. Pucciarelli 1, E. Stabile 3, C. Bancone 3, S. Capron 1, C. Testoni 1, L.S. de Sarno 1, C. Brucinella 1, C. Montevergine 1, Laboratory of Invasive Cardiology, Mercogliano, Italy; 1 University of Napoli “Federico II”, Department of Advanced Biomedical Sciences, Naples, Italy; 2 Second University of Naples, Naples, Italy; 3 Clinica Montevergine, Cardiac Surgery, Mercogliano, Italy; 2 University of Foggia, Foggia, Italy

Acute kidney injury (AKI) after transcatheter aortic valve implantation (TAVI) is frequent and is associated with adverse outcomes. Past studies have attributed AKI to several peri-procedural features including impaired kidney function at baseline. The relationship between patient blood management, baseline kidney function and this complication is less well defined. This study aimed to fill this gap in knowledge.

Data from the institutional prospective transfemoral TAVI registry were collected in 293 consecutive patients. Patients were stratified according to the Chronic kidney disease (CKD) classification, in to two groups: group A (CKD classes 0, 1 and 2) and group B (CKD classes 3, 4 and 5). Patients in group A had the group of preoperative anaemia (according to World Health Organization definition), post-procedural hemoglobin (Hb) drop ( < 2g/dl, 2-4g/dl and > 4g/dl) and blood transfusions on AKI were evaluated. Anaemia, Hb drop and transfusions were then forced into multivariable logistic models for study outcome.

Incidence of AKI was 17.2% in group A and 14.7% in group B. Anaemia was significantly associated with AKI in both groups. Similarly, Hb drop was significantly associated with AKI with a clear trend toward a higher incidence in parallel with the degree of postprocedural anemia. Transfusion was associated with a significantly increase in the incidence AKI in both groups, with a marked additive effect in the preoperatively anaemic patients. Multivariable logistic regression revealed transfusion as an independent predictor of AKI in group A (OR 1.98, 95% CI: 1.05-3.88; p < 0.001) and baseline anaemia in group B (OR 2.21; 95% CI: 1.88- 4.98; p <0.001).

This study portrays that optimization of patient blood management is crucial to TAVI outcomes, presence of anaemia and/or chronic kidney disease allows better risk stratification and should prompt new management algorithms.

Abstract P2629 – Table 1

<table>
<thead>
<tr>
<th>Responders (N=17)</th>
<th>Non-responders (N=13)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Median 71 yrs (range 37–83)</td>
<td>Median 66 yrs (range 51–79)</td>
</tr>
<tr>
<td>Mean PCWP (Right heart study)</td>
<td>22 mmHg</td>
<td>29 mmHg</td>
</tr>
<tr>
<td>Pulmonary Artery Systolic Pressure (Right heart study)</td>
<td>60 mmHg</td>
<td>59 mmHg</td>
</tr>
<tr>
<td>Pulmonary Vascular Resistance Index (PVR)</td>
<td>7.3 [U/min 100 [ml]]</td>
<td>7.5 [U/min 100 [ml]]</td>
</tr>
<tr>
<td>Change in PVRI post Reversibility test with iloprost</td>
<td>3.3 [WU/ml]</td>
<td>0.0 [WU/ml]</td>
</tr>
<tr>
<td>Cardiac Index (litre/min/m²)</td>
<td>2.54 [litre/min/m²]</td>
<td>0.13 [litre/min/m²]</td>
</tr>
<tr>
<td>Left Ventricle diastolic dimension on transthoracic echo, Pre-study</td>
<td>53 millimeter</td>
<td>66 millimeter</td>
</tr>
<tr>
<td>RV/Tricuspid Annular Plane Systolic Excursion (TAPSE) on transthoracic echo, Pre-Study</td>
<td>1.8 cm (range 2.3–0.8)</td>
<td>1.25 cm (range 2.0–0.5)</td>
</tr>
<tr>
<td>Left Atrium (LA) area on Apical 4ch view (TTE)</td>
<td>27 cm² (range 17–44)</td>
<td>34 cm² (range 24–47)</td>
</tr>
</tbody>
</table>
P2631 | BEDSIDE
Soluble ST2 for risk stratification and the prediction of mortality in patients undergoing transcatheter aortic valve implantation
A. Stundt, F. Courtz, P.J. Leimkuehler, M. Weber, S. Pingel, A. Sedaghat, R. Schueler, E. Grube, G. Nickenig, J.M. Sinning. University Hospital Bonn, Heart Center, Department of Cardiology, Bonn, Germany

Background: Risk scores were developed to estimate perioperative risk and in-hospital mortality after cardiac surgery and have not been validated for TAVI yet. Soluble ST2 (sST2) is a novel biomarker that has been shown to be linked to cardiac hypertrophy, fibrosis, and ventricular dysfunction and, therefore, could be considered as a parameter for further risk stratification in TAVI patients.

Purpose: The aim was to assess the prognostic performance of sST2 for short- and long-term mortality and whether it is suitable for risk stratification.

Methods: In 462 patients, serum creatinine, troponin I, NT-proBNP and sST2 levels were measured. Primary endpoint was in-hospital mortality; other outcomes were recorded according to VARC-2 criteria.

Results: In 462 TAVI patients, a median baseline sST2 level of 20.0 ng/ml was found. Elevated sST2 levels were significantly associated with both in-hospital mortality (survivors: 19.8 (13.8–28.2) ng/ml vs. non-survivors: 24.5 (16.3–38.9) ng/ml; P=0.027) and all-cause mortality at 1 year (survivors: 19.0 (13.6–27.2) ng/ml vs. risk survivors: 22.4 (15.0–36.0) ng/ml; P=0.005). In ROC analysis, sST2 had the highest AUC for the prediction of all-cause mortality at 30 days. However, renal function was superior for the prediction of all-cause mortality at 1 year. In addition, we stratified our cohort according to the median level of NT-proBNP (2.960 pg/ml) and the sST2 cut-off level of 35 ng/ml in four groups (figure). Patients with an elevation of both biomarkers had a significantly worse prognosis.

Conclusions: Baseline sST2 is strongly associated with adverse short-term outcome, and might be useful for the prediction of in-hospital outcome. sST2 provides additional prognostic information beyond established biomarkers for the prediction of 1-year outcome.

P2632 | BEDSIDE
Transfemoral transcatheter aortic valve implantation in lower risk patients: 30-day and long-term outcomes
C. Rodriguez, E. Durand, M. Godin, C. Tran, A. Cribier, H. Eitchaninoff. University Hospital of Rouen, Interventional Cardiology, Rouen, France

Background: Transcatheter aortic valve implantation (TAVI) is an alternative to surgical aortic valve replacement (SAVR) in patients with severe symptomatic aortic stenosis (AS) at high surgical risk. A predictive Logistic Euroscore (Log ES) >15% usually defines the high-risk population. However, TAVI is performed in a number of pts with a Log ES <15% due to comorbidities not included in the calculation of the Log ES but increasing the risk of SAVR. The results of TAVI in this subgroup of “low-risk” patients needs to be assessed.

Population and methods: From January 2010 to December 2013, 351 consecutive patients underwent transfemoral TAVI with the Edwards Sapien XT prosthesis using exclusively local anesthesia. We compared the clinical characteristics and outcomes at 30 days in two groups according to the Log ES <15% (Low risk: LR): n=175 (49.3%), or >15% (High risk: HR). n=176 (51.1%). Long-term survival was analyzed by Kaplan Meier analysis. Valve Academic Research Consortium (VARC-2) classification of TAVI complications was used.

Results: Mean Log ES was 10.3±3.1% and 24.4±9.6% in the LR and HR groups, respectively. Patients in the LR group were younger (82.1±7.6 vs. 85.3±5.5 years, p<0.0001), more often female (55.1% vs. 44.9%, p=0.04), and had more frequently a history of previous CABG (2.6% vs. 6.8%, p=0.01). Procedural success was high and similar in the two groups (98.3% in both groups). There was no significant difference between the two groups in major vascular complications (16.6% vs. 14.8%, p=0.66), life-threatening bleedings (8.0% vs. 9.7%, p=0.71), major acute stroke (3.4% vs. 1.1%, p=0.17), myocardial infarction (2.9% vs. 1.1%, p=0.28) and permanent pace maker (5.7% vs. 5.1%, p=0.82). There was a trend for lower 30-day mortality in the LR group (4.0% vs. 7.9%, p=0.09). Kaplan-Meier survival curves comparing LR and HR patients are shown in the figure and survival was significantly higher in LR patients at one (85.4% vs. 78.7%), two (76% vs. 68.4%) and four (69.1% vs. 41.4%) years (log rank p=0.02).

Conclusions: In lower risk patients (Log ES <15%), TAVI is associated with similar procedural success and complications. However, 30-day and long-term survival is significantly higher in lower risk patients.

P2633 | BEDSIDE
Risk scores and biomarkers for the prediction of 1-year outcome after transcatheter aortic valve replacement
J.M. Sinning1, K.C. Wollert2, A. Sedaghat3, C. Widera2, C. Hammerstingl1, M. Vasa-Nicotera1, E. Grube1, G. Nickenig1, N. Werner1, T. Kempf2. 1Medizinische Klinik, Universitätsklinikum Bonn, Bonn, Germany; 2Hannover Medical School, Klinik für Kardiologie und Angiologie, Hannover, Germany

Background: Up to 50 percent of the patients still die or have to be rehospitalized during the first year after transcatheter aortic valve implantation (TAVI). This emphasizes the need for more strategic patient selection. The aim of our study was to compare the prognostic performance of 4 risk scores (logistic EuroSCORE, EuroSCORE II, STS-PROM, GAV score) and 5 circulating biomarkers of inflammation and/or myocardial dysfunction (hsCRP, GDF-15, IL-6, IL-8, NT-proBNP) to predict all-cause mortality and rehospitalisation after TAVI.

Methods: We calculated the hazard ratios and c-statistics of risk scores and biomarkers for the risk of death (N=80) and the combination of death or rehospitalisation (N=132) during the first year after TAVI in 310 consecutive TAVI patients. The magnitude of the increase in model performance when combining risk scores and biomarkers was evaluated by the change in the c-statistic (ΔAUC), integrated discrimination improvement (IDI), and continuous net reclassification improvement [NRI (<0)].

Results: The EuroSCORE II and GDF-15 had the strongest predictive value for 1-year mortality (EuroSCORE II, AUC 0.711; GDF-15, AUC 0.686) and for the composite endpoint (EuroSCORE II, 0.690; GDF-15, 0.682). When added to the EuroSCORE II, GDF-15 enhanced the prognostic performance of the score and enabled substantial reclassification of patients. Combinations of increasing tertiles of the EuroSCORE II and GDF-15 allowed to stratify the patients into subgroups with mortality rates ranging from 8.5 to 49.1% and death/rehospitalisation rates ranging from 15.3 to 68.4%.

Conclusions: Our study identified the EuroSCORE II and GDF-15 as the most promising predictors of a poor outcome after TAVI. Risk score/biomarker combinations may support the decision making process in TAVI patients.
of cardiomyocytes or reactivation of certain fetal genes. In the pathologic cardiac hypertrophy model of ascending aortic constriction, Selumetinib provided significant ERK inhibition in the stressed heart but not in the other organs. This selective ERK inhibition prevented LV wall thickening, LV mass increase, fetal gene reactivation and cardiac fibrosis. In another distinct physiologic cardiac hypertrophy model of a swimming rat, Selumetinib provided a similar anti-hypertrophy effect, except that no significant fetal gene reactivation or cardiac fibrosis was observed.

Conclusions: Selumetinib, a novel oral anti-cancer drug with good safety records in a number of Phase II clinical trials, can inhibit ERK activity in the heart and prevent cardiac fibrosis. These promising results indicate that Selumetinib could potentially be used to treat cardiac hypertrophy. However, this hypothesis needs to be validated in human clinical trials.

Acknowledgement/Funding: Natural Science Foundation of China (grant number: 81300169,81270289)

P2635 | BEDSIDE
Clinical profile and outcomes of peripartum cardiomyopathy in a southeast Asian tertiary centre: the PERIPHI study
L.R.C. Cueva1, N.C. Manapat1, J.R. Jalique1, 2 *Philippine Heart Center, Department of Adult Cardiology, Manila, Philippines; 2Philippine Heart Center, Department of Education, Training and Research, Manila, Philippines

Background: Peripartum cardiomyopathy is a rare form of dilated cardiomyopathy characterized by heart failure and left ventricular dysfunction associated with pregnancy. While clinical characteristics of these patients have been previously described in literature, there is limited data regarding the natural history and predictors of outcomes of these patients in Asia, most specifically in Filipino patients.

Methods: A review of 39 patients diagnosed with peripartum cardiomyopathy was performed. Clinical and echocardiographic data were analyzed. Patients were followed up for the occurrence of death and major adverse events (MAE) and outcomes were correlated with patient variables.

Results: The mean age of the patients was 28.4±6.9 and the mean ejection fraction (EF) was 27.8±8.4%. Heart failure was the most common symptom (98%) and 16 patients had an initial EF of ≥25% (41%) and only 2 patients in this subgroup experienced improvement in EF. 29 patients experienced death and/or EF ≤47.4%. Significant variables associated with the occurrence of MAEs were arrhythmia at initial presentation (OR 3.38,p<0.026) and no improvement of EF in 6 months (OR 0.319,p=0.024) Variables associated with mortality were initial EF (OR 0.52,p<0.033), EF ≥25% (OR 1.20,p=0.019), Fractional shortening (OR 0.88,p<0.024) and recovery of LV function (OR 0.232,p≤0.05). Kaplan Meier survival curve showed that patients whose ejection fraction recovered in 6 months experienced a 75% freedom from MAE at almost two years. The occurrence of death is highest in the first two years before reaching an almost 60% free incidence from mortality. Patients with an ejection fraction of less than 25% had a mortality rate of 50% in two years. Patients with ejection fraction of ≥25% had a 90% likelihood of survival for 8 years. Patients whose EF recovered in 6 months were alive for almost 7 years.

Conclusion: Peripartum cardiomyopathy is associated with significant morbidity and mortality. The degree of left ventricular dysfunction on presentation, the absence of recovery of EF as well as improvement of EF within 6 months were predictive for mortality and the occurrence of major adverse events. This study emphasizes the need for aggressive treatment and monitoring early in the course of disease in order to improve outcomes.

Acknowledgement/Funding: none

P2636 | BEDSIDE
Effect of tafamidis on the progression of cardiac involvement in patients with familial amyloid polyneuropathy

Introduction: Transthyretin familial amyloid polyneuropathy (TTR-FAP) is a rare inherited amyloidosis caused by mutations of the transthyretin protein. The V30M variant leads to neurodegeneration, cardiac conduction defects and infiltrative cardiomyopathy. Tafamidis was designed to stabilize the TTR in its tetrameric form inhibiting the dissociation into monomers which is the rate-limiting step in TTR-FAP. Tafamidis can delay peripheral neurologic impairment but little is known about its effect on cardiac involvement.

Purpose: To evaluate the impact of tafamidis on the progression of the infiltrative cardiomyopathy and cardiovascular autonomic neuropathy.

Methods: Prospective study of consecutive patients with V30M TTR-FAP followed annually and submitted to echocardiogram, 24-hour Holter, 123-I metaiodobenzylguanidine (MIBG) myocardial imaging and ambulatory blood pressure monitoring (ABPM). Data prior to initiation of tafamidis was compared to that at 24 months after therapy.

Results: Of de 284 FAP patients participating in the study, 44 (mean age=43±12 years; 50% female) were enrolled for treatment with tafamidis. During a median follow up of 24 months, no patient died. The treatment was stopped in 5 patients (11.4%) due to adverse effects or progression of the disease, one of these patients was selected for liver transplantation. The initial echocardiogram showed a mean septal thickness of 10±3 mm, E/A ratio of 1.2±0.4 and E wave deceleration time of 207±57 msec. Five patients had left ventricular thickening (septal thickness ≥12 mm) and diastolic dysfunction (E/A <1.0 or >2.5). After 24 months of treatment all echocardiographic parameters remained stable. The Holter parameters, including the heart rate variability variables remained also stable during follow-up. The mean value of late heart-to-mediastinum (H/M) MIBG uptake ratio was 1.70±0.31 before tafamidis and it was compromised (≤1.60) in 35% patients. At 24 months there was no statistically significant change in late H/M. In contrast, ABPM revealed statistically significant increases in daytime (120±13 vs. 122±19 mmHg, p=0.005) and nighttime systolic BP (111±15 vs. 113±16 mmHg, p<0.011) and in pulse pressure (45±9 vs. 46±11 mmHg, p=0.001).

Conclusion: These results suggest that treatment with tafamidis may have stabilized the progression of cardiac involvement in patients with early stages of FAP. However due to the limited duration of follow-up we must be cautious given the slowly progressive nature of the disease.
tion of the outflow gradient in symptomatic HOCM pts. may thus also modify the risk profile. A multi-center initiative to aggregate additional pt.-years is warranted.

P263 | BENCH
Predictive value of tei index for patients with cardiac amyloidosis
D. Liu1, K. Hu1, P. Nordbeck1, S. Herrmann1, M. Cikic2, B. Kramer1, G. Ertl1, S. Stoerk1, F. Weidemann2,3.
1University of Wuerzburg, Department of Internal Medicine I, Comprehensive Heart Failure Center, Wuerzburg, Germany; 2University Hospital Centre Zagreb, Zagreb, Croatia; 3Katharinen-Hospital, Medical Clinic II, Unna, Germany

Background: We previously reported that longitudinal systolic and diastolic deformation parameters derived from speckle tracking imaging (STI) could predict the outcome of patients with cardiac amyloidosis (CA).

Purpose: Left ventricular (LV) Tei index is a known parameter reflecting combined systolic and diastolic myocardial performance. In this study, we thus tested the hypothesis that Tei index could also predict outcome of CA patients and compared the prognostic values between Tei index and previously reported deformation parameters.

Methods: LV systolic and diastolic functions including tissue-Doppler-derived LV tei index and STI-derived strain imaging were evaluated by echocardiographic in 60 consecutive CA patients (age 64±10 years, 55% male) and 30 normal controls (age 61±8 years, 60% male). All patients completed clinical follow-up (median 274, quartiles 90–900 days). The endpoint was all-cause death.

Results: LV Tei index was significantly higher in CA group (0.70±0.24) as compared with normal group (0.45±0.09). In CA group, Tei index was positively associated with LV wall thickness and negatively associated with ejection fraction and global longitudinal systolic and diastolic strain rate values. Furthermore, Tei index tended to be positively associated with E/E’ ratio. Cox regression analysis results showed that Tei index [hazard ratio (HR): 8.778, 95% confidence interval (CI) 1.752–43.989, P=0.008], global systolic strain (global SSSys, HR 1.101, 95% CI 1.013–2.118, P=0.026) and E to global diastolic strain rate ratio (ELSSRdias, HR 1.647, 95% CI 1.121–2.424, P=0.011) were univariate predictors of all-cause mortality after adjustment for age, gender, and body mass index. CA patients with Tei index ≥ 0.63 was associated with significantly increased risk of all cause death compared to those with Tei index < 0.63 (P=0.007).

Conclusions: Tei index allows simple and feasible assessment of LV systolic and diastolic function in patients with CA. Similar as deformation predictors, Tei index could also be used as a reliable predictor for outcome in CA.

P2640 | BEDSIDE
Coexistence of degenerative aortic stenosis and wild type transthyretin-related cardiac amyloidosis: a potentially dangerous association that can be non-invasively identified
S. Longhi1, M. Lorenzini1, C. Gagliardi1, A. Milandri1, E. Biagini1, P. Gustafsson2,3, F. Salka1, A. Marzocchi1, C. Rapezzi1, S. Herrmann1, M. Cikic2, B. Kramer1, G. Ertl1,1 University Hospital Policlinic S. Orsola-Malpighi, Cardiology, Department of Experimental, Diagnostic and Specialty Medicine – DIME, Bologna, Italy; 2University Hospital Policlinic S. Orsola-Malpighi, Nuclear Medicine Unit, Department of Experimental, Diagnostic and Specialty Medicine – DIME, Bologna, Italy

Background: Degenerative aortic stenosis (AS) and wild type transthyretin (TTR) amyloidosis (wt-ATTR) are common degenerative and clinical profile. It has been recently suggested that the coexistence of wt-ATTR and degenerative AS (co-occurrence that can be non-invasively identified) is potentially dangerous in patients undergoing AVR or TAVR. Therefore, we aimed to investigate the coexistence of degenerative AS and wt-ATTR cardiac amyloidosis in a cohort of consecutive CA patients.

Methods: We previously reported that longitudinal systolic and diastolic deformation parameters derived from speckle tracking imaging (STI) could predict the outcome of patients with cardiac amyloidosis (CA).

Conclusions: Coexistence of degenerative AS and wt-ATTR cardiac amyloidosis (a potentially dangerous condition in patients undergoing AVR or TAVR) can be suspected by clinical and echocardiographic elements and effectively diagnosed by 99mTc-DPD scintigraphy.
P2643 | BEDSIDE
Novel epsilon wave characteristics in arrhythmogenic cardiomyopathy
A. Protonotarios,1 A. Anastasakis2, E. Prappa3, C. Pitsatos2, V. Vlagouli2, D. Tousoulis4, L. Antoniades4, A. Tsatsopoulou1,1 Yannis Protonotarios Medical Center of Naxos, Naxos, Greece;2 University of Athens Medical School, 1st Department of Cardiology, Athens, Greece;3 Evangelismos General Hospital, 2nd Department of Cardiology, Athens, Greece;4 Nicosia General Hospital, Department of Cardiology, Nicosia, Cyprus

Purpose: Epsilon waves constitute hallmarks of arrhythmogenic cardiomyopathy (ACM) providing high diagnostic value; but limited information about their specific characteristics exist. We aimed to evaluate novel epsilon wave characteristics including wave duration, presence in the inferior leads and extension beyond lead V3 into an ACM population.

Methods: Eighty-six unselected patients fulfilling the 2010 Task Force diagnostic criteria were enrolled from a multi-center ACM cohort. Seventy-six of them were carriers of desmosomal mutations. All subjects were serially evaluated with standard 12-lead ECG and with two-dimensional echocardiography. Epsilon wave durations were evaluated in all precordial and inferior leads. Novel parameters including their duration and precordial/inferior lead extension were assessed. Epsilon waves were defined as reproducible low amplitude signals after the end of QRS complex up to the end of T wave. The waves were studied in all precordial and inferior leads. Epsilon wave duration was defined as the time interval between the low amplitude signals onset and offset; the highest measured value in precordial leads was recorded for each patient.

Results: Twenty-five subjects (29%) exhibited epsilon waves. They were detected in lead V3 and beyond in 9, while in the inferior leads in 7. Epsilon waves were associated with wall motion abnormalities of the right ventricular outflow tract (RVOT) (p=0.001) but not of the RV posterior wall (p=0.21), RV apex (p=0.30) or left ventricle (p=0.94). Patients with epsilon waves exhibited increased RVOT diameter (p=0.001). Cases with extension of epsilon waves beyond V3 showed increased epsilon wave duration (p=0.002) and RVOT diameter (p=0.04). Epsilon wave duration was positively correlated with RVOT diameter (r=0.70, p=0.001). Epsilon waves were associated with episodes of sustained ventricular tachycardia (p=0.004) but not with heart failure (p=0.41) or sudden cardiac death (p=0.31) during follow-up. Patients who experienced sustained ventricular tachycardia exhibited increased epsilon wave duration as compared to those who did not (p=0.003).

Conclusions: Epsilon waves may extend to the left precordial and inferior leads. Their presence, increased duration and left precordial lead extension signify overt structural disease and are associated particularly with RVOT involvement. Importantly, epsilon waves are associated with episodes of sustained ventricular tachycardia but not sudden cardiac death or heart failure.

CHRONIC PULMONARY HYPERTENSION
P2644 | BENCH
Beneficial effect of combined therapy with macitentan and sildenafil in a rat model of pulmonary arterial hypertension
K.H. Kim1, H.K. Kim1,2. Sejong General Hospital, Bucheon, Korea, Republic of;2 Seoul National University, Seoul, Korea, Republic of

Background: We investigated the efficacy of macitentan in combination with sildenafil on hemodynamic and morphological parameters in rats with monocrotaline-induced PH.

Methods: Two weeks after monocrotaline injection, elevated PASP was confirmed by echocardiography. Adult male SD rats (n=40) were equally randomized into group 1 (sham control), group 2 [MCT (60 mg/kg ip.)], group 3 [MCT+macitentan (10 mg/kg/d)], group 4 [MCT+macitentan + sildenafil (10 mg/kg/d + 50X2 mg/kg/d)]. RV afterload is assessed by measurement of PASP from TR velocity and right atrial pressure. For quantification of RV performance, TAPSE, FAC were measured. In a pressure-volume analysis performed at the 8th week.

Results: Serial echocardiograms revealed that significant pulmonary hypertension was developed three weeks after MCT injection and it was getting severe with time. The increases in right ventricular systolic pressure (RVSP) and ratio of right ventricular weight to body weight were significantly attenuated in the macitentan and combination with sildenafil groups [RVSP 57±2 for MCT only vs 48±1 for MCT + macitentan vs 36±2 for MCT + macitentan + sildenafil, p<0.05]. Combination therapy with macitentan and sildenafil had additive effects on decreased in cardiac fibrosis and pulmonary artery fibrosis, resulting in further improvement in pulmonary hemodynamics compared with treatment with macitentan alone. All rats treated with only macitentan alone or combination therapy were survived during 8 week follow-up, however 30% of MCT injection rats treated with saline were dead.

Conclusions: Combination therapy of macitentan and sildenafil more effective than macitentan treatment alone significantly prevent RV remodeling process without any cardiovascular toxic effects in the monocrotaline-induced PH model.

P2645 | BEDSIDE
Lack of pharmacokinetic interaction between the dual endothelin receptor antagonist macitentan and the combined oral contraceptive, ethinylestradiol and gestodene
N. Hurst1, M. Pellek2, P.N. Siddharta1, J. Dingemannse1.1 Actelion Pharmaceuticals Ltd, Clinical Pharmacology, Allschwil, Switzerland;2 CliPharmCologne, MEDA, Cologne, Germany

Background: Macitentan is a dual endothelin receptor antagonist (ERA) approved for the long-term treatment of pulmonary arterial hypertension. ERAs have been associated with tenovertagion and are contraindicated during pregnancy. Hormonal contraceptives (HCs) are cytochrome P450 (CYP) 3A4 substrates and their efficacy can be affected by CYP3A4 inducers. At supra-therapeutic concentrations, macitentan induced CYP3A4 in vitro.

Purpose: To evaluate the effect of macitentan 10 mg (therapeutic dose) in healthy women on the pharmacokinetics (PK) of a combined oral HC, containing 35 μg ethinyl estradiol (EE) and 1 mg norethisterone (NE), and to investigate the safety and tolerability of macitentan co-administered with this HC.

Methods: This open-label, randomized, two-way cross-over study included 26 subjects who received a single oral dose of the HC alone (reference) then concomitantly with macitentan at steady state (test), or vice versa, with a washout period of at least 3 weeks in between. PK, adverse events (AEs), vital signs (VS), electrocardiogram (ECG) variables, and clinical laboratory tests were monitored. No PK interaction was concluded if the 90% confidence intervals (Cis) of geometric mean ratios (test/reference) of the peak plasma concentration (Cmax) and the area under the plasma concentration-time curve from time 0 to infinity (AUC0-∞) of EE and NE were within the bioequivalence criteria of 0.8 to 1.25.

Results: All 26 subjects were randomized; mean age was 32.5 years (range 23–45) and mean body mass index was 24.2 kg/m2. All subjects were included in the safety analyses and 23 subjects were evaluable for the PK analyses. Cmax and AUC0-∞ of the HC were within the bioequivalence criteria. For EE, geometric mean ratios (90% Cis) of Cmax and AUC0-∞ were 0.92 (0.85, 0.98) and 0.95 (0.90, 0.99), respectively. These values of NE were 1.02 (0.95, 1.09) and 1.04 (0.98, 1.09), respectively. Overall, the HC, macitentan, and the HC-administered with macitentan were well tolerated. The most frequently reported AE was headache (69%). One serious AE (asthma bronchiale, assessed as related to the investigational drug) was reported 14 days after last macitentan administration. All AEs resolved without sequelae. No major changes from baseline in VS, ECG variables, and clinical laboratory tests were reported.

Conclusions: No PK interactions between macitentan and the HC were observed. Based on this study, the efficacy and safety of HCs are not affected by macitentan co-administration. In line with previous clinical results, macitentan 10 mg does not affect the PK of CYP3A4 substrates.

P2646 | BENCH
Audit of prostanoid use in a nationally designated PH centre
W. Gin-Sing1, S. Gibbs1, L. Howard1, M. Lau-Walker2, G. Lee3, G. Villa1.1 Imperial College Healthcare NHS Trust, Pulmonary Hypertension Service, London, United Kingdom;2 King’s College London, London, United Kingdom;3 Pulmonary Hypertension Service, University Hospitals of North Midlands, Northampton, United Kingdom

Background: Pulmonary hypertension (PH) is a rare disease which is managed in the UK by 7 designated specialist centres which results in some patients living a long distance from their nearest centre. Prostanoid therapy is recommended for patients with the most severe form of the disease. There are several prostanoids in use in the UK: Intravenous epoprostenol, treprostinil and iloprost. Prostanoids are complex to deliver and therefore patients are trained to be independent in their management with support from PH Nurse Specialists.

Purpose: This audit was conducted to investigate the use of prostanoid therapy in one of the designated adult PH centres. We wanted to assess whether there was equal access to therapy independent of the distance patients lived from the hospital, to describe the characteristics of the patients on prostanoid therapy compared to other patients in the same group and dosing levels.
Methods: All adult patients with pulmonary arterial hypertension (PAH) and chronic thromboembolic disease which was not operative (CTEPH-N0) under the care of the designated PH centre on the 31st January 2015 were identified using locally held data which has been entered into the National Audit of Pulmonary Hypertension. Demographics for the prostanoid group were compared to the PH and CTEPH-N0 population. Time from diagnosis, to starting prostanoids, time therapy and average dose were calculated.

Results: Prostanoid patients: mean time since diagnosis 7yrs (0–15.9), mean time to starting on prostanoid therapy 3yrs (0–11.2), mean time on prostanoid therapy 2.7yrs (5 days–11.1 years).

Conclusion: Patients on prostanoid therapy are younger, more female and have a higher functional class. Surprisingly there was a higher percentage of patients on prostanoids living further away from the PH centre suggesting that distance from the centre is not a barrier to therapy. The average dose of epoprostenol was 23ng/kg/min compared to 58.5ng/kg/min for those on treprostinil.

P2648 | BENCH
Comparison of caveolin-1 isoforms expression in the right ventricle and lungs of monocrotaline induced pulmonary hypertension
Comenius University, Faculty of Pharmacy, Bratislava, Slovak Republic

Background: Monocrotaline induced pulmonary arterial hypertension (PAH) is well known experimental model in rats. The underlying processes in the failing right ventricle and affected lungs are still not completely known. Isoforms caveolin-1 alpha and caveolin-1 beta seem to play a role in PAH.

Purpose: Therefore we hypothesized that expression of these proteins and their mRNA level might be changed in the right ventricle and lungs of monocrotaline induced pulmonary hypertension.

Methods: Group of 13 male Wistar rats was injected with monocrotaline (MC; 60 mg/kg) and 7 control rats (CON) received vehicle. Separate group of 20 (MON) and 10 (CON) rats was used for hemodynamic measurements. Animals were weighted frequently and vital functions were measured using MouseOx meter. Rats were sacrificed after 4 months or immediately if showing dyspnea, lethargy and significant weight loss.

Results: MON-treated rats had lower body weight when compared to controls (MON: 294±9 g vs. CON: 328±6 g, P<0.01). There was a significant elevation in the right ventricular systolic pressure (MON: 50.6±5.28 mmHg vs. CON: 21.5±2.49 mmHg, P<0.01). Right ventricular wall thickness was increased (MON: 0.29±0.02 mm vs. CON: 0.17±0.01 mm, P<0.05), as well as the weight of lungs (MON: 2.47±0.12 g vs. CON: 1.27±0.04 g, P<0.01). Caveolin-1 expression in the right ventricle was diminished (MON: 66±14 vs. CON: 160±9) and in lungs was significantly decreased (MON: 30±11 vs. CON: 100±7, P<0.01). The expression of phosphorylated isoform pSer14Cav-1 when calculated as pSer14Cav-1/Cav-1 ratio was not changed in the right ventricle (MON: 98±35 vs. CON: 100±16), while in lungs was significantly increased (MON: 135±646 vs. CON: 100±24, P<0.05). Furthermore, the mRNA level of caveolin-1 alpha isoform was significantly reduced in the right ventricle (MON: 0.54±0.04 vs. CON: 1.0±0.10, P<0.01) and so was in lungs (MON: 0.57±0.07 vs. CON: 1.0±0.03, P<0.01). Caveolin-1 beta isoform mRNA was significantly lowered in the right ventricle (MON: 0.30±0.03 vs. CON: 1.0±0.19, P<0.01) as well as in lungs (MON: 0.43±0.06 vs. CON: 1.0±0.05, P<0.01).

Conclusion: Altered levels of caveolin-1 isoforms in the right ventricle and lungs might play an important role in the progression of pulmonary hypertension in this model. Additionally, the increased level of pSer14Cav-1 in lungs and its unchanged amount in the right ventricle can point to a different underlying processes in these organs.

Acknowledgement/Funding: APVV-0887-11, VEGA 1/0981/12, VEGA 1/0564/12

P2649 | BENCH
Involvement of angiotensin converting enzyme 2 in pulmonary hypertension
A. Darago1, M. Fagyas1, T. Vincze1, A. Peter2, I. Manyine Siket 1, I. Edes2, Z. Papp1, A. Toth1.
1 Medical and Health Science Center, Institute of Cardiology, Szeged, Hungary; 2 Medical and Health Science Center, Institute of Cardiology, Debrecen, Hungary

Introduction: Pulmonary hypertension (PH) is a rare disease characterized by hypertension of the pulmonary arterial wall, reduced vessel lumen, increased pulmonary vascular resistance leading to right heart failure. The mortality rate is about 60% within 5 years. It is proposed here that angiotensin II metabolism plays a role in the pathomechanism of PH. Angiotensin II is formed by the angiotensin converting enzyme (ACE) and removed by its homologue ACE2.

Materials and methods: Clinical data and sera of 25 patients with PH and 25 patients with systemic hypertension (control) were collected. The amount of ACE (by ELISA) and the activity of ACE and ACE2 (by synthetic fluorescence substrate) were determined.

Results: Patients with PH had a significantly higher ACE activity (40.4±6 U/L) when compared with the control group (22.6±2 U/L, p<0.01). ACE2 activity was inversely proportional with the ejection fraction of left ventricle (p<0.05) and with the tricuspid annular systolic excursion (p<0.05, r=0.365, P=0.035). Multiple regression analysis showing that ACE and ACE2 were significantly associated with CI (TRPG: R=0.494, P=0.003; TAPSE: R=0.504, P=0.002), Multiple regression analysis incorporating clinical, laboratory findings, hemodynamics and echocardiographic parameters, revealed that CI and E' were significantly associated with CI at rest (LVEDD: β= 0.447, P<0.001; CI: β = 0.599, <0.001).

Purpose: To evaluate the role of ACE and ACE2 in pulmonary hypertension.

P2650 | BEDSIDE
Comparison of the effects of bosentan on endothelial function in patients with pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension
Nagoya University Graduate School of Medicine, Nagoya, Japan

Background: Although bosentan, a dual endothelin receptor antagonist, is effective for the treatment of pulmonary arterial hypertension (PAH), which is often complicated by the presence of peripheral endothelial dysfunction (PED) associated with impaired flow-mediated vasodilation (FMD), little is known about its mode of action.

Purpose: We used FMD assessment to investigate the effects of orally adminis-
tered bosentan on endothelial function in patients with PAH or inoperable chronic thromboembolic pulmonary hypertension (CTEPH).

**Methods:** Eighteen patients diagnosed with PAH and nine patients diagnosed with inoperable CTEPH were enrolled in the study. All patients underwent cardiac catheterization at baseline and FMD assessment before and after 3 months of bosentan treatment. Reference normal values for FMD were -5%.

**Results:** The mean age of the patients (male, 5; female, 22) was 55±10 years. At baseline, mean pulmonary arterial pressure (mPAP) was 47±12 mmHg and FMD was 5.8±2.37%. Bosentan was well tolerated by all patients: no cases of drug-related liver dysfunction were observed. There were no significant differences in mPAP, cardiac index, and pulmonary vascular resistance between the two groups of patients at baseline. The prevalence of PED with FMD -5% was 56% and 33% in the PAH and CTEPH groups, respectively; there was no significant difference in FMD between the two groups at baseline. There was also no significant correlation between FMD and pulmonary vascular resistance, and FMD and plasma brain natriuretic peptide levels (r=-0.04, r=-0.14, respectively) at baseline. In patients with PAH, FMD was significantly increased after bosentan treatment (6.01±2.37% vs. 8.07±1.18%; p<0.0001). FMD was also significantly improved after bosentan treatment in patients with PAH associated with collagen tissue disease (6.48±1.07% vs. 8.83±1.66%; p=0.023) and in those with PAH associated with other comorbidities and idiopathic PAH (5.76±1.69% vs. 7.68±0.80%; p=0.001). However, in patients with CTEPH, there was no significant difference in FMD after bosentan treatment (5.33±2.37% vs. 6.12±2.96%; p=0.62).

**Conclusions:** Bosentan therapy improved FMD in patients with PAH but not in those with inoperable CTEPH. In addition, FMD was not correlated with PAH severity. Therefore, FMD is useful for assessing the effects of therapeutics on peripheral endothelial function in patients with PAH.

P2651 | BEDSIDE

**Baseline characteristics and outcome of adult patients with pulmonary hypertension in Africa: results from the Pan-African Pulmonary Hypertension Cohort (PAPUCO) study**

F. Thiennemann1, A. Dzudie2, A.O. Mocumbi3, L. Blauweit4, M.U. Saní5, K.M. Karaye6, I. Mbanze7, A.O. Mocumbi8, K. Sliwa9, F. Thienemann1

1. University of Cape Town, Institute of Infectious Diseases and Molecular Medicine, Cape Town, South Africa; 2. Douala General Hospital, Douala, Cameroon; 3. Instituto Nacional de Saúde, Maputo, Mozambique; 4. Mayo Clinic, Division of Cardiovascular Diseases, Rochester, United States of America; 5. Aminu Kano Teaching Hospital, Department of Medicine, Kano, Nigeria; 6. Eduardo Mondlane University, Faculty of Medicine, Maputo, Mozambique; 7. University of Cape Town, Hatter Institute for Cardiovascular Research in Africa, Cape Town, South Africa

** Purpose:** The epidemiology of PH in Africa and the distribution of its multitude of aetiologies has not yet been described, but limited reports suggest that the incidence of PH in Africa is higher than that reported from developed countries, owing to the pattern of diseases prevalent in the region.

**Methods:** We here present data from the Pan African Pulmonary Hypertension Cohort (PAPUCO), a prospective multinational cohort registry on incident and prevalent PH. The results after 1 year of follow-up are shown in the table 1. Survival at 1, 3 and 5 years from diagnosis for PE vs MT groups was 96.9% vs 92.3%, 90.8% vs 81.7% and 84.7% vs 64.5%, respectively (p<0.009).

**Conclusion:** In CTEPH, these data confirm better outcomes due to PE compared to MT, demonstrating the potential of Spanish CTEPH patients undergoing PE, which seems to be due to a lower referral rate for operability assessment. **Acknowledgement/Funding:** Bayer Schering Pharma for supporting this Registry (RHEAP)

P2653 | BEDSIDE

**Sleep-disordered breathing in pulmonary arterial hypertension PAH and in pulmonary hypertension due to left ventricular dysfunction - comparison of clinical characteristics**

K. Wiko1, B. Uznanska-Loch1, K. Leni2, A. Dydula3, E. Trzos1, D. Miskowiec1, J.D. Kasprzak1, M. Kurpesa1.

1 Medical University of Lodz, Chair and Department of Cardiology, Bieganski Hospital, Lodz, Poland; 2 Medical University of Lodz, Lodz, Poland

**Introduction:** Sleep-disordered breathing (SDB) affects up to 70% of patients (pts) with heart failure (HF) caused by left ventricular dysfunction and is an important determinant of worse clinical outcome in such patients. Prevalence of SDB in PAH pts and its clinical implications remain unclear.

**Purpose:** Comparison of the prevalence of SDB among pts with different etiology of pulmonary hypertension with evaluation of SDB clinical importance.

**Methods:** 81 pts optimally treated for HF were screened for SDB using Holter ECG monitoring commercial software, with estimation of apnea-hypopnea index (eAHI). Study population was divided into two groups: 39 HF pts (coronary artery disease, left ventricular ejection fraction LVEF ≤ 55%, SAP>30 mmHg, NYHA II-IV) and 42 PAH pts (19 idiopathic, 17 congenital heart defects, 6 connective tissue diseases).

**Results:** While similar in NT-proBNP values, study groups differed regarding several clinical parameters. Pts in HF group were older (63 vs 50 years in PAH group, p<0.001), were predominantly males (78% vs 40% in PAH group, p<0.001), and had lower SPAP (40 vs 93 mmHg, p<0.000001) and lower LVEF (33 vs 56%, p<0.000001). SDB defined as eAHI > 15 was found in 64% of HF pts and in 36% of PAH patients. Mean eAHI was higher in HF than in PAH group
GROW-UP CONGENITAL HEART DISEASE AND SURGERY

P2654 | BEDSIDE
Survival into adulthood of patients with congenital heart disease in Sweden
M. Delbogg, A. Rosengren, G. Lappas, P. Eriksson, Z. Mandalenakis, Sahlgrenska Academy, University of Gothenburg, Dept. of Molecular & Clinical Medicine/Cardiology, Gothenburg, Sweden

Background: Recent reports from western countries have showed a substantial increase in the number of patients with congenital heart disease during the last decades. Nevertheless, there is a lack of evidence about estimating survival into adulthood for children with congenital heart disease in Sweden.

Purpose: The aim of the present study was to investigate the survival trends in children with congenital heart disease who reaching adulthood in Sweden.

Methods: We linked data from the Swedish patient and Cause of Death Registers to study all children who were born between 1 January 1970 and 31 December 1993 with a diagnosis of congenital heart disease according to the International Classification of Diseases (8th, 9th and 10th edition). Follow-up data collection was performed for all patients until 31 December 2011; mean age at diagnosis was 5 years, mean follow-up was 13 years. Patients were divided into four groups according to the birth period (first group 1970–1975, second group 1976–1981, third group 1982–1987 and forth group 1988–1993).

Results: We identified 21,564 patients (51.8% men, 48.2% women) with congenital heart disease who were registered in Sweden. At the last year of follow-up (2011), 20,084 patients with congenital heart disease (93.1%) were still alive. Children from the first and second group had no significant difference in survival to adulthood. However, children from the third and forth group had a significant improvement in survival: 1.37 times higher (95%, p < 0.001, CI 1.16–1.63) respectively. 2.42 times higher (95%, p < 0.001, CI 2.02–2.92) compared to the first group; These findings were independent of the gender, age of diagnosis or the complexity of heart malformations (according to Marelli classification).

Conclusions: Children with congenital heart disease have a subsequent increase of survival to adulthood during the last 40 years in Sweden. Patients who were born in the last birth period had 60% increased survival compared to patients surgically closed early in life whereas small shunts in most cases are left without intervention. The long-term prognosis in congenital VSD is generally good but patients are still exposed for the risk of long-term complications. The aim of this study was to clarify the incidence of endocarditis in adults with VSD. In the general population, the incidence is estimated to 0.08/1000 inhabitants/year.

Methods: The national registry for congenital heart disease was searched for adult patients (>18 years of age) with main diagnosis VSD (Eisenmenger physiology excluded). 779 patients were identified and the national in-patient registry was then searched for hospitalisations due to endocarditis during the last 10 years but over the age of 18.

Results: The mean observation time was 8.9 years. 17 patients were treated for endocarditis, seven men and ten women, mean age at endocarditis 46.3±12.2 years. Thirteen had small shunts without previous intervention, 5 of these had their endocarditis before first entry in the registry. Four patients had repaired VSD and aortic valve replacement before the endocarditis episode, all of these 4 patients needed reoperation and one patient died from complications.

Conclusion: The overall incidence of endocarditis was 1.7/1000 patientyears for their endocarditis after first entry in the registry and also 1.7/1000 patientyears in the subgroup with small shunts without previous intervention. In this contemporary cohort, patients with VSD are at high risk of endocarditis, up to 20 times the risk in the general population.

Acknowledgement/Funding: The Swedish Heart-Lung foundation, Sweden; Umeå university, Umeå, Sweden; The County of Västerbotten, Sweden; The Heart Foundation of Northern Sweden

P2655 | BEDSIDE
The natural history of valvular pulmonary stenosis: outcome up to 40 years after surgical repair
J.A.A.E. Cuypers1, M.E. Menting1, E.M.W.J. Utens2, W.A. Helbing3, M. Witsenburg3, A.E. Van Den Bosch3, R.T. Van Dornburg3, F.J. Meiboom4, A.J.J.C. Bogers1, J.W.Rooz-Heesselink1, Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands; 2Erasmus Medical Center, Department of Child and Adolescent Psychiatry and Psychology, Rotterdam, Netherlands; 3Erasmus Medical Center, Department of Paediatric Cardiology, Rotterdam, Netherlands; 4University Medical Center Utrecht, Department of Cardiology, Utrecht, Netherlands; 5Erasmus Medical Center, Department of Cardio-thoracic Surgery, Rotterdam, Netherlands

Purpose: To provide prospective information on long-term outcome after surgical correction of valvular pulmonary stenosis (PS).

Methods: A cohort of consecutive patients is followed longitudinally for 37±4 years after surgical correction of PS during childhood between 1968–1980. Survival information was available in 93% of 89 patients. Of 46 eligible survivors, 29 participated in the in-hospital examination, 15 gave permission to use their hospital records (in total 96%). Cumulative survival in the whole cohort up to 40 years (Fig. 1) was 95% when perioperative mortality was excluded. There were 3 late deaths: car accident, sudden death during sleep and unknown. Cumulative event-free survival was 67% after 40 years: 25% needed a reintervention, 12% underwent pacemaker implantation and 9% had supraventricular arrhythmias. Early reinterventions were mainly for residual PS, late reinterventions for pulmonary regurgitation. Subjective health status was good. Exercise capacity was normal in 74%. RV fractional area change was <35% in 13%, LVEF by biplane Simpson method was abnormal in 41%. The use of a transannular patch (TAP) and younger age at surgery were predictive for late events (HR 3.02 [95% CI: 1.09–8.37] and HR 0.81/year [95% CI 0.66–0.98] respectively). Not surprisingly, reintervention was the most common event associated with use of a TAP. Use of inflow occlusion instead of cardiopulmonary bypass showed a trend towards more reinterventions (HR 3.19 [95% CI: 0.97–10.47]).

Conclusion: Survival up to 40 years after successful repair of PS is nearly as good as survival in the general population. Subjective health status is good and there is a low incidence of arrhythmias. Reinterventions, however, are necessary in one quarter of the patients.

Acknowledgement/Funding: Dutch Heart Foundation grant number 2009-8-073

P2656 | BEDSIDE
Risk of hemorrhagic stroke in children and young adults with congenital heart disease

Background: The risk of hemorrhagic stroke in children and young adults with congenital heart disease is not well established. Patients with congenital heart disease may be at increased risk of hemorrhagic stroke potentially due to concomitant intracranial vascular malformations reported to be associated with certain diagnoses.

Purpose: We aimed to study the absolute and relative risk of hemorrhagic stroke in children and young adults with congenital heart disease.

Methods: Data from the Swedish patient and Cause of Death Registers were retrieved to study all patients (n=26,568) who were born between 1st January 1970
and 31st December 1993 with a diagnosis of congenital heart disease and without previous stroke at the age of congenital heart disease diagnosis. Ten controls for each patient (n=265,680) matched for age, sex and county, were randomly selected from the general population. Follow-up data was collected for patients and controls until December 2011 (mean follow-up 9.8 years).

Results: Among patients with congenital heart disease (51.4% men, 48.6% women, mean age at diagnosis 5 years), 71 (0.27%) developed hemorrhagic stroke compared to 161 (0.06%) among controls. The risk of developing hemorrhagic stroke was 4.68 times greater in young adults with congenital heart disease (95% CI 3.54–6.20, p < 0.001) compared to controls. Almost 40% of congenital hemorrhagic strokes (28/71) were found in patients with less complex congenital malformations such as in the second Marelli group (septal defects, patent ductus arteriosus, coartation of aorta and Ebstein’s anomaly); The risk of hemorrhagic stroke was associated with the second Marelli group, HR 4.29 (95% CI 2.03–9.00, p < 0.001) compared to controls. Furthermore, patients with a complex congenital heart disease such as in Marelli group 1 (transposition of great vessels, tetralogy of Fallot, atrioventricular septal defect, hypoplastic left heart syndrome, double inlet ventricle and common arterial trunk) had a risk of hemorrhagic stroke 3.34 higher (95% CI 1.82–6.12, p < 0.001) compared to controls.

Conclusions: Our results show that the risk to develop hemorrhagic stroke is significantly higher in children and young adults with congenital heart disease compared to general population. However, in absolute terms the risk is low. Further the repeated clinical evaluation of mechanisms of hemorrhagic stroke in young patients with congenital heart disease.

Acknowledgement/Funding: Grants from the Sahlgrenska Academy, Swedish Medical Research Council, and partly by grants from Stroke Centre West in Sweden.

P2650 | BEDSIDE

Macitentan superior to bosentan in pulmonary arterial hypertension due to congenital heart disease?

I.M. Blok1, A.C.M.J. Van Rei1, M.J. Schuring1, R.H.A.C.M. De Bruin-Bon1, A.P.J. Van Dijk2, A.H. Zwinderen1, B.J.M. Mulder1, B.J. Bouma1, 1Academic Medical Center of Amsterdam, Cardiology, Amsterdam, Netherlands; 2University Hospital Nijmegen, Cardiology, Nijmegen, Netherlands

Background: Recently macitentan, a new oral endothelin receptor antagonist, was approved in Europe for the treatment of pulmonary arterial hypertension (PAH). However, it is unclear whether patients with PAH due to congenital heart disease (CHD) who currently use bosentan would benefit from a switch to macitentan.

Methods: In this prospective observational study adult PAH-CHD patients, currently on bosentan treatment, were evaluated with a standardized treatment protocol, including six-minute walk distance (6-MWD), World Health Organization (WHO) functional class, and laboratory tests, carried out every 3 months. After baseline measurements bosentan was switched to macitentan. At three months we repeated the clinical evaluation. We used paired samples t, chi square, and logistic regression analysis for baseline measurements bosentan was switched to macitentan. Results: Currently 35 PAH-CHD patients were switched to macitentan (mean age 41±15 years, 43% male, 34% Down syndrome, 74% Eisenmenger syndrome). No serious adverse events were reported. After three months macitentan treatment, WHO classification improved in 8 (28%) and worsened in 2 (7%) patients. No serious adverse events were reported. After three months macitentan treatment, WHO classification improved in 8 (28%) and worsened in 2 (7%) patients. No significant change in haemoglobin or liver enzymes was detected.

Conclusions: Our preliminary data suggests that a switch from bosentan to macitentan in PAH-CHD patients is safe and improves clinical status.
seems to be a more prominent role for biomarkers in decision-making for treatment in PAH-CHD patients.

P2664 | BEDSIDE
Chronological changes in mitral regurgitation after atrial septal defect closure in adults; predictors of aggravation of mitral regurgitation
S. Nishimura, C. Izumi, M. Amano, M. Miyake, H. Kondo, T. Tamura, K. Kaitani, Y. Nakagawa, Tenri Hospital, Department of Cardiology, Tenri, Japan

Background: Association between atrial septal defect (ASD) and mitral regurgitation (MR) is well known. Some patients show improvement of MR, but others show aggravation or development of MR after ASD closure. Data about predictors of changes in MR after ASD closure are limited. The purpose of this study is to clarify the chronological changes in MR after ASD closure and the predictors of aggravation of MR.

Methods: We retrospectively investigated 161 consecutive adult patients who underwent surgical ASD closure between 1987 and 2014 in Tenri Hospital. Thirty-two patients with concomitant mitral valve surgery (n=15), aortic valve surgery (n=6), or other congenital heart disease repair (n=11) at ASD closure were excluded; hence 129 patients (mean age; 53±14 years) were enrolled. MR grade was qualitatively classified into 4 grades (none, mild, moderate, severe) by echocardiography. Aggravation of MR was defined as ≥2 grades increase after ASD closure. Cardiac catheter and transthoracic echocardiographic characteristics and cardiac events (cardiac death and eventual mitral valve surgery) were examined.

Results: The mean follow-up period was 77 months. Preoperative grade of MR was none in 78 patients, mild in 48 patients, moderate in 3 patients. Aggravation of MR after ASD closure was seen in 16 patients (12%) (group P), the remaining 113 patients (88%) were defined as group N. In group P, aggravation of MR was detected at 0–5 years after ASD closure in 8 patients, 5–15 years in 2 patients, 15 years in 6 patients. Prevalence of pre and postoperative atrial fibrillation (AF) was higher (pre: 63% vs 33%, P=0.02, post: 69% vs 19%, P<0.01), preoperative left atrial dimension (LAD) and defect size were larger (LAD: 43.7mm vs 37.6mm, P<0.01, defect size: 32.2mm vs 25.8mm, P=0.03), and length of posterior mitral leaflet was shorter (6.8mm vs 8.3mm, P<0.01) in group P than group N. In group P, the mechanism of aggravated MR was due to mitral annular dilation not tethering.

Conclusion: Predictors of aggravation of MR after ASD closure were presence of AF, left atrial enlargement, large ASD size, and contracted posterior mitral leaflet. Contracted posterior leaflet, in combination with mitral annular dilation associated with AF, may lead to poor coaptation of mitral leaflets. Careful follow-up is needed for patients with AF or contracted posterior mitral leaflet.

P2665 | BEDSIDE
Decreased diastolic ventricular kinetic energy in young Fontan patients demonstrated on four-dimensional cardiac magnetic resonance imaging
P. Sjöberg1, E. Heiberg2, H. Arheden1, P. Liuba2, M. Carlsson1, 1 Skane University Hospital, Department of Clinical Physiology, Lund University, Lund, Sweden; 2 Skane University Hospital, Pediatric Heart Centre, Lund University, Lund, Sweden

Background: Quantification of ventricular kinetic energy (KE) in patients with single ventricle and Fontan circulation has not been investigated and might provide better understanding of the physiology and find early stages of a failing ventricle.

Purpose: Our aim was to determine if kinetic energy in the ventricle of Fontan patients using cardiac magnetic resonance (CMR) differs from healthy controls.

Methods: Eleven patients (3 females, median age 12, range 3–29) with functionally single ventricle and Fontan circulation underwent CMR with 1.5-T Philips scanner including a four-dimensional phase-contrast flow sequence. Eight healthy volunteers (2 females, median age 26, range 23–36) was used as a reference. Ventricular segmentation was performed in 30 time frames per cardiac cycle and imported to the 4D flow dataset. Ventricular KE calculated as KE=1/2mv2 was performed over all voxels inside the ventricle and calculated on CINE images.

Results: Mean KE indexed for stroke volume (SV) and peak KE indexed for SV in systole and diastole are shown in figure 1. Diastolic KE indexed for SV was lower than the systolic KE and diastolic KE was significantly lower than in controls (−15.2±2.9% vs −22.7±2.4%, respectively, p<0.001). Longitudinal deformation was significantly impaired in the anterior and both anterior and posterior septal walls. In ASO patients global circumferential strain (−23.9±4.8% vs −25.9±4.1%, respectively, p=0.06) and LV torsion (12.1±4.8° vs 13.1±5.4°, respectively, p=0.351) were similar to those measured in controls. Multivariate Analysis global LV longitudinal strain was significantly correlated only with age at surgery (P=0.005; Coeff.= 0.046; Std.Error= 0.016).

Figure 1. Kinetic energy in Fontans and controls
EXERCISE IS THERAPY IN HEART DISEASE

P2666 | BEDSIDE
Effects of functional electrical stimulation of lower limb muscles on circulating endothelial progenitor cells, CD34+ and VEGF-A in heart failure with reduced ejection fraction

N. Magoufis1, J. Parissis2, A. Karavias1, D.T. Farmakis1, V. Mantzaraki2, M. Peppas3, I. Konomidou2, G. Filippatos2, V. Pyrgakis1, J. Lekakis1, General Hospital of Athens G. Gennimatas, Department of Cardiology, Athens; 1Athikon Hospital, 22nd University Department of Cardiology, Athens; 2Athikon University Hospital, 2nd Department of Internal Medicine, Athens, Greece

Background: Functional electrical stimulation (FES) of lower limb muscles, an alternative mode of exercise in patients not able or willing to train physically, is effective in improving clinical status and endothelial-dependent vasodilatation in heart failure (HF). We sought to evaluate the effects of FES on circulating levels of vascular endothelial growth factor-A (VEGF-A), endothelial progenitor cells (EPC) and CD34+ monocytes in HF with reduced LVEF (HFrEF).

Methods: 27 HF r/e exercise training patients, aged 69±8 years, with NYHA class III/IV symptoms and mean LVEF 0.27±0.05 in 6-week FES or sham procedure. We measured circulating levels of VEGF-A, EPC and CD34+ monocytes at baseline and after therapy along with clinical, functional and biochemical biomarkers.

Results: Baseline demographics, HF severity measures (NYHA class, LVEF, α-CD34, β-CD34, β-VEGF-A, α-EPC, β-EPC, α-Delta1- EPC, β-Delta1- EPC) were still lower for patients (p<0.05) in comparison to controls, leading to a TEM/EPC ratio in favor of EPC (p<0.001). After 6 months training, we observed a decrease in TEM/EPC ratio for patients (p<0.05) compared to the CON group. At the end of week 6, capillaries for CD45+ and unaltered LV stiffness in both males and females.

Conclusions: Our results confirm that there is a more pronounced exercise-induced LV hypertrophy in females that has no functional consequence compared to the males. The gender-specific response of the LV to exercise is modulated by characteristic molecular pathways.

P2669 | BEDSIDE
Exercise training leads to an increase of the proangiogenic TIE2 monocyte/ EPC ratio in patients with peripheral arterial disease over 6 months

J.F. Dopheide, J. Rubrech, A. Trumpp, P. Geissler, T. Gori, M.P. Radsak, T. Muenzel, C. Espinola-Klein. University Hospital of Mainz, Mainz, Germany

Background: Tie2+ monocytes (TEM) and endothelial progenitor cells (EPC) play a crucial role in neangiogenesis. In peripheral arterial disease (PAD) exercise training can promote angiogenesis and thus ameliorate the severity of the disease.

Methods: 40 PAD patients with intermittent claudication (IC, Fontaine Stage IIA and b) were asked to perform either a supervised (SET) (n=20) or a non-supervised exercise training (NET) (n=20). Peripheral blood leukocytes were analysed from whole blood by flow cytometry (Beckman-Coulter Navios 10/3). Monocytes and EPC were identified by different gating strategies in relation to size and granularity (FSC/SSC) and surface molecules (CD14/CD6/CD54/CD34) and analysed for CD14+/CD16/Tie2 or CD34+/VEGF-R2+/CD45-, respectively. The results were compared with an age matched control group (n=20).

Results: At admission patients in total showed an increased proportion of TEM and reduced proportion of TEM (both p<0.05). Comparison of SET vs. NET showed a higher proportion of TEM for the SET group, and thus an increased TEM/EPC ratio in favour of EPC (p<0.001). After 6 months training, we observed a decrease in TEM/EPC ratio for patients (p<0.01) with a shift of the TEM/EPC ratio in favour of TEM (p<0.01), leading to no difference between patients and controls in regard to EPC and their ratio. TEM proportions though were still lower for patients (p<0.05). Comparison of SET vs. NET showed a higher proportion of TEM for the SET group, and thus an increased TEM/EPC ratio (both p<0.05). The absolute walking distance in the SET group was higher than in the NET group. The exercise training with prolonged hypoxia recovery offers better metabolic benefits than exercise training alone for the obese Zucker rats. This advantage was closely associated with effective weight reduction.

P2667 | BENCH
Gender differences in morphological and functional aspects of athletes’ heart in a rat model


Background: Long-term exercise training is associated with characteristic morphological and functional changes of the myocardium, resulting in a condition called athlete’s heart. Referring to the latest studies, sex hormones may be involved in the regulation of exercise-induced left ventricular (LV) hypertrophy.

Purpose: We aimed at understanding the gender-specific functional and morphological alterations in the LV and the underlying molecular changes in a rat model of athlete’s heart.

Methods: We divided our young, adult male and female rats into control and exercised groups. Athlete’s heart was induced by swim training. The exercised rats were exposed to 200 min/day swimming for 12 weeks. Control rats were taken into the water for 5 min/day. Following the training period we assessed LV hypertrophy with echocardiography. LV pressure-volume (P-V) analysis was performed to calculate ventricular function. Additionally, molecular biological studies (qRT-PCR, Western blot) were performed. Interaction between gender and training was tested by two-way ANOVA.

Results: Echocardiography showed LV hypertrophy which was confirmed by LV wall thickness, whereas LV function was more preserved in females. Post-mortem measured heart weight/tibial length ratio (+31.2% female vs. +14.5% male, p<0.05) also verified gender differences in LV hypertrophy. The induction of Akt signaling was more significant in females compared to the males (p<0.05 female vs. +27.4% male, p<0.05). There is a characteristic difference in the mitogen-activated protein kinase (MAPK) pathway as suppressed phosphorylation of p44/42 MAPK (Erk) was observed in female exercised rats, but not in male ones. α-myosin heavy chain (MHC)α/-MHCβ ratio did not differ in males, but increased markedly in females (+140.6% female vs. +16.9% male, p<0.05). Despite the more significant hypertrophy in females, characteristic functional parameters of athletes’ heart did not show notable differences between the genders during invasive hemodynamic measurements. LV P-V analysis showed increased stroke volume and stroke work, improved contractility and mechanical efficiencies and unaltered LV stiffness in both males and females.

Conclusions:

EXERCISE IS THERAPY IN HEART DISEASE

P2668 | BENCH
Hyperinsulinemia and overweight in obese Zucker rats effectively suppressed by exercise training with hypoxia recovery

W.S. Hu, Shung Ho Hospital, New Taipei City, Taiwan, ROC

It is currently unknown whether hypoxia training can effectively suppress over- weight and hyperinsulinemia in genetically obese animals. In this study, both lean and obese Zucker rats were randomly assigned into the following groups: control (CON, n=7), exercise training (EX, n=7), hypoxia (HYP, n=7) and exercise training with hypoxia recovery (EX+HYP, n=7). During a 6-week training period, rats performed swimming exercise progressively from 30 to 180 min/day, and recovered under hypoxia (14% oxygen for 8 h day−1). Obese Zucker rats exhibited substantially greater fasting insulin levels, and exaggerated glucose and insulin responses following an oral glucose challenge compared with lean rats. At the beginning of week 6, capillaries for CD45+ (CD45), capillaries for CD34+ (CD34) and capillary fibra proportions of the plantar muscle in the EX group were significantly greater than the CON group (PB0.05), but no additive effect of hypoxia on exercise training was observed. Our data demonstrate that exercise training with prolonged hypoxia recovery offers better metabolic benefits than exercise training alone for the obese Zucker rats. This advantage was closely associated with effective weight reduction.

EXERCISE IS THERAPY IN HEART DISEASE

P2669 | BEDSIDE
Exaggerated exercise blood pressure response is related to increased arterial stiffness, asymmetrical dimethylarginine and osteoprotegerin in essential hypertension

K. Dimitriadis, C. Tsoufis, T. Kalos, S. Galanakos, K. Kyriazopoulos, F. Lagiou, L. Nikolopoulou, D. Tousoulis. First Cardiology Clinic, University of Athens, Hippokration Hospital, Athens, Greece

Background and introduction: A hypertensive response to exercise (HRE)
is associated with high cardiovascular risk, while elevated levels of asymmetric dimethylarginine (ADMA) and osteoprotegerin (OPG) are related to atherosclerotic progression.

**Purpose:** In this study we sought to determine the relationships of HRE with ADMA, OPG and arterial stiffness in essential hypertension.

**Methods:** Our population of 240 newly diagnosed never treated non-diabetics with stage I to II essential hypertension (155 men, mean age=51 years, office blood pressure (BP)=150/96 mmHg) with a negative treadmill exercise test (Bruce protocol) was divided into those with HRE (n=70) (peak exercise systolic BP >210mmHg in men and >190 mmHg in women) and those without HRE (n=170). Arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV) values.

**Results:** Patients with HRE compared to those without HRE had greater 24-h systolic BP (143±9 vs 131±8 mmHg, p<0.05), while did not differ regarding metabolic profile and left ventricular mass index (p=NS). Patients with HRE as compared to those without HRE exhibited greater levels of ADMA (0.63±0.04 vs 0.52±0.05 µmol/l, p<0.001), OPG (5.4±0.1 vs 4.1±0.5 pmol/l, p<0.001) and PWV (9.5±1.7 vs 7.5±0.9 m/sec, p<0.001), independently of confounders. In the total population, peak exercise systolic BP was related to 24-h systolic BP (r=0.249, p<0.05), PWV (r=0.278, p<0.003), ADMA (r=0.260, p<0.007) and OPG (r=0.214, p<0.05). Regarding OPG, it was associated with 24-h systolic BP (r=0.285, p<0.001), ADMA (r=0.284, p<0.05) and PWV (r=0.424, p<0.001), independently of confounders. Multiple regression analysis showed that 24-h systolic BP (b=0.210, p<0.003), male sex (b=0.270, p<0.05), ADMA (b=0.225, p<0.006) and OPG (b=0.188, p<0.05) were independent predictors of peak exercise systolic BP.

**Conclusions:** In essential hypertension, a HRE is accompanied by a state of increased arterial stiffness, endothelial dysfunction and progressive atherosclerosis. The interrelationships of ADMA and OPG with exercise BP response support that diffuse vascular dysfunction contributes to HRE-related risk in hypertension.

P2671 | BENCH

Long-term change of physical activity towards a physically active lifestyle is associated with reduced arterial stiffness in elderly males: results of the SAPALDIA 3 cohort study

S. Endes, E. Schaffner, S. Caviezel, J. Dratva, M. Wanner, B. Martin, C. Schindler, N. Kuenzi, N. Probst-Hensch, A. Schmidt-Trucksäss, on behalf of SAPALDIA Team. University of Basel, Department of Sport, Exercise and Health, Basel, Switzerland; Swiss Tropical and Public Health Institute - University of Basel, Basel, Switzerland; University of Zurich, Institute of Social and Preventive Medicine, Zurich, Switzerland

**Background and purpose:** Longitudinal analyses of physical activity (PA) and arterial stiffness in populations of older adults are scarce. We examined associations between long-term change of PA and arterial stiffness in the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA). SAPALDIA 3 (2010–2011) assessed PA in SAPALDIA 2 (2002–2003) and SAPALDIA 3 (2010–2011) using a short questionnaire with a cutoff of at least 150 minutes of PA per week for sufficient activity. Arterial stiffness was measured oscilometrically by means of the brachial-ankle pulse wave velocity (baPWV) in SAPALDIA 3. We used multivariable mixed linear regression models adjusted for several potential confounders in 2605 subjects aged 50–80 years.

**Results:** Adjusted baPWV means were significantly lower in persons showing a PA change from insufficiently active in SAPALDIA 2 to active in SAPALDIA 3 and in persons being sufficiently active in both assessments (each p<0.05) compared to subjects with insufficient activity in both surveys irrespective of the PA intensity in the entire cohort. Only males showed a significant lower baPWV associated with a long-term physically active lifestyle in sex-specific analyses, especially when performed with moderate-to-vigorous intensity (each p<0.05) (Figure). Keeping up or changing to a physically active lifestyle is associated with lower arterial stiffness in older males. The beneficial effect of PA on arterial stiffness observed only in males might be due to more time spent in moderate-to-vigorous PA compared to females.

P2672 | BEDSIDE

Increased activity of renin-angiotensin-aldosterone system induces vascular endothelial damage causing the excessive blood pressure elevation even during moderate exercise in hypertensive patients

K. Yabu, T. Masuda, M. Ogura, R. Shimizu, D. Kamekawa, Y. Kamada, T. Tanaka, A. Aoyama, M. Yamaoka-Tojo, J. Ako, Katsato University, Graduate School of Medical Sciences, Sagamihara, Japan; Katsato University, Department of Rehabilitation, Sagamihara, Japan; Katsato University School of Medicine, Department of Cardiovascular Medicine, Sagamihara, Japan

**Background:** Excessive blood pressure (BP) elevation during exercise is frequently observed in hypertensive (HT) patients who showed autonomic imbalance. Elevated sympathetic activity activated the renin-angiotensin-aldosterone system (RAAS) and accelerated vascular endothelial damage and arteriosclerosis. This study aimed to investigate whether the inhibition of RAAS ameliorated the excessive BP elevation during exercise in HT patients.

**Methods:** Thirty HT patients, 64±16 years, were treated with angiotensin II receptor blocker (ARB-treated group) or amloidide (AML-treated group) for 8 months in crossover method. At the end of each treatment period, patients performed a cycle ergometer exercise test at moderate intensity. We measured peak systolic BP (SBP) during the exercise test and determined SBP elevation from baseline (∆SBP). Excessive BP elevation during exercise was defined as ≥ mean±SD in ∆SBP obtained from 28 control subjects. We assessed the change of plasma adrenaline (ADRN) before and after the exercise test (∆ADRN) as a parameter of sympathetic activity. We measured serum high-sensitivity C-reactive protein (hs-CRP) and thrombomodulin as parameters of vascular endothelial damage in addition to plasma renin and aldosterone. These parameters were compared between the AML- and ARB-treated groups.

**Results:** The proportion of patients with excessive BP elevation during exercise and ∆SBP were significantly lower in the ARB-treated group than in the AML-treated group (Figure). ∆ADRN, hs-CRP and thrombomodulin were significantly lower in the ARB-treated group than in the AML-treated group (P<0.05, respectively).

**Conclusion:** Increased activity of RAAS induced vascular endothelial damage resulting in the excessive BP elevation during exercise even at moderate intensity in HT patients.
Exercise is therapy in heart disease

III-IV, left ventricular ejection fraction inferior to 35%, 26% ischemic, submitted to CRT. 39 patients were randomized either to group A, 6 months HIIT twice a week exercise program (19 p) or to Group B, non-exercise (20 p). Besides those, 61 p were not randomized (group C) because they lived far away from rehabilitation center and were not able to attend exercise sessions. All 100 p were evaluated before and at 24 months after CRT by: clinical functional class (NYHA evaluation); echocardiography, for left ventricular ejection fraction (LVEF) and left ventricular end systolic (LVESV) and end diastolic (LVEDV) volumes; cardio pulmonary test, for peak oxygen consumption (VO2p) and duration; 12-MIBG scintigraphy, for early heart-mediastinum rate (eHMR), late heart-mediastinum rate (lHMR) and wash-out (WO).

Results: Comparing the 2 randomized study groups (A and B), clinical functional class variation (Δ) (p=0.01), ΔWO (-18.970±29.565 vs 13.21±18.274; p=0.012) and ΔHMR (-0.137±2.020; p=0.021) were significantly better in the exercise group.

Comparing group A (exercise) to B and C together (non-exercise, with and without randomization), clinical functional class variation (Δ) (p=0.004), and ΔWO (-18.970±29.565 vs 8.289±18.492; p=0.003) were significantly better in the exercise group. HMR was almost significantly better, also in the exercise group. A (0.045±0.1 vs −0.798±0.187; p=0.055).

Comparing A to B and A to C, together, variation of LVEF, LVEDV, LVESV, VO2p and exercise test duration, had no significant difference (p>ns).

Conclusion: Exercise is therapy in heart disease patients submitted to CRT, improved by itself clinical functional class and nervous system autonomic function. No significant difference was observed between exercise and non exercise patients, relatively to variation of left ventricular function and volumes or variation of peak oxygen consumption and exercise test duration.

Acknowledgement/Funding: FCT GRANT PTDC/DES/120249/2010

P2674 | BEDSIDE

Effects of exercise training on cardiac autonomic activity in heart transplant and left ventricular assist device patients—assessment of heart rate profile

K. Fan, J. Ng, G. Yip, C. Ko, M. Wong, K. Chan, K. Cheng, C. Tsui. Grantham Hospital, Hong Kong, Hong Kong SAR, People’s Republic of China

Background: Cardiac rehabilitation exercise training programs improve exercise capacity in cardiac failure patients (pts). Chronotropic incompetence and abnormal HR recovery reflecting profound abnormalities of autonomic activity have been reported in chronic heart failure. We studied the effects of exercise training in pts with left ventricular assist devices (LVAD) and post heart transplantation (HT) by assessing chronotropic response (CR) and heart rate recovery immediate after exercise (HRR1). HRR1 was almost significantly better, also in the exercise group. A (0.045±0.1 vs −0.798±0.187; p=0.055).

Methods: A total of 23 pts (15 HT (56% men; mean age 50 yrs) and 8 LVAD (100% men; mean age 55 yrs) underwent a 12 weeks supervised exercise program starting 3 months after surgery. Symptom-limited cardio pulmonary exercise tests were performed at baseline and at the end of the program. Chronotropic response to exercise was evaluated by the percentage of chronotropic reserve

Results: The results are shown in Table. There were significant improvement in exercise capacity in both groups. Exercise training resulted in significant improvement of exercise capacity in LVAD pts without significant effects on CR. On the contrary, exercise training allowed higher levels of physical activities with significant improvement of CR in HT pts but not HRR1, consistent with underlying pathophysiology of denervated transplanted heart.

Comparison of HT and LVAD gps

<table>
<thead>
<tr>
<th>Heart rate group</th>
<th>LVAD group</th>
<th>Baseline</th>
<th>3 mths</th>
<th>P value</th>
<th>LVAD group</th>
<th>Baseline</th>
<th>3 mths</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MET level</td>
<td></td>
<td>5.3±1.6</td>
<td>8.2±2.4</td>
<td>0.0001</td>
<td>2.1±1.2</td>
<td>2.4±1.1</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td>Resting HR (bpm)</td>
<td></td>
<td>90.9±14.9</td>
<td>96.8±15.4</td>
<td>0.11</td>
<td>85.8±12.1</td>
<td>84.7±17.1</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Peak HR (bpm)</td>
<td></td>
<td>110.7±17.8</td>
<td>125.7±19.2</td>
<td>0.004*</td>
<td>97.0±6.0</td>
<td>106.4±20.1</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>HRR1 (bpm)</td>
<td></td>
<td>2.9±1.6</td>
<td>4.0±2.6</td>
<td>0.05</td>
<td>3.8±1.6</td>
<td>4.2±2.6</td>
<td>0.037</td>
<td></td>
</tr>
<tr>
<td>CR (%)</td>
<td></td>
<td>35.15±10.7</td>
<td>57.2±9.2</td>
<td>0.02*</td>
<td>20.1±10.0</td>
<td>28.6±10.0</td>
<td>0.08</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: The opposite divergent relationship of HRR1 and CR among post HT pts and LVAD pts reflected different pathophysiological processes from different treatment strategies. Heart rate profile can potentially represent a simple, non-invasive tool to assess outcome during cardiac rehabilitation for these special groups of pts.

P2675 | BENCH

Results from a benthic multicenter study on the combination of exercise training + electrical myostimulation treatment in chronic heart failure (HF-CREMS study)

B. Verges1, M.-C. Illou2, B. Pavvy3, J.P. Mabire4, C. Bosse Plon5, Y. Morvan6, E. Kessler7, M. Ghammer8 on behalf of French Working Group of Cardiac Rehabilitation. 1Clinique les Rosiers, Cardiac rehabilitation. 2Dijon. 3AP-HP Hospital Broussais, Paris. 4Hospital Center Liere Vendee-Ocean, Mahecourt. 5CH d’Outreau, Croquebeuf. 6Clinique St Yves, Rennes. 7Cardiac rehabilitation, Joigny. 8CH St Luc, Abreschviller. 9Centre de reeducation Cardiaque, Tracy-Le-Mont, France

Background: Exercise training (ET) (aerobic and resistance training) as part of a comprehensive cardiac rehabilitation is recommended for patients with cardiac heart failure (CHF). It is a valuable method to improve exercise tolerance. Some studies reported a similar improvement with quadrupical electrical myostimulation (EMS), but very few data are known about the effect of combination of the two methods.

Purpose: To determine whether addition of low frequency EMS to ET may improve exercise capacity and/or muscular strength in CHF patients. Primary end-point: improvement of peak VO2. Secondary endpoints: improvement of muscle strength, sub maximal parameters (ventilatory threshold, 6 min walking test), quality of life.

Methods: 91 patients were included (mean age: 58±9 y; NYHA III: 52±48%, LVEF: 29±7%) in a multicenter study. The patients were randomized into two groups: ET; 41 patients and ET + EMS; 50 patients. All patients underwent 20 ET sessions. In addition, in the ET+EMS group, patients underwent 20 low frequency (10 Hz) quadrapical EMS sessions (20”on/20”off, 1 hour/session). Before and at the end of the protocol, all the patients performed a cardio pulmonary stress test, a 6 min walking test, evaluation of muscular circumference, strength and biological assays (CPK, LDH, Aldolase, and Myoglobin).

Results: Data analysis revealed a significant improvement of exercise capacity in all patients (15±25% in ET group and 14±22% in ET + EMS group. Results were better for sub maximal parameters (gain of ΔVO2max: 17 ± 14% for ET group vs 8 ± 10% and for muscular circumference and strength. No statistically significant difference among the two groups was found.

Conclusion: Our data, from this large multicenter randomized study, show that combination of ET + EMS does not demonstrate any significant additional improvement in exercise capacity. Thus, we may consider, in CHF patients enrolled in a rehabilitation program, not to add EMS if patients are able to perform a conventional aerobic training.

P2676 | BEDSIDE

Changes in cardiorespiratory fitness predict incident hypertension: a population-based long-term study

S.Y. Jae1, S. Kuri2, B. Franklin1, J. Laukkanen3, 1university of seoul, Seoul, Korea, Republic of; 2University of Eastern Finland, Institute of Public Health and Clinical Nutrition, Kuopio, Finland; 3William Beaumont Hospital, Preventive Cardiology and Cardiac Rehabilitation, Royal Oak, United States of America

Background: Although cardiorespiratory fitness (CRF) has been associated with the risk of hypertension, little is known about changes in CRF over time to predict the risk of incident hypertension. Our aim was to investigate whether changes in CRF over a decade predict the risk of incident hypertension, independent of risk factors, in initially normotensive men.

Methods: Participants from the Kuopio Ischemic Heart Disease Study underwent symptom-limited maximal exercise testing using a cycle ergometer at baseline and at 11-year follow-up. This prospective study included 431 participants (mean aged 50±7.6 years) without hypertension at baseline and at a second examination. Changes in CRF were calculated as the difference in maximal oxygen uptake between baseline (mean VO2max 33.8 ml/kg/min) and during a second examination (mean VO2max 28.7 ml/kg/min), conducted at the 11-year follow-up. The change in CRF (%) was classified on the basis of tertiles as percentage. Hypertension was defined as systolic and diastolic blood pressure ≥140/90 mm Hg and/or hypertension diagnosed by a physician.

Results: During 10 years of additional follow-up after the second examination, 158 men (37%) developed hypertension. Good baseline CRF as a continuous variable (per 1 mL/kg/minute) was associated with a lower risk of incident hypertension (hazard ratio 0.89, 95% confidence interval, CI 0.86 to 0.93, p<0.001) in a multivariate adjusted model. An average decline in CRF was 5.1 mL/kg/min (15.0%) over a decade. Men who demonstrated the largest decline in CRF level (change range: –24% to –62%) had a 3.92-fold (95% CI 2.00 to 7.69, p<0.001) risk of incident hypertension compared to men with the smallest change in CRF level (change range: −6% to 82%), after adjusting for age, follow-up time, alcohol consumption, cigarette smoking, serum low and high density lipoprotein cholesterol, body mass index, energy expenditure of physical activity and baseline level of VO2max.

Conclusion: This 21-year follow-up study demonstrated that more marked decreases in CRF were independently associated with risk of incident hypertension.

P2677 | BEDSIDE

Physical inactivity increases endostatin and osteopontin in patients with coronary artery disease

M. Sponder1, M.F.S. Fritzer-Szekeres2, R.M. Marculescu2, B.L. Litschauer3, J.S.J. Strametz-Juranek1. 1Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna; 2Medical University of Vienna, Department of Medical and Chemical Laboratory Diagnostics, Vienna; 3Medical University of Vienna, Department of Clinical Pharmacology, Vienna, Austria

Background: The balance between the angiostatic factor endostatin (ES) and...
angiogetic factor osteopontin (OPN) is essential in physiological and pathological angiogenesis. Several circumstances such as the grade of physical fitness might influence this equilibrium and are of distinct interest when investigating mechanisms in coronary artery disease (CAD).

Methods: The present explorative cross-sectional study investigates the influence of physical inactivity on ES and OPN levels in 181 male and 71 female patients with angiographically verified CAD. ES was measured in serum, OPN in plasma by ELISA. Univariate analysis of variance (ANOVA) was used to test for the influence of physical activity on ES and OPN levels and age, BMI, sex and diabetes status were included as covariates.

Results: ES and OPN levels were dependent on reported physical exercise level. There was a nearly linear reduction observable in ES from 252 ng/ml in non-active patients to 176 ng/ml in very active patients corresponding a decrease of more than 30% and a reduction in OPN from 150 ng/ml in non-active patients to 113 ng/ml in very active patients corresponding a decrease of more than 25%. ES and OPN intercorrelated significantly (r=0.42; p<0.001). The ES and OPN concentration decreased significantly with increasing activity level (F=5.5; p<0.001 and F=3.8; p<0.01 resp.).

Conclusions: This study is the first to show a linear decrease in ES and OPN levels in CAD-patients depending on the grade of physical activity. Lower levels of ES and OPN in physically active patients might be a sign of increased angiogenesis and decreased inflammation and calcifying activity and therefore contribute to the understanding of the damaging effect of physical inactivity in cardiovascular disease.

CARDIOVASCULAR ADAPTATION TO EXERCISE

P2679 | BENCH
Left ventricular contractility of athlete’s heart: assessment by speckle tracking echocardiography and invasive pressure-volume analysis in rats


Background: Long-term exercise training is associated with characteristic structural and functional cardiac adaptation (athlete’s heart), which involves improved cardiac contractility. Contractile function is considered to be precisely measurable only by invasive hemodynamics.

Purpose: We aimed to correlate strain values measured by speckle tracking echocardiography (STE) with sensitive contractility parameters of pressure-volume (P-V) analysis in a rat model of exercise-induced left ventricular (LV) hypertrophy.

Methods: LV hypertrophy was induced in exercised group (n=10) by swim training (12 weeks, 200 min/day). Untrained rats (n=12) were taken into the water for 5 min/day. Echocardiography was performed using a 13 MHz linear transducer (12 weeks, 200 min/day). Untrained rats (n=12) were taken into the water for 5 min/day. Echocardiography was performed using a 13 MHz linear transducer with sensitive contractility parameters of pressure-volume (P-V) analysis. LV P-V analysis was performed using a pressure-ductility microcatheter and load-independent contractility indices were obtained. We used Pearson correlation to observe the relation between pressure-conductance microcatheter and load-independent contractility indices recordings for speckle-tracking analysis. LV P-V analysis was performed using a 5 min/day. Echocardiography was performed using a 13 MHz linear transducer with sensitive contractility parameters of pressure-volume (P-V) analysis in both groups compared with the sedentary groups (C: 0.311±0.06; O: 0,312±0.05; OF: 0.326±0.12; T: 0.198±0.05; TF: 0.294±0.05ms). The improvement in intrinsic contractile function induced by exercise training. STE was improved in trained animals. The improvements of metabolic and autonomic function induced by ET (T and TF groups) was accompanied by better diastolic function as expressed by lower isovolumetric relaxation time (IVRT) (C: 38.7±5.2; O: 41.4±3; OF: 35.2±2.5; T: 27.5±1.4; TF: 31.2±2.7ms) and E/A ratio (C: 1.83±0.12; FT: 1.66±0.12ms). The left ventricle performance index MPI (C: 0.31±0.06; O: 0.31±0.05; TF: 0.326±0.12; T: 0.198±0.05; TF: 0.294±0.05) was improved in trained animals. The improvements of metabolic and autonomic parameters were correlated with the maintenance of diastolic function reinforcing the preventive role of ET in the management of SM.

Acknowledgement/Funding: capses
Results: The prevalence of VE was similar in athletic (6.0% (n=34)) and non-athletic (6.0% (n=75)) individuals. Of the athletes who demonstrated VE, 50% had a single VE. The commonest type of VE was of right ventricular outflow tract (RVOT) origin in both groups (figure). Comparison of echo indices between athletes with and without VE did not demonstrate any significant difference in left ventricular cavity size, relative wall thickness or RVOT dimensions. On the contrary, athletes with VE had significantly greater maximal LV wall thickness and larger right ventricular dimensions (RVD1, RVD2, RVD3) compared to athletes with VE. No athlete demonstrated a cardiomyopathy phenotype.

Conclusions: Our study indicates that VE is rare in young individuals and that athletic activity is not associated with an increased prevalence of VE. Although VE was not associated with structural heart disease, further long-term follow-up is necessary to elucidate their exact significance.

Acknowledgement/Funding: Cardiac Risk in the Young

P2682 | BEDSIDE
Dynamic coupling between atrio-ventricular duration and RR-interval in phase-reification analysis shows rate-dependent intranodal conduction facilitation related to physical conditioning status
Federal University of Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil

Introduction: Dynamic coupling between atrio-ventricular duration (AVD) and RR-interval relates to AV conduction facilitation and susceptibility to supraventricular arrhythmia. Phase-reification of RR-interval series allows separation of acceleration (AC) and deceleration (DC) phases, reflecting sympathetic and parasympathetic influence on heart rate, respectively. This study assessed the effect of physical fitness status on dynamic AVD and phase-reification-driven RR-interval coupling.

Methods: Healthful sedentary (HS, n=10, 8±7.1 METs) and elite runners (ER, n=10, 19.6±1.4 METs) males, age, weight and height matched, were studied. All underwent 15-min resting ECG recording in controlled conditions, RR-interval series were analyzed using histogram distribution, split in 100-ms-width classes, from 700ms to 1200ms. For each class, mean of normal RR-intervals (MRR) and mean of the peak-to-peak P-R to heart wall interval (MPR) were calculated and analyzed in RR-intervals pairs of AC and DC phases. Regression of MPR vs. MRR were calculated, and slope compared between groups. (α=0.05)

Results: No overall intergroup differences regarding MPR was observed. Whereas, at lower MRR, MPR was larger in ER, at higher MRR, MPR was larger in HS (Figures A and B). In both groups, PR/RR slope was steeper in DC than AC. Significant inter and intra-group PR/RR slope differences were observed in both phases (Figures A and B).

Conclusion: Dynamic AVD and RR-interval coupling shows phase-reification-dependent behavior, with steepest PR/RR slopes observed during parasympathetic (DC) interval variation. Additionally, in elite runners, AVD increases as RR interval decreases, indicating a reverse cardiac cycle length-dependent facilitation of intra-nodal conduction.

P2682 | BEDSIDE
Left atrial morphological and electrical remodeling in athletes: a prospective, longitudinal combined ECG and speckle-tracking study
F. D’Ascenzi1, M. Solari1, M. Focardi1, M. Biagi1, F. Cassano1, P.2682 | BEDSIDE
Dynamic coupling between atrio-ventricular duration and RR-interval in phase-reification analysis shows rate-dependent intranodal conduction facilitation related to physical conditioning status
Federal University of Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil

Introduction: Dynamic coupling between atrio-ventricular duration (AVD) and RR-interval relates to AV conduction facilitation and susceptibility to supraventricular arrhythmia. Phase-reification of RR-interval series allows separation of acceleration (AC) and deceleration (DC) phases, reflecting sympathetic and parasympathetic influence on heart rate, respectively. This study assessed the effect of physical fitness status on dynamic AVD and phase-reification-driven RR-interval coupling.

Methods: Healthful sedentary (HS, n=10, 8±7.1 METs) and elite runners (ER, n=10, 19.6±1.4 METs) males, age, weight and height matched, were studied. All underwent 15-min resting ECG recording in controlled conditions, RR-interval series were analyzed using histogram distribution, split in 100-ms-width classes, from 700ms to 1200ms. For each class, mean of normal RR-intervals (MRR) and mean of the peak-to-peak P-R to heart wall interval (MPR) were calculated and analyzed in RR-intervals pairs of AC and DC phases. Regression of MPR vs. MRR were calculated, and slope compared between groups. (α=0.05)

Results: No overall intergroup differences regarding MPR was observed. Whereas, at lower MRR, MPR was larger in ER, at higher MRR, MPR was larger in HS (Figures A and B). In both groups, PR/RR slope was steeper in DC than AC. Significant inter and intra-group PR/RR slope differences were observed in both phases (Figures A and B).

Conclusion: Dynamic AVD and RR-interval coupling shows phase-reification-dependent behavior, with steepest PR/RR slopes observed during parasympathetic (DC) interval variation. Additionally, in elite runners, AVD increases as RR interval decreases, indicating a reverse cardiac cycle length-dependent facilitation of intra-nodal conduction.

P2682 | BEDSIDE
Left atrial morphological and electrical remodeling in athletes: a prospective, longitudinal combined ECG and speckle-tracking study
F. D’Ascenzi1, M. Solari1, M. Focardi1, M. Biagi1, F. Cassano1, P.2682 | BEDSIDE
Dynamic coupling between atrio-ventricular duration and RR-interval in phase-reification analysis shows rate-dependent intranodal conduction facilitation related to physical conditioning status
Federal University of Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil

Introduction: Dynamic coupling between atrio-ventricular duration (AVD) and RR-interval relates to AV conduction facilitation and susceptibility to supraventricular arrhythmia. Phase-reification of RR-interval series allows separation of acceleration (AC) and deceleration (DC) phases, reflecting sympathetic and parasympathetic influence on heart rate, respectively. This study assessed the effect of physical fitness status on dynamic AVD and phase-reification-driven RR-interval coupling.

Methods: Healthful sedentary (HS, n=10, 8±7.1 METs) and elite runners (ER, n=10, 19.6±1.4 METs) males, age, weight and height matched, were studied. All underwent 15-min resting ECG recording in controlled conditions, RR-interval series were analyzed using histogram distribution, split in 100-ms-width classes, from 700ms to 1200ms. For each class, mean of normal RR-intervals (MRR) and mean of the peak-to-peak P-R to heart wall interval (MPR) were calculated and analyzed in RR-intervals pairs of AC and DC phases. Regression of MPR vs. MRR were calculated, and slope compared between groups. (α=0.05)

Results: No overall intergroup differences regarding MPR was observed. Whereas, at lower MRR, MPR was larger in ER, at higher MRR, MPR was larger in HS (Figures A and B). In both groups, PR/RR slope was steeper in DC than AC. Significant inter and intra-group PR/RR slope differences were observed in both phases (Figures A and B).

Conclusion: Dynamic AVD and RR-interval coupling shows phase-reification-dependent behavior, with steepest PR/RR slopes observed during parasympathetic (DC) interval variation. Additionally, in elite runners, AVD increases as RR interval decreases, indicating a reverse cardiac cycle length-dependent facilitation of intra-nodal conduction.

P2684 | BEDSIDE
Circulatory power and exercise ventilatory power during exercise over time during sequential combination therapy in pulmonary arterial hypertension
A. Hirashiki, Y. Kamimura, Y. Nakano, S. Adachi, T. Okumura, K. Takeshita, M. Tourohara, T. Kondo. Nagoya University Graduate School of Medicine, Nagoya, Japan

Background: Many potential therapeutic options are now available for patients with pulmonary arterial hypertension (PAH). However, the optimum strategy for implementation of combination therapy remains controversial. In addition, little is known about exercise capacity under sequential combination therapy.

Purpose: We investigated exercise capacity over time by using relatively new indexes, namely circulatory power (CP) and exercise ventilatory power (EVP), in cardiopulmonary exercise testing (CPX) of PAH patients.

Methods: Forty-two patients diagnosed with PAH (World Health Organization functional classes II to IV) were enrolled in the study. An endothelin receptor antagonist (ERA) was used as first-line treatment. A phosphodiesterase-5-inhibitor (PDE-5I) was the preferred combination partner, followed by the addition of intravenous epoprostenol if needed. All patients underwent cardiac catheterization at baseline and CPX at baseline and after 3, 6, and 12 months. Circulatory power (CP) was defined as the product of peak oxygen uptake (VO2) and peak systolic blood pressure (SBP). Exercise ventilatory power (EVP) was defined as peak SBP divided by the minute ventilation/volume of carbon dioxide produced (VE/VCO2) slope.

Results: Mean patient (male, 16; female, 26) age was 57±12 years. At baseline, mean pulmonary arterial pressure was 44±12 mm Hg, peak VO2 was 12.4±4.4 mL/kg/min, and VE/VCO2 slope was 54.5±20.4. At baseline, both CP and EVP during CPX significantly correlated with pulmonary vascular resistance (r=−0.487, P<0.0001, LVEDV 231 vs 229mLs, P=0.856, RV 257 vs 254mLs, P=0.747) but all measures of cardiac displacement towards the axilla were greater (%LatD=45.6% vs 37.9%, P=0.0001, %Septal 54.2±18.6% vs 46.8±3.9%, P=0.001, and %CTHTX=43.6±3.5%, P=0.048, %Septal 54.2±18.6% vs 46.8±3.9%, P=0.001, and %CTHTX=43.6±3.5%, P=0.048).

Conclusions: In healthy EAs, TWIV2–3 is associated with displacement of the RV towards the left axilla rather than RV dilatation or hypertrophy. TWIV2–3 inversely may be explained by the position of the RV relative to the surface ECG leads.
During the follow-up period, 59 deaths from pulmonary embolism were disposed by prolonged television watching. However, no prospective study has examined the association between prolonged television watching and pulmonary embolism. Several papers have reported that pulmonary embolism was present in 10% of patients in the sportcheck study.

**Results:** In 83% (95% CI: 70%-96%) of participants hsTnT exceeded 14 ng/l (99th percentile value) and in 51% (95% CI: 37%-64%) of participants cTnT exceeded the detection limit (0.01 ng/ml). The measured pooled change scores for cTnT were +31.53 ng/l (95% CI: 13.46–49.61), for cTnI +39.70 ng/l (95% CI: 21.36; 58.03), for BNP +10.42ng/l (95% CI: 4.26; 16.57), for NT-proBNP +67.30ng/l (95% CI: 49.93; 84.68), and for D-dimer +262.27ng/ml (95% CI: 155.86; 358.69). RV-EF increased and RV-EF decreased after exercise, while no significant change was observed in LV-EF.

**Conclusions:** Our analysis underlines that cTnT, hsTnT, cTnI, NT-proBNP, BNP, and D-dimer levels can significantly increase after endurance exercise. In addition, transient right ventricular dilation and dysfunction can be observed. All these can mimic PE, ACS, heart failure or cardiac injury. An accurate interpretation of elevated biomarkers after strenuous exercise is thus mandatory.

**Acknowledgement/Funding:** Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

**Background:** Acute coronary syndrome (ACS) and pulmonary embolism (PE) are two of the most common cardiovascular emergencies. Different biomarkers and echocardiography assessment are used to diagnose and risk stratify patients with the suspicion of PE and ACS. Although highly accurate, each of these biomarkers has its own caveats, for instance, several studies have demonstrated that elevated levels of biomarkers can be markers for pulmonary embolism after strenuous exercise.

**Purpose:** It is still little known about the frequencies, magnitude of concentration changes, and underlying causes of biomarker increases after endurance exercise. We aimed to investigate these in this study.

**Methods:** We performed a meta-analysis of biomarker changes (cTnT, hsTnT, cTnI, NT-proBNP, and D-dimer) and cardiovascular imaging parameters after endurance exercise. We searched for studies published in English language from 1997 to 2014 that assessed these biomarkers or cardiac function and provided the exercise protocol directly after endurance exercise. Altogether, 45 studies could be included: 33 ones met the inclusion criteria for cTnT, 4 for hsTnT, 12 for cTnI, 7 for NT-proBNP, 17 for BNP, 7 for D-dimer, 7 for right ventricular ejection fraction (RV-EF), 8 for right ventricular end diastolic diameter (RV-EDD), and 21 for left ventricular ejection fraction (LV-EF).

**Results:** In 83% (95% CI: 70%-96%) of participants hsTnT exceeded 14 ng/l (99th percentile value) and in 51% (95% CI: 37%-64%) of participants cTnT exceeded the detection limit (0.01 ng/ml). The measured pooled change scores for cTnT were +31.53 ng/l (95% CI: 13.46–49.61), for cTnI +39.70 ng/l (95% CI: 21.36; 58.03), for BNP +10.42ng/l (95% CI: 4.26; 16.57), for NT-proBNP +67.30ng/l (95% CI: 49.93; 84.68), and for D-dimer +262.27ng/ml (95% CI: 155.86; 358.69). RV-EF increased and RV-EF decreased after exercise, while no significant change was observed in LV-EF.

**Conclusions:** Our analysis underlines that cTnT, hsTnT, cTnI, NT-proBNP, BNP, and D-dimer levels can significantly increase after endurance exercise. In addition, transient right ventricular dilation and dysfunction can be observed. All these can mimic PE, ACS, heart failure or cardiac injury. An accurate interpretation of elevated biomarkers after strenuous exercise is thus mandatory.

**Acknowledgement/Funding:** Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

**Background:** Acute coronary syndrome (ACS) and pulmonary embolism (PE) are two of the most common cardiovascular emergencies. Different biomarkers and echocardiography assessment are used to diagnose and risk stratify patients with the suspicion of PE and ACS. Although highly accurate, each of these biomarkers has its own caveats, for instance, several studies have demonstrated that elevated levels of biomarkers can be markers for pulmonary embolism after strenuous exercise.

**Purpose:** It is still little known about the frequencies, magnitude of concentration changes, and underlying causes of biomarker increases after endurance exercise. We aimed to investigate these in this study.

**Methods:** We performed a meta-analysis of biomarker changes (cTnT, hsTnT, cTnI, NT-proBNP, and D-dimer) and cardiovascular imaging parameters after endurance exercise. We searched for studies published in English language from 1997 to 2014 that assessed these biomarkers or cardiac function and provided the exercise protocol directly after endurance exercise. Altogether, 45 studies could be included: 33 ones met the inclusion criteria for cTnT, 4 for hsTnT, 12 for cTnI, 7 for NT-proBNP, 17 for BNP, 7 for D-dimer, 7 for right ventricular ejection fraction (RV-EF), 8 for right ventricular end diastolic diameter (RV-EDD), and 21 for left ventricular ejection fraction (LV-EF).

**Results:** In 83% (95% CI: 70%-96%) of participants hsTnT exceeded 14 ng/l (99th percentile value) and in 51% (95% CI: 37%-64%) of participants cTnT exceeded the detection limit (0.01 ng/ml). The measured pooled change scores for cTnT were +31.53 ng/l (95% CI: 13.46–49.61), for cTnI +39.70 ng/l (95% CI: 21.36; 58.03), for BNP +10.42ng/l (95% CI: 4.26; 16.57), for NT-proBNP +67.30ng/l (95% CI: 49.93; 84.68), and for D-dimer +262.27ng/ml (95% CI: 155.86; 358.69). RV-EF increased and RV-EF decreased after exercise, while no significant change was observed in LV-EF.

**Conclusions:** Our analysis underlines that cTnT, hsTnT, cTnI, NT-proBNP, BNP, and D-dimer levels can significantly increase after endurance exercise. In addition, transient right ventricular dilation and dysfunction can be observed. All these can mimic PE, ACS, heart failure or cardiac injury. An accurate interpretation of elevated biomarkers after strenuous exercise is thus mandatory.

**Acknowledgement/Funding:** Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

**Background:** Acute coronary syndrome (ACS) and pulmonary embolism (PE) are two of the most common cardiovascular emergencies. Different biomarkers and echocardiography assessment are used to diagnose and risk stratify patients with the suspicion of PE and ACS. Although highly accurate, each of these biomarkers has its own caveats, for instance, several studies have demonstrated that elevated levels of biomarkers can be markers for pulmonary embolism after strenuous exercise.

**Purpose:** It is still little known about the frequencies, magnitude of concentration changes, and underlying causes of biomarker increases after endurance exercise. We aimed to investigate these in this study.

**Methods:** We performed a meta-analysis of biomarker changes (cTnT, hsTnT, cTnI, NT-proBNP, and D-dimer) and cardiovascular imaging parameters after endurance exercise. We searched for studies published in English language from 1997 to 2014 that assessed these biomarkers or cardiac function and provided the exercise protocol directly after endurance exercise. Altogether, 45 studies could be included: 33 ones met the inclusion criteria for cTnT, 4 for hsTnT, 12 for cTnI, 7 for NT-proBNP, 17 for BNP, 7 for D-dimer, 7 for right ventricular ejection fraction (RV-EF), 8 for right ventricular end diastolic diameter (RV-EDD), and 21 for left ventricular ejection fraction (LV-EF).

**Results:** In 83% (95% CI: 70%-96%) of participants hsTnT exceeded 14 ng/l (99th percentile value) and in 51% (95% CI: 37%-64%) of participants cTnT exceeded the detection limit (0.01 ng/ml). The measured pooled change scores for cTnT were +31.53 ng/l (95% CI: 13.46–49.61), for cTnI +39.70 ng/l (95% CI: 21.36; 58.03), for BNP +10.42ng/l (95% CI: 4.26; 16.57), for NT-proBNP +67.30ng/l (95% CI: 49.93; 84.68), and for D-dimer +262.27ng/ml (95% CI: 155.86; 358.69). RV-EF increased and RV-EF decreased after exercise, while no significant change was observed in LV-EF.

**Conclusions:** Our analysis underlines that cTnT, hsTnT, cTnI, NT-proBNP, BNP, and D-dimer levels can significantly increase after endurance exercise. In addition, transient right ventricular dilation and dysfunction can be observed. All these can mimic PE, ACS, heart failure or cardiac injury. An accurate interpretation of elevated biomarkers after strenuous exercise is thus mandatory.

**Acknowledgement/Funding:** Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan.
P2689 | BEDSIDE

The impact of different types of aerobic exercise on vascular function
D. Athanasiaou1, G. Siassos1, G. Terzis2, A. Stasinaki3, E. Dimitropoulos1, E. Okonomou1, M. Zaromytidou1, M. Kourouzis1, S. Tsalamandris1, D. Tousoulis1. 1University of Athens Medical School, 1st Cardiology Department, “Hippokration” Hospital, Athens, Greece; 2University of Athens, Faculty of Physical Education and Sports Science, Athens, Greece

Background: Chronic exercise training improves endothelial function in individuals with cardiovascular diseases. Endothelial function and arterial stiffness are key players in the pathophysiology of atherosclerotic disease.

Purpose: To investigate the acute effects of continuous moderate-intensity aerobic exercise (CAE) and high intensity interval aerobic exercise (hIAE) on endothelial function, central and peripheral arterial stiffness in healthy subjects.

Methods: Twenty healthy men (mean aged 23±3 y) were recruited in this cross over study. They participated in two exercise sessions: a) CAE: volume at 50% of maximum aerobic work on a cycle ergometer for 30 min and b) hIAE: interval maximum aerobic work on a cycle ergometer for 30 min. Endothelial function was evaluated by flow-mediated dilation (FMD) in the brachial artery. Carotid femoral pulse wave velocity (cfPWV) was measured as an index of the central aortic stiffness, while femoral tibial PWV (ftPWV) was measured as an index of peripheral arterial stiffness. Measurements were carried out before and immediately after each exercise session.

Results: There was no statistically significant difference in baseline measurements of the participants before CAE and hIAE, concerning FMD, cfPWV and ftPWV (p>NS for all). Importantly, both CAE (8.57±2.53% vs. 6.37±1.48%, p<0.001) and hIAE (11.5±7.5% vs. 5.85±1.77%, p<0.001) caused a significant improvement in FMD compared to baseline measurements. Moreover, CAE and hIAE had no impact in cfPWV, compared to baseline measurements (p>NS for both). Interestingly, compared to baseline measurements, CAE (8.17±1.48/sec vs. 9.25±2.6/sec; p<0.05; Wilcoxon) and hIAE (8.25±0.8/sec vs. 9.14±1.07/sec vs. p=0.002) significantly improved ftPWV.

Conclusion: Endothelial function is favorably affected by both continuous moderate-intensity aerobic exercise and high intensity interval aerobic exercise which may enhance endothero protective effects of exercise on atherosclerosis progression. Importantly, only peripheral arterial stiffness improved by both types of aerobic exercise. Further studies are needed to elucidate how different patterns of aerobic training can affect cardiovascular health.

EXERCISE, PHYSICAL ACTIVITY AND SPORT IN HEALTH

P2690 | SPOTLIGHT

Suppressed middle-acidosis by oral bicarbonate ingestion affected stroke volume responses during an all-out long sprint cycling event
P.M. Lepretre1, C. Hanon2, C. Thomas3, S. Dore4, R. Delfour-Peyrethon5, S. Perrey5, D. Bishop6. 1Pôle Sports de Médecine du Sport, Evry, France; 2Clinique des Maladies des Grossesses, Parturientes, Fœtus et nouveau-nés, Centre hospitalier d’Evry, Evry, France; 3Faculté des Sciences Fondamentales, département des Sciences et Techniques des Activités Physiques et Sportives, Evry, France; 4Université de Nantes, UFR-STEPS, Lab. Motricité, Interactions, Performance, EA 4334, Nantes, France; 5Université Montpellier, UFR-STEPS, MHD Euromed, Montpellier, France; 6Victoria University, Institute of Sport, Exercise and Active Living, Melbourne, Australia

Background: Improvement in long sprint performance would be the result of oxygen uptake response (VO2). The inability of subjects to produce and maintain a high aerobic energy flow could impair the long sprint performance. Very high-intensity exercises resulted in a marked elevation in ATP utilization and induced considerable metabolic and ionic perturbations in contracting skeletal muscles which could affect VO2 response. Berger reported that metabolic acidosis induced by sodium bicarbonate ingestion had no effect on faster VO2 responses but altered slow VO2 adjustment. Due to the large active muscle mass, the peak of VO2 (VO2peak) is limited by maximal cardiac output (CO) rather than peripheral factors during exhaustive cycling exercise. Together, these findings raised the question about the influence of metabolic acidosis on cardiac output (CO) response especially at the end of very-high intensity exercise.

Purpose: To determine whether acid-base balance status affects the cardiorespiratory response and cycling sprint performance.

Methods: 11 well-trained male cyclists performed on a cycle ergometer 1) a progressive exercise to determine VO2peak and 2) two 70-s all-out supra-maximal exercise in random iso-kinetic conditions with (ALK) or without (PLAC) bicarbonate oral ingestion. Heart rate (HR) and stroke volume (SV) were measured (by impedance) continuously during all tests.

Results: The induced acidosis had no effect on VO2 at rest (p>NS) but during high VO2 value (96.6±9.2% of VO2peak) compared to PLAC in course of which, high value of VO2 was lower than VO2peak (92.2±6.3% of VO2peak, p<0.01). The highest CO values measured during both all-out trials were not different from maximal CO measured during the incremental exercise (P = NS) However, CO induced a higher HR values at rest (ALK: 142.8±17.8 vs. PLAC: 130.5±20.6 bpm; p<0.05), a higher SV value (incremental test: 133.5±12.1 vs. ALK: 150.3±28.9; p<0.05) during exercise. Highest VO2 values were attained at 51.4±13.4 and 53.6±7.8 s during PLAC and ALK events, (P = NS). A faster CO response was found compared to VO2 kinetic at the onset of ALK exercise. At the end of both all-out conditions, significant VO2 drop (P<0.01) was correlated to CO and SV decreases in ALK conditions.

Conclusion: There is experimental evidence that the bulk O2 delivery to the limb may limit the VO2 responses in the transient phase and induced alkalosis affects CO and VO2 during the whole all-out trial.

Acknowledgement/Funding: French Ministry of Sports

P2691 | BEDSIDE

Usefulness of chest pain units as fast-track screening for ACS in low-intermediate risk patients

Purpose: The potential advantages of chest pain units (CPU) for rapid exclusion of ACS are many, including an appropriate risk stratification, unnecessary inpatient admissions, costs and length of stay of patients presenting with acute chest pain with low-intermediate risk. Our aim was to analyse the usefulness of a chest pain unit in a university teaching hospital in terms of appropriate patient selection, risk stratification and need for admission of patients presenting with acute chest pain over the entire period of the study.

Methods: A total of 105 patients presenting chest pain of low-intermediate risk in the ED managed in the CPU were included over a two and a half year period. After negative cardiac biomarker determination and normal or inconclusive ECG, an exercise treadmill test (ETT) or stress myocardial perfusion imaging (MPI) upon patients characteristics. Data was analysed using SSPS statistical system.

Results: The median age was 56 (13SD) years, 59 (56.2%) were males, with 51 (48.6%) HT, 17 (16.2%) DM, 44 (41.9%) hypercholesterolemia, 26 (24.8%) smokers, 24 (22.8%) CAD and 2 (1.9%) had a history of chronic abuse of cocaine and alcohol, with a mean GRACE score of 71.7 (SD 21.7), 7 (6.6%) being over 100. Mean time in observation prior to the test was 16.4 hours. An ETT was performed in 90 (85.7%), whilst MPI was performed in the latter 15 (14.3%). Overall performance during the stress tests was excellent with a mean 7.62 METS and a mean 7.09 DUKE index. 75 (71.4%) with diagnostic negative test were discharged and evaluated as outpatients. 20 patients presented an non-diagnostic test, thus requiring early follow-up consults in less than 30 days with testing. A positive result of either ETT or MPI in 10 (9.5%) was indication of invasive coronary angiography; in 4 (3.8%) patients no significant CAD was found and 6 (5.7%) had at least 1 vessel disease with indication of PCI. A patient with 106 GRACE score with non-diagnostic ETT was discharged and presented the following day with STEMI.

Conclusion: Patients managed in a CPU are at low-intermediate risk for CAD. ETT or MPI only identified disease in 5.7%, and furthermore, it failed to identify disease in a patient with intermediate risk. Most patients were discharged home without hospital admission but where evaluated as outpatients. Therefore, a CPU may reduce hospital admission, but still consumes resources for patients at low risk and it seems that patients at intermediate risk for CAD presenting with acute chest pain may benefit from further study.

P2692 | BEDSIDE

Exertional oscillatory ventilation as a long-term prognostic factor for patients with post-acute coronary syndrome

Background: Previous studies have shown widespread prevalence of respiratory instabilities comorbid with cardiovascular disease. Prevalence of exertional oscillatory ventilation (EOV) across post-acute coronary syndrome (post-ACS) population has never been revealed.

Methods: We studied consecutive 209 post-ACS patients (median age = 59.3 years; 89.0% male; LVEF: 59.1±11.8%) who underwent cardipulmonary exercise testing in cardiac rehabilitation from 2009 to 2014. EOV was visually determined by cyclic fluctuations in minute ventilation that lasted for >60% of the exercise duration and an amplitude of > 15% of the average amplitude of cyclic fluctuations at rest.

Results: EOV was present in 24 patients (11.5%). During 639.2±539.4 days of follow up, major adverse cardiac events (MACE; including cardiac death, myocardial infarction and congestive heart failure) occurred in 20.8% (5/24) in patients with EOV vs. 9.2% (9/95) in patients without EOV (p = 0.08).

Conclusion: EOV may represent an independent clinical predictor of recurrent cardiac events after post-ACS.
with EOV (EOV group) and 5.95% (11/185) in patients without EOV (non-EOV group) (p<0.01). No significant differences were observed for medical treatment (beta-blocker, ACE/ARB and Diuretics) between the groups. VE/VO2 slope (29.4 vs. 28.1, p=0.29) was similar between the EOV group and non-EOV group. EOV group had significantly higher NT-proBNP levels (3942 vs. 1866.0 pg/ml, p=0.03) and lower UEF (54.1 vs. 59.7, p=0.03) than non-EOV group, but the prevalence of clinically diagnosed heart failure was similar between the groups (29.2% for EOV group vs. 16.2% for non-EOV group, p=0.12). Kaplan-Meier survival analysis revealed that EOV was associated with a poor prognosis in patients with post-ACS.

Conclusion: EOV often coexists with the post-ACS setting and the presence of EOV reflects an unfavorable prognosis.

P2694 | BEDSIDE
Heart rate variability detects psychophysiological stress induced by realistic force-on-force training of police personnel
D. Brisindra, F. Floravanti, A.R. Sorbo, A. Venuti, R. Fenci. Catholic University of the Sacred Heart, Biomagnetism Center, Clinical Physiology, Rome, Italy

Purpose: Acute tactical stress (ATS) can reduce the performance of police officers (POs) on complex tasks such as decision-making and management of emotions in self-defense situations. ATS may also suppress the ability to keep situational control. In the real world this may dramatically increase inappropriate use of force and liability. Thus, realistic tactical training (RTT) is mandatory for POs and it is increasingly performed with scenarios simulating real-world force-on-force incidents. In the present study, we aimed to evaluate individual stress response to RTT and determine which parameters were more efficient to assess ATS providing separation between HS and LS.

Results: All POs were in good psychological balance, with no evidence of individual tendency to respond with abnormal levels of state anxiety/anger to the test challenges. HR increment (p=0.001) was not different in differentiating between LS and HS. At univariate analysis several HRV features were significantly different (p<0.01) between LS and HS conditions. At the DA the two stress conditions were separated with 80.4% PA even cross-validating the results, combining most significant (p<0.005) HRV features in the formula F1 = 1.156 x HRVt - 0.018 x VLFpower - 0.061 x SD2 - 1.156 x DF2 - 1.243 (LS if F1 > 0).

Conclusions: ATS induced by police RTT determines changes of cardiac autonomic modulation which are different in LS and HS scenarios. DA of HRV provides a realistic force-on-force training of police personnel

P2695 | BEDSIDE
Diagnostic value of automatically measured ST-segment changes in individual ECG leads to detect myocardial ischemia during exercise ECG

Background: Exercise ECG is a widely available cardiac stress test, but currently provides insufficient diagnostic accuracy even when done by experienced cardiologists. It is currently unclear which ECG parameters on which leads provide best diagnostic accuracy.

Methods: We enrolled 813 consecutive patients referred for exercise stress myocardial perfusion imaging (MPI) into this prospective single-center study. Amplitude of ST-depression and ST-slope were analysed in an automated fashion from digital ECG recordings at J+40ms, J+60ms and J+80ms in all 12 leads. Time of analysis was the 10 seconds in which the ST-depression was maximal. To evaluate diagnostic accuracy, we calculated the area under the receiver operating characteristics curves (AUC). Optimal cut-off points were derived using the Youden-index. Myocardial ischemia as assessed by MPI was defined as a summed difference of T > 2 or presence of a transient systolic dilation.

Results: Myocardial ischemia was detected by MPI in 294 (36%) patients. The diagnostic accuracy of ST-deviation, as quantified by AUC, was best in lead V6 at J+80ms (AUC 0.63 CI 0.59–0.67), with an optimal cut-off at −0.04mV (sensitivity 54%, specificity 68%). Lead I was the second best lead and showed a similar diagnostic value (J+80ms AUC 0.62, CI 0.58–0.66). ST-slope showed best results also in V6 (J+80ms AUC 0.64, CI 0.60–0.68) with an optimal cut-off at -0.75mV/s (sensitivity 85%, specificity 57%).

P2696 | BEDSIDE
Stage 3 or 4 chronic kidney disease disrupts the improvement in exercise capacity after hospital discharge in patients with ischemic heart disease
R. Matsuzaa1, T. Masuda2, K. Kamiya1, N. Hamazaki2, K. Nozaki1, S. Tanaka1, E. Maekawa1, J. Ako1, Kitasato University Hospital, Department of Rehabilitation, Sagamihara, Japan; 2Kitasato University, Department of Rehabilitation, School of Allied Health Sciences, Sagamihara, Japan; 3Kitasato University Graduate School of Medical Sciences, Department of Cardio-angiology, Sagamihara, Japan; 4Kitasato University School of Medicine, Department of Cardiovascular Medicine, Sagamihara, Japan

Background: Poor exercise capacity is well known to increase mortality after hos-
Exercise, physical activity and sport in health

V. Vassilikos, A. Delignianis, Aristotle University of Thessaloniki, Laboratory of Sports Medicine, Thessaloniki, Greece; 2Aristotle University of Thessaloniki, 2nd Podepeducic Clinic of Internal Medicine, Thessaloniki, Greece; 3Aristotle University of Thessaloniki, 3rd Cardiology Department, Thessaloniki, Greece

Purpose: Exercise-induced arterial adaptations hold important implications for cardiovascular health. The aim of the study was the investigation of carotid intima-media thickness, arterial elastic properties and peak exercise time in men with erectile dysfunction (ED), exercise stress testing (EST), while principally important to detect coronary artery disease, it is also essential to define cardiovascular (CV) risk through evaluation of maximal exercise capacity and vascular pathologies. Aim of this study was to investigate the association between ED and EST parameters.

Methods: 180 ED patients and 50 men without ED underwent maximal EST. Exercise parameters including exercise capacity (metabolic equivalents, METS), peak exercise time, heart rate (HR) at 6 METS, peak exercise HR recovery (HRR) at 1 and 2 min and chronotropic index (CI) were evaluated in all individuals. Endothelial function was evaluated with brachial flow-mediated dilatation (FMD).

Results: Table shows EST parameters of the two study groups. ED patients had lower peak exercise time and exercise capacity (P<0.001) and reduced CI (P<0.01) compared to men without ED. There was a significant association of ED severity with exercise duration, peak workload, HRR 2 minutes after exercise, and CI (all P<0.05). There also was a positive correlation of HRR and CI with FMD (all P<0.05).

Conclusions: This study shows interrelationships between exercise capacity, HRR, CI and ED. Abnormal HRR and CI are associated with systemic endothelial dysfunction. These findings elucidate pathophysiological links and may have important implications for the estimation of CV risk in ED patients.

P2697 | BENCH
Regular trainings in patients with advanced heart failure (NYHA III) after ICD and CRT-D implantations: good or bad in terms of QoL and depression symptoms
E. Smolis-Bak, R. Dabrowski, I. Kowalik, H. Rymuza, H. Hzewd. National Institute of Cardiology, Warsaw, Poland

Background: Congestive heart failure (CHF) often causes emotional symptoms. Patients (pts) need complex care which should consist of optimal pharmacological treatment, exercise training and psychological therapy. The aim of the study was evaluation of the impact of regular trainings in pts with advanced heart failure after ICD and CRT-D (n=61) implantations. All pts underwent rehabilitation program in hospital and at home. Patients were randomly assigned to exercise group (ExG, n=69), mean age 62.4±9.6 years (ICD: 36, CRT-D: 33 pts), with 3–5 exercise sessions per week, during 6 months (endurance training, general physical condition training with elements of resistance exercises) and control group (CG, n=69), mean age 62.3±9.7 with CHF of ischemic and non-ischemic origin, after ICD (n=77) and CRT-D implantations: good or bad in terms of QoL and depression symptoms.

Methods: Study group consisted of 138 pts (11 women), age 47–75 years, mean: 62.3±9.7 with CHF of ischemic and non-ischemic origin, after ICD (n=77) and CRT-D (n=61) implantations. All pts underwent rehabilitation program in hospital and at home. Patients were randomly assigned to exercise group (ExG, n=69), mean age 62.4±9.6 years (ICD: 36, CRT-D: 33 pts), with 3–5 exercise sessions a week, during 6 months (endurance training, general physical condition training with elements of resistance exercises) and control group (CG, n=69), mean age 62.3±9.7 years (ICD: 36, CRT-D: 33). Before discharge and after 6 and 18 months the depression level according to Beck Depression Inventory (BDI) and QoL, according to Nottingham Health Profile (NHP) were estimated. Physical abilities limitations, energy level, pain, emotional reactions, sleep disturbances, social isolation, problems with work, family life and sexual life were analyzed as well.

Results: At the baseline both groups had scores specific for mild depressions symptoms according to BDI: ExG: 11.3±7.4 vs. CG: 11.5±7.7 (ns). After 6 and 18 months significant improvement was observed in ExG, respectively: 9.4±6.1, p<0.03 and 7.9±5.1, p<0.001 (no depression symptoms). In consecutive studies results were similar in CG: 11.2±9.3, ns, and 10.7±7.7. In NHP tests evaluation sleep disturbances were significantly reduced in ExG, before: 2.2±1.7 vs. 1.7±1.6 after 6 months, p=0.0002, vs. 1.5±1.4 after 18 months, p<0.0001. Limitations of physical activities were reduced in ExG: 2.4±1.7, p<0.0001 vs. 1.6±1.4, p<0.0001 vs. 1.6±1.4-p<0.0001, respectively. In ExG emotional reactions control was better, p<0.0001, and level of energy increased, p<0.01. In CG only pain feelings were reduced, p<0.05. Social life and family life scores were significantly higher in ExG vs CG (p<0.05).

Conclusions: Regular trainings significantly reduced level of depression symptoms and improved quality of sleep in patients with advanced CHF (NYHA III) after ICD and CRT-D implantations. Rehabilitation activities reduced limitations in physical activity, increased level of energy and control of emotional reactions.
P2701 | SPOTLIGHT
Neighbourhood environmental attributes associated with walking in South Australian adults: differences between urban and rural areas
N. Berry1, T. Sugiyama2, R. Nolan3, J. Dollman4, N. Coffey2. 1 Flinders University, School of Nursing and Midwifery, Adelaide, Australia; 2 University of South Australia, School of Population Health, Adelaide, Australia; 3 SA Health, Public Health and Chronic Systems, Adelaide, Australia; 4 University of South Australia, School of Health Sciences, Adelaide, Australia

Background and Introduction: The benefits of walking for cardiovascular health are well established. Despite this, participation is poor and worse in rural areas compared to urban areas. Most studies on perceptions of neighbourhood walkability and walking have been conducted in urban areas, thus little is known about how walkability is related to rural areas.

Purpose: To examine associations of perceived walkability with adults’ walking in urban and rural South Australia (SA).

Methods: In 2013, 2402 adults (aged ≥18 years) participated in a computer-assisted telephone interview survey in SA. Perceptions of neighbourhood walkability were determined by six questions relating to two domains, route (paths, aesthetics) and destination (shops, parks). Responses ranged from 1 (strongly disagree) to 4 (strongly agree). For each participant, overall walkability (OW), route-related walkability (RW) and destination-related walkability (DW) were calculated as a mean of the relevant items. Self-reported walking was categorised as no walking or some walking in the previous week. Data were stratified by area of residence: urban (n=1738) and rural (n=664), and analysed using logistic regression, adjusting for age, work status, self-reported health, marital status, education and income.

Results: There was a significant difference in walking participation between urban and rural residents with 25.8% in rural areas reporting no walking compared to 18.5% in urban areas (p<0.001). There were significant differences in perceived walkability between urban and rural areas with greater mean scores in urban areas compared to rural areas across all three domains of walkability (p<0.001). DW: 3.27±0.59 vs 2.72±0.82; OW: 3.22±0.77 vs 2.61±1.00 and RW: 3.29±0.61 vs 2.77±1.82. For each domain of walkability, there was an association between walkability and walking participation in urban areas. Each additional unit in OW, DW, and RW was associated with a 1.44 times (95% CI: 1.17, 1.76, p<0.001), 1.35 times (95% CI: 1.16, 1.58, p<0.001), and 1.34 times (95% CI: 1.09, 1.65, p=0.005) greater odds of walking, respectively. There were no significant associations for any domain of walkability in rural areas.

Conclusion(s): Consistent with past studies, walking participation was associated with the perception of neighbourhood walkability in urban areas. However, this was not observed in rural areas. Environmental influences on walking are likely to differ between urban and rural areas. Further research in rural areas is required to inform environmental and policy initiatives to increase rural walking participation.

P2701 | BEDSIDE
Does moderate but regular exercise alter the baroreceptor response in pregnancy?
R.E. Carpenter1, O. Uzun2, S.J. Emery3, D. Rassi1, M.J. Lewis1. 1 Swansea University, Swansea, United Kingdom; 2 University Hospital of Wales, Cardiff, United Kingdom; 3 Singleton Hospital, Obstetrics and Gynaecology, Swansea, United Kingdom

Background: The influence of exercise ‘training’ on baroreceptor function during pregnancy is largely unknown. A previous report suggested that diminished baroreceptor sensitivity (BRS) and reduced cardiac parasympathetic tone in late pregnancy may be prevented by physical exercise.

Purpose: We sought to test the above hypothesis using a large group of women, a controlled and standardised exercise programme, and multiple physiological assessments during and following pregnancy.

Methods: Fifty-one healthy pregnant women were recruited and randomly assigned to exercise or non-exercise groups. Exercise groups attended weekly aerobic exercise classes from the 20th week of pregnancy onwards. Beat-to-beat cardiovascular assessments including stroke volume (SV), heart rate variability (HRV) and BRS were performed antenatally at 12–16 (T1), 26–28 (T2), 34–36 (T3) weeks and 12 weeks following birth (PP) during supine and standing postures and during rest and exercise.

Results: BRS was reduced (p=0.025) by mid-pregnancy in the supine position only, and the exercising group showed a further significant reduction (p=0.006) by late pregnancy. HRV was reduced (p=0.002) by mid-pregnancy in the supine position and remained reduced until late pregnancy (p<0.0001), whilst exercise caused a further reduction (p=0.029) in HRV by late pregnancy. SV was reduced (p<0.0005) by mid-pregnancy but was not influenced by exercise (p=0.950).

Conclusion: Regular moderate antenatal exercise significantly reduced BRS and HRV in late pregnancy. Diminished parasympathetic cardiac activity during late gestation was exaggerated by exercise and is a likely cause of the reduced BRS. These presumably advantageous influences of exercise could enhance maternal preparedness for labour via a relative cardiac sympathetic dominance.

Acknowledgement/Funding: Welsh Government NISCHR Health Studentship; Cooperative Pharmacy

EXERCISE TRAINING AND PHYSICAL ACTIVITY

P2702 | BEDSIDE
Changes in Cardiorespiratory fitness and Incidence of Myocardial perfusion defects and Major Adverse Cardiac Events
M. Al-Mallah1, A. Ahmed1, W. Qureshi2. 1 National Guard Hospital, King Faisal Cardiac Center (KACC), Riyadh, Saudi Arabia; 2 Wake Forest University, Winston-Salem, United States of America

Background: Cardiorespiratory fitness (CRF) is an independent predictor of outcomes. It is not clear if changes CRF is associated with incidence of myocardial perfusion defects and major adverse cardiac events (MACE).

Methods: We included 948 patients without known coronary artery disease who underwent 2 clinically indicated exercise stress tests more than 1 year apart (median 5.6 years, IQR 3.2–9.2 years). The first test was a normal exercise treadmill test and the second test was a nuclear exercise test (SPECT). Patients who underwent revascularization in between the two tests were excluded. Cardiorespiratory fitness was estimated using metabolic Equivalents (METs). Multivariable Cox Analysis was used to determine the independent predictors of MACE.

Results: Of the included cohort, 145 patients (15.1%) had a drop of 2 METS or more in CRF. Patients with decline in CRF had higher incidence of new perfusion defects (34.7% vs. 21%, p=0.001) as well as MACE rate (15.9% vs. 7%, p<0.001). Using multivariable analysis, the drop in CRF was an independent predictor of MACE after adjusting for confounders (Hazard ratio 1.69, 95% 1.02–2.81, p=0.041).

Conclusions: Our analysis suggest that drop in CRF in associated with increased incidence of myocardial perfusion defects and is an independent predictor of MACE.

P2703 | BEDSIDE
Screen time is a risk factor for higher exercise blood pressure independent of moderate-to-vigorous physical activity or fitness in adolescents
B. Weisser1, C. Hacke2. 1 Christian-Albrechts-University Kiel, Kiel, Germany; 2 University Medical Center Hamburg Eppendorf, Hamburg, Germany

Background: In the present study, the influences of sedentary behaviour (screen time), physical activity and fitness on systolic resting and exercise blood pressure (BP) were investigated in 532 subjects aged 12–17 years.

Methods: Systolic exercise BP was measured at 1.5 Watt/kg body weight (standardized cycle ergometry). Fitness was determined as the physical working capacity at a heart rate of 170/min. (PWC170). The subjects were classified according to screen time (low: ≤2 h/day as recommended or high: >2 h/day) and to moderate-to-vigorous physical activity (MVPA; low: 60 min on >5 days per week, high: 60 min on >5 days per week). For the calculation of odds ratios, logistic regression analysis was used.

Results: Resting BP was lower (−2.3 mmHg, p=0.03) in the group with lower screen time (<2 h/ day) adjusted for age, sex, height and BMI (111.9±11.3 vs. 114.2±11.1 mmHg). After further adjustment for fitness, the difference was no longer significant. In contrast, systolic exercise BP remained significantly lower (−3.7 mmHg, p=0.02) after correction for all variables (148.1±16.9 vs. 151.8±16.9 mmHg). The odds ratio for a systolic exercise BP above the 90th percentile was 1.97 (95% confidence interval 1.11–3.5, p<0.05) in the group with a high screen time. Furthermore, the influence of screen time on exercise BP was independent of physical activity (p=0.023).

Discussion: Even with high MVPA, high screen time was associated with a higher exercise BP (Table). In the present study, sitting (or totally inactive) time was associated with a higher exercise BP independent of the amount of physical activity.

Table 1. Exercise BP, screen time and MVPA

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Mean systolic exercise BP (mmHg)</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>High screen time/low activity</td>
<td>154.4 mmHg</td>
<td>151.6–157.1 mmHg</td>
</tr>
<tr>
<td>Low screen time/low activity</td>
<td>149.7 mmHg</td>
<td>145.8–151.5 mmHg</td>
</tr>
<tr>
<td>High screen time/high activity</td>
<td>148.1 mmHg</td>
<td>143.7–152.5 mmHg</td>
</tr>
<tr>
<td>Low screen time/high activity</td>
<td>144.3 mmHg</td>
<td>140.1–148.6 mmHg</td>
</tr>
</tbody>
</table>

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475 by guest on 07 February 2019
Thus, activity and inactivity might not be the extremes of the same continuum but could be two separate risk factors, at least for exercise blood pressure in adolescents. In addition, lifestyle parameters of activity, sedentary behaviour and fitness had a greater effect on exercise blood pressure than on resting blood pressure.

**P2704 | BEDSIDE**

**Improvement aerobic capacity leads to cognitive function benefits in patients with chronic kidney disease on hemodialysis**


**Objective:** To evaluate the effect of intradialytic aerobic training on functional capacity and cognitive function in patients with chronic kidney disease (CKD) on hemodialysis (HD).

**Methods:** We selected fifteen patients on HD Facility. We conducted an exercise test (Bruce protocol) on a treadmill to exclude patients with coronary artery disease, obtain the values of maximum heart rate (MHR) and assess aerobic capacity through the maximum volume of oxygen consumption (VO2max) estimated. Patients were tested for 6-minute walk (6MW) to assess functional capacity. For screening cognitive function, patients answered the instrument Mini Mental State Examination (MMSE). The ability patients were included in a protocol with intradialytic aerobic training on a cycle ergometer. The exercise was conducted during the first hour of the HD session, 30 minutes, three times a week for four months. Was used the 65–75% of maximum heart rate training range, controlled by frequency heart counter FS2 Polari. All assessments were repeated at the end of the training program. “T” test was applied and the results were presented as mean ± SD.

**Results:** The results showed an improvement in aerobic capacity (p<0.03), accompanied by improved functional capacity (p<0.01) and cognitive function (p<0.01).

**Characteristics of patients**

<table>
<thead>
<tr>
<th>Before protocol (n=15)</th>
<th>After protocol (n=15)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) 50.6±16.95 7% abnormal, 7% normal</td>
<td>50.6±16.95 7% abnormal, 7% normal</td>
<td>=</td>
</tr>
<tr>
<td>BMI (kg/height²) 25.7±5.64 25.7±5.56 0.78</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>VO2 max (ml/kg/min) 28.2±19.16 21.1±19.02 0.03</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>6MW (m) 523.7±70.10 608.1±71.78 0.01</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Cognitive function (MMSE’S point) 24.0±3.00 26.4±2.92 0.01</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Glycemia (mg/dl) 112.1±36.52 193.6±26.75</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dl) 11.4±1.32 12.6±1.33 0.05</td>
<td>=</td>
<td></td>
</tr>
<tr>
<td>BMI, body mass index; VO2max, maximum volume of oxygen consumption; 6MW, six minutes walk test; MMSE, Mini Mental State Examination.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** We found that intradialytic aerobic training has a beneficial effect on functional capacity and cognitive function in CKD patients on HD.

**Acknowledgement/Funding:** JSPS KAKENHI Grants (nos. 60598944 and 25461058).

---

**P2705 | BEDSIDE**

**Determinants of exercise capacity in patients with preserved left ventricular ejection fraction and reduced left ventricular ejection fraction**

S. Kikuchi, N. Ikehara, T. Goto, K. Waki, N. Ohto. Nagoya City University Graduate School of Medical Sciences, Department of Cardio-Renal Medicine and Hypertension, Nagoya, Japan

**Background:** It is important to evaluate exercise capacity objectively to detect the development of heart failure (HF) in patients with heart disease. The pathology of exercise capacity is multifactorial, and cardiac function is recognized as one of the most important determinants.

**Purpose**

We assessed the determinants of exercise capacity in patients with preserved left ventricular ejection fraction (EF) and reduced EF.

**Methods:** Eighty-one consecutive patients with preserved LVEF, and thirty-eight consecutive patients with reduced LVEF who underwent both Doppler echocardiography at rest and during cardio-pulmonary exercise testing (CPX) were enrolled. We measured LVEF, peak early diastolic transmural flow velocity (E), peak late diastolic transmural flow velocity (A), early diastolic mitral annular velocity (e'), systolic mitral annular velocity (s'), and propagation velocity of LV early diastolic filling flow (Vp) by Doppler echocardiography. After echocardiographic examination, a symptom-limited exercise testing was performed with a simultaneous respiratory gas analysis, and peak oxygen consumption (pVO2) was determined. Blood hemoglobin (Hb), serum creatinine (Cr), and brain natriuretic peptide (BNP) levels were obtained on the same day. Logarithmic transformation was applied for BNP level.

**Results:** Significant correlations were observed between age, Hb, BNP, A, e', as well as E/e' and pVO2 in patients with both preserved EF (r=−0.33, p<0.006, r=−0.35, p<0.006, r=−0.35, p=0.002, r=−0.42, p<0.001 and r=−0.41, p<0.001, respectively) and reduced EF (r=−0.65, p<0.001, r=−0.53, p=0.008, r=−0.41, p=0.01, r=−0.35, p=0.03, r=0.43, p=0.009, and r=−0.43, p<0.008, respectively). Furthermore, Vp and s' were significantly correlated with pVO2 in patients with preserved EF (r=−0.35, p<0.001, r=−0.30, p=0.006 significantly), and there was a significant correlation between Cr and pVO2 in patients with reduced EF (r=−0.38, p=0.002). In multivariate regression analysis, Vp (p=0.41, p=0.0002), e' (p=0.16, p=0.02) and A (p=0.22, p=0.03) were selected as significant determinants for pVO2 (r=−0.59, p<0.001) in patients with preserved EF, and age (p=0.45, p=0.002), Bp (p=0.30, p=0.03) and BNP (p=0.28, p=0.03) were selected as significant determinants for pVO2 (p=0.76, p<0.001) in patients with reduced EF.

**Conclusion:** Left ventricular diastolic function is the prime determinant of exercise capacity in patients with preserved EF. On the other hand, cardiac function has a less impact on exercise capacity in patients with reduced EF.

**Acknowledgement/Funding:** JSPS KAKENHI Grants (nos. 60598944 and 25461058).
Usefulness of exercise testing in prediction of short-term outcome among patients with stable coronary artery disease

A.M. Kiviinemi1, T.V. Kentta1, M.J. Junttila1, J.S. Perkiomaki1, O.-P. Piira1, S. Lepojärvi1, O. Ukkola1, A.J. Hautala2, M.P. Tulpoo2, H.V. Huikuri3 on behalf of The ARTEMIS investigators. 1University of Oulu, Oulu University Hospital, Medical Research Center Oulu, Oulu, Finland; 2 Verve Research, Oulu, Finland

Background: Impaired exercise capacity (EC) and heart rate responses to exercise and recovery, indicating abnormal cardiac autonomic function, predict outcomes of various populations. However, exercise testing is not routinely used in risk assessment in patients with stable coronary artery disease (CAD).

Purpose: To test the hypothesis that composite index of EC and exercise heart rate responses is a powerful determinant of short-term cardiac risk in stable CAD.

Methods: Patients with angiographically verified stable CAD (n=1740, 67±8 years, 1199 men, 88% using β-blockers) underwent a symptom-limited exercise test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate response/heart rate responses is a powerful determinant of short-term cardiac risk in stable CAD. β-blockers) underwent a symptom-limited exercise test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate re-β-blockers) underwent a symptom-limited exercise test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate re-β-blockers) underwent a symptom-limited exercise test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate re-β-blockers) underwent a symptom-limited exercise test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate re-β-blockers) underwent a symptom-limited exercise test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate re-β-blockers) underwent a symptom-limited exercise test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate re-

Results: Twenty-two patients (1.3%) were hospitalized due to heart failure and 19 exercise and supine recovery. The EC was normalized using reference value based test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate re-

>β-blockers) underwent a symptom-limited exercise test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate re-

Results: Twenty-two patients (1.3%) were hospitalized due to heart failure and 19 exercise and supine recovery. The EC was normalized using reference value based test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate re-

>β-blockers) underwent a symptom-limited exercise test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate re-

Results: Twenty-two patients (1.3%) were hospitalized due to heart failure and 19 exercise and supine recovery. The EC was normalized using reference value based test on cycle ergometer. Maximal chronotropic response index (CRI, heart rate re-

Analysis/Funding: The Finnish Technology Development Centre, the Finnish Foundation for Cardiovascular Research and the Academy of Finland and the Finnish Foundation for Cardiovascular Research.

Conclusions: The 6-MST is a feasible and acceptable method for assessing exercise capacity in older adults which also allows physiological changes to be accurately monitored throughout exercise.

P2710 | BEDSIDE
Prognostic value of double product reserve during cardiopulmonary exercise test in patient with idiopathic dilated cardiomyopathy

D. Han, J.C. Youn, S. Park, S.H. Lee, D. Choi, S.M. Kang. Yonsei University College of Medicine, Division of Cardiology, Severance Cardiovascular Hospital, Seoul, Korea, Republic of

Background: The double product reserve (DPR) is as indirect indicator of myoc aridal oxygen uptake and it has been known to be related to clinical outcome in patients with ischemic heart disease. However, the prognostic value of DPR in patients with idiopathic dilated cardiomyopathy (DCM) is not well known.

Purpose: We aimed to evaluate the relationship between DPR and parameters of cardiopulmonary exercise test and its prognostic value in patients with idiopathic DCM.

Methods: We measured DPR (calculated as the product of peak systolic blood pressure (SBP) and peak heart rate (HR) subtracted from the product of resting SBP and resting HR) in 142 consecutively enrolled idiopathic DCM patients (49 male, 53.3±14.5 years, mean ejection fraction 29.5±6.6%). Primary endpoint was cardiovascular (CV) events defined as all-cause mortality, cardiac transplantation or rehospitalization due to HF aggravation.

Results: DPR was well correlated with Peak VO2 (r=0.712, p<0.001) and VE/VCO2 slope (r=0.614, P<0.001). The CV events occurred in 24 patients during follow up period (median 20.3 months). When the patients with idiopathic DCM were divided by DPR according to Youden index, low DPR (<9205) was associated with poor clinical outcome (P=0.002). Multivariate Cox regression analysis revealed that DPR was an independent predictor of CV events (P=0.047) in idio-patic DCM patients when controlled for age, sex, left atrial volume index, estimated glomerular filtration rate and New York heart association functional classification.

Conclusions: DPR was well correlated with metabolic gas exchange measure-ments and was an independent prognostic marker in patients with idiopathic DCM. These findings may explain the novel relationship between myocardial oxygen uptake and clinical outcome in these patients.

P2711 | BEDSIDE
Physically active lifestyle does not protect overweight and obese subjects from developing fatal or non-fatal cardiovascular event: The 10-year (2002-12) Follow-up of Attica Study

C. Chrysohou1, D. Panagiotakos1, E. Georgioussopoulou1, C. Pitsavos1, J. Skoumas1, C. Chatzinikolaou2, N. Skourlis3, V. Metalla3, C. Stefanadis1, D. Tousoulis1. 1University of Athens, Athens, Greece; 2Harokopio University, Athens, Greece

Background: Obesity is linked to increased cardiovascular disease (CVD) risk, whereas physical activity is considered as protective against CVD development. Physical activity is also related to favorable cardio-metabolic effects, indepen-dently of the weight status of the subjects. Although, the combined effect of obe-sity status and physically active lifestyle, has rarely been studied in prospective studies. The aim of this work was to explore the link between body mass, physical activity and 10-year incidence of CVD.

Methods: The ATTICA study was carried out in the Athens area during 2001–2002 and included 3042 participants free of CVD at baseline (49.8% men, aged 18–89). Body Mass Index (BMI) of the participants was calculated after measuring their height and weight. Overweight/obesity was defined as BMI equal or greater than 25kg/m². Physical activity status was assessed using the valid-od IPQ-questionnaire. Inactive subjects were considered people with less than 2000mets/week. During 2011–2012, 2583 out of the 3042 baseline partici-pants attended the 10-year follow-up of the ATTICA study (15% lost-to-follow-up).

Results: Being overweight/obese and physically active was not proved protec-tive terms of cardiorespiratory effort and perceived exertion but the “learning effect” is ~25% improvement in steps. Measures of cardiorespiratory effort and perceived exertion showed acceptable agreement with a 6MWT.

Acknowledgement/Funding: British Heart Foundation & Wellcome Trust
Exercise training and physical activity / Decreasing cardiovascular risk in vulnerable populations

P2712 | BENCH
Aerobic exercise improves vascular insulin sensitivity by upregulating cholinergic anti-inflammatory pathway in spontaneously hypertensive rats

Z.X. Hou1, Y. Zhang1, C.J. Mi1, W.J. Xing1, L. Yang1, L. Tao2, F. Gao3 on behalf of Insulin.
1 Fourth Military Medical University, Department of Physiology, Xi’an, China, People’s Republic of
2 Xijing Hospital, The Fourth Military Medical University, Department of Cardiology, Xi’an, China, People’s Republic of
3 University, Department of Cardiology, Xi’an, China, People’s Republic of

Background: Exercise has been recommended as a part of lifestyle modifications to prevent and manage hypertension. Both experimental and clinical studies have shown that exercise improves insulin sensitivity and lowers blood pressure. However, the underlying mechanisms remain largely undefined.

Purpose: Vascular insulin resistance contributes to elevated peripheral vascular resistance and subsequent hypertension. This study was designed to explore whether chronic aerobic exercise starting during the early stage of hypertension improves vascular insulin sensitivity and the underlying mechanisms.

Methods: Young spontaneously hypertensive rats (SHRs) and their normotensive Wistar-Kyoto (WKY) control rats were subjected to an 8-wk free-of-loading swim training session (60 min/d, 5d/wk).

Results: SHRs exhibited higher systolic blood pressure, accompanied by increased systemic insulin resistance and vascular insulin resistance as evidenced by impaired vasodilator response to insulin in mesenteric arterioles compared with WKY rats. SHRs also exhibited elevated levels of inflammatory cytokines (TNF-α and IL-1β) and reduced expression of vascular acetylcholine transporter (VACHT), α7 nicotinic acetylcholine receptor (α7nAChR) and phosphorylation of janus kinase 2 (Jak2) in mesenteric arterioles. Long term exercise training resulted in significantly reduced blood pressure and alleviated systemic insulin resistance as well as vascular insulin resistance in mesenteric arterioles in SHRs. Exercise also decreased inflammatory cytokines (TNF-α and IL-1β) and increased expression of VACHT, α7nAChR and phosphorylation of Jak2 in mesenteric arterioles in SHRs. Furthermore, chronic treatment with PNU-282887 (0.5 mg/kg/d), a selective α7nAChR agonist, not only mimicked the effects of exercise in attenuating vascular insulin resistance and lowered blood pressure in SHRs but also reduced inflammatory cytokines and ROS in mesenteric arterioles of SHRs.

Conclusions: Long term exercise training starting at the early stage of hypertension alleviates hypertension through improving vascular insulin sensitivity in part via upregulating α7nAChR-mediated cholinergic anti-inflammatory pathway in SHRs.

Acknowledgement/Funding: NSFC (81270301)

P2713 | BEDSIDE
The influence of short-term exercise training on QT dispersion and double product in diabetic patients after coronary artery bypass graft surgery

V. Stoikov1, M. Deljanin Ilic1, S. Ilic1, M. Stoikov2, D. Petrovic3, S. Saric1, S. Andronov2, J. Cvetkovic2, V. Mitic2, D. Vujicic2, University of Novi, Medical Faculty, Institute of Cardiology, Niska Banja, Serbia
Introduction: Coronary patients with diabetes are at high risk of cardiovascular and arrhythmic events. QT dispersion (QTd) is a measure of inhomogeneous repolarization of the myocardium and is used as an indicator of arrhythmogenicity. Abnormally high QTd has been correlated with risk of cardiac death in coronary patients.

Purpose: The aim of this study was to establish the influence of short-term exercise training on QT dispersion and double product (DP) in diabetic patients after coronary artery bypass graft surgery (CABG).

Methods: The study involved 165 patients after CABG, in the sinus rhythm without significant atrioventricular block. Average age of patients was 56.8 ± 12.1 years. Fifty-two patients were with diabetes mellitus, and 113 were without diabetes. In all subjects clinical examination, standard ECG and exercise test on treadmill according to Bruce protocol, were performed and after that patients were included in program of physical training for three weeks. Patients were instructed to follow a training program using the bicycle ergometer (10 min, 2 times a day) and walking. The patients continued to take the same medications in same doses. From standard ECG corrected QT dispersion (QTc) was calculated.

Results: Before starting with the program of physical training, patients with diabetes had significantly higher values of QTc (56.2±14.9 vs 47.0±17.1 ms; p < 0.005), and significantly lower values of DP (11878.4±784.7 vs 11248.8±629.9 beat/min x mmHg; p<0.005 in patients with diabetes). After three weeks, significant reduction of QTc was found (from 56.2±14.9 to 47.7 ±13.8 ms; p < 0.025 in patients with diabetes and from 47.0±17.1 to 41.0±15.9 ms; p < 0.001 in patients without diabetes). After three weeks, significant reduction of DP was found (from 11878.4±784.7 to 11248.8±629.9 beat/min x mmHg; p<0.005 in patients with diabetes and from 11515.4±837.7 to 11020.9±535.7 beat/min x mmHg; p<0.001 in patients without diabetes). In diabetic patients, after program of physical training, significant reduction of glycemia was found (from 8.3±2.4 to 7.1±1.6 mmol/L; p<0.005).

Conclusions: The study showed that patients with diabetes had a higher value of QTc, probably due to diffuse interstitial fibrosis. Short-term exercise training has a favourable effects on QT dispersion and double product in patients after CABG. In patients without diabetes physical training had more favourable effects on the followed parameters. Physical training led to the significant decrease of myocardial oxygen uptake at rest and probably decreased the possibility of arrhythmic events.

DECREASING CARDIOVASCULAR RISK IN VULNERABLE POPULATIONS

P2714 | BEDSIDE
The association of statin adherence and in-stent restenosis

C. Cocos1, O. Abaci2, B.B. Kocas1, G. Cetinkil1, S. Arslan1, A. Yildiz1, M. Ersanli
1 Cardiology Institute of Istanbul University, Istanbul, Turkey
2 Xijing Hospital, The Fourth Military Medical University, Department of Cardiology, Xi’an, China, People’s Republic of

Background: Half of patients discontinue statin therapy within the first year, and adherence decreases during follow-up period. However data about the effects of statin treatment on stent restenosis is confusing and no studies have described the relationship between statin adherence and in-stent restenosis (ISR).

Purpose: In our study, therefore we investigated the statin adherence and ISR among percutaneous coronary intervention patients (PCI) who were prescribed a statin at discharge.

Methods: We retrospectively analyzed 908 patients whom underwent bare-metal stent implantation and have been performed control coronary angiography (CA) also have continuous insurance coverage between PCI and CA to determine statin adherence. We used the pharmacy-based proportion of days supplied (PDS) to quantify statin adherence during the period between PCI and control CA.

Results: Percentage of patients adherent to statin according to prescription records (≥80% PDC for statins), was 26% in the ISR (+) group and 33% in the ISR (-) group (P<0.03). In multivariate logistic regression analysis, statin adherence was an independent predictor of ISR [OR=2.04, CI (1.01–4.13), p<0.04].

Conclusions: The principal findings of our study were (1) statin non-adherence 1 year after PCI was higher compared with other studies and (2) statin non-adherence in patients with PCI was associated with increased ISR.

P2715 | BEDSIDE
A community pharmacy-based cardiovascular risk screening service implemented in a resource-limited country

Z. Jahangard-Rafsanjani1, N. Hakimzadeh1, K.H. Gholsari2, A. Sarayani1,2, A.G. Hemmati1,2
1 University of Medical Sciences, Tehran, Iran (Islamic Republic of)
2 Tehran University of Medical Sciences, Tehran, Iran (Islamic Republic of)

Background: Effective cardiovascular risk screening is one of the strategies to reduce the burden of cardiovascular diseases (CVD). The role of community pharmacies in such screening services needs further investigation particularly in resource-limited countries.

Purpose: To assess the feasibility and effect of a pharmacy-based cardiovascular screening in an urban referral community pharmacy in Iran.

Methods: In a cross sectional study, 287 clients aged between 30–75 years without previously diagnosed CVD, diabetes or recent health check-up for blood glucose and lipid profile were screened. The screening service was free of charge and was advertised by means of posters inside and at the entry point of the pharmacy. Measurement of all major cardiovascular risk factors (BP, lipid profile, blood glucose), exercise habits, existing medical conditions and medications, family history, was performed by the investigator (student pharmacist). Framingham risk score was calculated and high risk individuals were given a clinical summary sheet signed by the investigator and were encouraged to follow up with their family physician. Each client was contacted one month after recruitment and their adherence to the follow up recommendation were documented.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475 by guest on 07 February 2019
Liraglutide is more effective than lifestyle changes in modulating subcutaneous and visceral fat distribution, liver steatosis, insulin sensitivity and beta-cell function after comparable weight loss.

Background: Obesity, insulin resistance and beta cell deterioration are key issues in the development and progression of type 2 diabetes (T2DM) and its vascular complications.

Methods: Twenty-six metformin-treated obese subjects with impaired glucose tolerance (IGT), impaired fasting glucose (IFG) or newly diagnosed T2DM, were included. From July 2010 to May 2013, 3145 consecutive (mean age 65.9 years, 52% male) patients at high cardiovascular risk in Brazil (8% smoker, 13% family history of coronary artery disease) were included in this study. Patients who received the follow up recommendation had made an appointment with their physician. Moreover, 7.5% were under work-up by the physician. Of the 438 subjects with mean age 58.0±8.34 years, 47% were male. Results are shown in Table 1, presented as mean changes from IA to EOP. A Chi2 test examined the association between stratified CRF and depression; the odds ratio (OR) or 95% confidence interval (CI) were calculated. A retrospective analysis of the relationship between cardio-respiratory fitness (CRF) and depression in high risk individuals who attend a preventive cardiology programme (P2718) was evaluated.

Results: The screening program in community pharmacy has the potential to identify clients who might have elevated cardiovascular risk factors. However, the cost of such services might be a barrier to their widespread utilization. A plan to increase the adherence of clients to follow up recommendations is required.

Acknowledgement/Funding: Brazilian society of Cardiology

P2717 | BEDSIDE
Liraglutide may provide better weight loss compared to lifestyle changes: results of a randomized placebo-controlled trial

Results: Data from 287 participants were analyzed: 200 (69.7%) male; 52 (18%) smoker, 134 (47%) had a family history of CVD, 187 (65%) had diabetes (mean 10.1 ± 2.2 mmol/L) and remained unchanged during follow-up (29.2% at baseline, 28.4% at 6 months, and 27.8% at 12 months; p < 0.05). About 50% of diabetic patients had glycated hemoglobin levels below 7%, 55.9% of the hypertensive patients had blood pressure below the guideline-recommended targets (140/90 mmHg), and 41% of the overall population remained with LDL above 100mg/dL. During a 12 month follow-period, 232 patients (7.4%) suffered a MACE (combined endpoint of all-cause mortality, nonfatal myocardial infarction, stroke, or nonfatal cardiac arrest). Multivariate logistic regression analysis showed that the main independent predictor of MACE was statin use for at least 6 months (odds ratio [OR] 0.48, 95% confidence interval [CI] 0.36–0.63).

Conclusions: There are important gaps in adherence of evidence-based therapies for patients at high cardiovascular risk in Brazil. Statin use was independently associated with a risk reduction of combined MACE, regardless presence of previous cardiovascular events.

Acknowledgement/Funding: Tehran University of Medical Sciences

P2718 | BEDSIDE
A retrospective analysis of the relationship between cardio-respiratory fitness (CRF) and depression in high risk individuals who attend a preventive cardiology programme

Background: Targeted reduction of multi-factorial CVD risk factors underpins preventive cardiology. Low CRF and depression are two established risk factors for CVD. Reduction of depression is a known benefit of exercise and regular exercise results in improved CRF; however, few studies have investigated the relationship between CRF and depression.

Purpose: A retrospective cohort analysis investigating the relationship between CRF and depression in high risk individuals who attend a preventive cardiology programme.

Methods: Data of collected during a 12–16 week programme incorporating weekly exercise sessions and educational workshops. All patients had initial (IA) and end of programme assessments (EOP) including calculation of Maximal Exercise Capacity (METmax) establishing CRF and Hospital Anxiety and Depression Sub-Scale (HADS-D) measuring depression.

Results: Of the 438 subjects with mean age 58.0±8.34 years, 47% were male. Results are shown in Table 1, presented as mean changes from IA to EOP. A Chi2 test examined the association between stratified CRF and depression; the odds ratio (OR) or 95% confidence interval (CI) were calculated. A retrospective analysis of the relationship between cardio-respiratory fitness (CRF) and depression in high risk individuals who attend a preventive cardiology programme (P2718) was evaluated.

Conclusion: Small negative correlations between METmax and HADS-D were demonstrated at IA and EOP, indicating as CRF increases, depression decreases. However, this association was not evident when investigating a change over time. Potentially, due to relatively low prevalence of depression at baseline and change in METmax or HADS-D at EOP (p < 0.05), however, no significant correlation was found between change of METmax and HADS-D at EOP (p < 0.0587, p = 0.2796).

Table 1. Mean changes from IA to EOP

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean change from IA to EOP (SE)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in METmax</td>
<td>1.63 (0.07)</td>
<td>1.49, 1.77</td>
</tr>
<tr>
<td>Mean changes in HADS depression score</td>
<td>−1.56 (0.10)</td>
<td>−1.89, −1.29</td>
</tr>
<tr>
<td>Mean change in HADS anxiety score</td>
<td>−1.15 (0.14)</td>
<td>−1.43, −0.86</td>
</tr>
<tr>
<td>Mean change in METmax</td>
<td>−0.98 (0.23)</td>
<td>−3.39, −2.47</td>
</tr>
<tr>
<td>Mean change in EQ-VAS</td>
<td>11.22 (1.17)</td>
<td>8.91, 13.52</td>
</tr>
<tr>
<td>Mean change in BMI</td>
<td>−1.03 (0.07)</td>
<td>−1.45, −1.15</td>
</tr>
</tbody>
</table>

Conclusion: Small negative correlations between METmax and HADS-D were demonstrated at IA and EOP, indicating as CRF increases, depression decreases. However, this association was not evident when investigating a change over time. Potentially, due to relatively low prevalence of depression at baseline and change in METmax or HADS-D at EOP (p < 0.05) was not great enough to show significant correlations. Analysis over a longer time period is recommended to investigate this association further.
viation of nuclear factor-kappa B in myocardium. Although eicosapentaenoic acid (EPA) reduces oxidative stress, it is unclear whether EPA inhibits the AGEs production and prevents the progress of LVH. This study aimed to investigate the effect of long-term EPA administration on LVH in HT patients.

**Methods:** We recruited 65 HT patients whose resting blood pressure was controlled at 140/90 mmHg. In crossover method, all patients were administered 1,800 mg of EPA ethyl-ester daily and antihypertensives for 10 months in the EPA(+) group and only antihypertensives for 10 months in the EPA(−) group. We measured serum concentrations of EPA and arachidonic acid (AA). Serum malondialdehyde-modified LDL-cholesterol (MDA-LDL) and plasma pentosidine were measured as parameters of oxidative stress and AGEs, respectively. Left ventricular mass index (LVMI) was assessed as a parameter of LVH. All parameters were measured before and after the observation period and compared between the two groups. We calculated the changes in pentosidine and LVMI from baselines to those measured after the observation period (Δpentosidine and ΔLVMI).

**Results:** EPA and EPA/AA ratio were significantly higher in the EPA(+) group than in the EPA(−) group (P < 0.01, respectively). MDA-LDL, pentosidine and LVMI were significantly lower in the EPA(+) group than in the EPA(−) group (P < 0.05, respectively). Pentosidine was positively correlated with ΔLVMI (n=0.31, P=0.05).

**Conclusion:** Long-term administration of EPA prevented the progress of LVH via reducing oxidative stress and AGEs in HT patients.

**P2720 | BEDSIDE**

Effects of exercise-based cardiac rehabilitation on HDL function in patients with coronary artery diseases, independently of lipid-lowering medication

**Background:** It remains unclear how exercise-based cardiac rehabilitation (CR) affect HDL function and HDL subtraction in addition of lipid-lowering medication (LLM).

**Methods:** Apolipoproteins and cholesterol in HDL2 and HDL3 separated by heparin-Mn precipitation method and cholesterol efflux capacity (CEC) using a cell-based system were measured at the baseline and at the end of the 6-month CR program in 48 patients with coronary artery diseases, aged of 68. Twenty-seven male and 7 female patients were started with LLM or were treated with increased doses of LLM, while the others were treated with the same doses of placebo during the follow-up period.

**Results:** (Table) HDL-cholesterol, apolipoprotein A1, HDL2-cholesterol, and HDL2-apolipoprotein A1 significantly increased, irrespective of the modification of LLM. Increases of CEC were significantly associated with increases in HDL-cholesterol, Apolipoprotein A1, HDL2-cholesterol, and HDL2-apolipoprotein A1.

**Conclusion:** CR can improve the reverse cholesterol transport, independent of LLM, resulting in the secondary prevention.
P2724 | BEDSIDE
Adherence to Mediterranean diet reduces the risk for 10-year type 2 diabetes development. The role of TNF-a and homocystein as possible mediators

D.B. Panagiotakos1, E. Kolovereu2, C. Pitsavos3, C. Chrysohou2, E. Georgoupiopoulou1, N. Skourli1, I. Skoumas1, D. Tousoulis2, C. Stefanidis3 on behalf of AtTomo MDS.1 1Harokopio University, Athens, Greece; 2Hippokration Hospital, University of Athens, Athens, Greece

Background and introduction: beyond its cardioprotective effects, Mediterranean diet (MD) has been reported to have a potential for anti-diabetic protection.

Purpose: To investigate the effect of long term adherence to MD on ten-year diabetes incidence, and examine inflammatory and oxidative stress biomarkers as candidate mediators of this relationship.

Methods: At baseline (2001–2), a random sample of 1514 men and 1258 women (<18 years) without any clinical evidence of cardiovascular disease, were enrolled in the study. Several socio-demographic, clinical, biochemical and other variables were studied in relation to diabetes development (i.e., fasting blood glucose > 125 mg/dl or the use of anti-diabetic medication, WHO, ICD-10 criteria). In 2011–2012 the ten-year review. Adherence to MD was evaluated using MediDietScore (range 0–55) and score tertiles (low, moderate and high adherence to the diet) were calculated. Between 2011–2012 the ten-year follow up was performed.

Results: 191 new diabetes cases were recorded. The ten-year incidence of diabetes was calculated 13.4% and 12.4% in men and women respectively. Moderate and high adherence to MD were found to reduce the risk of diabetes by 49% (95% CI: 0.30, 0.88) and 62% (95% CI: 0.16, 0.88) respectively, compared with low adherence. Trend analysis revealed a logarithmic relationship (p=0.042). Men with waist circumference <94 cm and women <80 cm were found to benefit the most. Whole grains, fruits and had the greatest predictive ability. When markers of inflammation and oxidative stress were taken into consideration, the anti-diabetic effect of MD was found to be partially explained by TNF-a and homocystein levels.

Conclusion(s): the present study demonstrates the beneficial role of adherence to MD in diabetes primary prevention. Anti-inflammatory components of MD may be responsible to some extent for this protection, which extends MD’s therapeutic role in diabetes primary prevention. Anti-inflammatory components of MD may be responsible to some extent for this protection, which extends MD’s therapeutic role in diabetes primary prevention.

Acknowledgement/Funding: The study was funded by an Independent Investigator Grant from Pfizer Pharmaceuticals to Imperial College London.
and the incidence of MACE which was defined as all cause mortality, repeated MI, revascularization as well as doing Cox regression analysis.

**Results:** Baseline characteristics were similar between four groups. At one year follow up, MACE in the BMS, 1st generation DES, 2nd generation plus new generation DES, and biodegradable DES groups were 12.3%, 8.1%, 5.3% and 3.9%, respectively (p=0.0001). There were 104 cases of stent thrombosis of all cohorts, and the incidence of stent thrombosis was the lowest in the biodegradable DES group among the 4 groups (2.5%, 2.0%, 1.4%, 0.7%, p=0.007). After the adjustment of age, male gender, SETMI, LV EF, stent number and length, stent type was significant predictor for one year MACE (Odds ratio of 1st, 2nd new generation biodegradable polymer coated stent group compared to BMS group: 0.62, 0.37, 0.27, respectively, p<0.05 for all).

**Conclusion:** Biodegradable polymer coated stent was the most efficacious and safest stent in acute MI at one year follow up.

---

**P2727 | BEDSIDE**

Comparative outcomes of zotarolimus-eluting stents in British Columbia: a real world analysis of 17,747 patients using propensity score and instrumental variable methods

M.B. Iqbal1, I.J. Nadra1, J.N. Din1, C. Hendry1, A. Fung2, E. Aymong3, A.W. Chan4, S. Hodget1, S.D. Robinson1, A. Della Siega1, Victoria Heart Institute, Victoria, Canada;4 Vancouver General Hospital, Vancouver, Canada;3 Royal Columbian Hospital, Vancouver, Canada;2 St Paul’s Hospital, Vancouver, Canada;5 Kelowna General Hospital, Kelowna, Canada

**Background:** Resolute zotarolimus-eluting stents (R-ZES) utilize the same platform and anti-restenotic drug as the Endeavor zotarolimus-eluting stents (E-ZES), but a more biocompatible polymer provides better drug-release kinetics. There are limited data on the long-term comparative efficacy of R-ZES and the preceding E-ZES.

**Methods:** We analyzed all patients who received either E-ZES or R-ZES between 2008-2013 in the British Columbia Cardiac Registry (n=17,746). We analyzed mortality and target vessel revascularization (TVR) at 2 years. Cox multivariate models were used to determine predictors for outcomes. To address bias due to measured and unmeasured confounders, propensity-matched analyses and instrumental variable (IV) analyses were performed.

**Results:** A total of 9,918 patients (56%) received E-ZES and 7,828 patients (44%) received R-ZES. Compared to E-ZES, R-ZES was associated with lower 2-year mortality (4.1% vs. 6.4%, p<0.001) and 2-year TVR (6.8% vs. 10.7%). R-ZES was an independent predictor for survival (HR=0.73, 95% CI: 0.61-0.87, p<0.001) and lower TVR (HR=0.88, 95% CI: 0.78-0.98, p=0.022). This was confirmed in propensity-matched cohorts (n=10,416) and R-ZES was predictive of survival (HR=0.89, 95% CI: 0.84-0.97, p<0.001) and lower TVR (HR=0.86, 95% CI: 0.75-0.98, p=0.032). Using enrollment year as an IV, IV analyses demonstrated R-ZES to be associated with reduced 2-year mortality (abs diff=3.7%, 95% CI: -4.7—-2.7, p<0.001) and reduced 2-year TVR (abs diff=5.0%, 95% CI: -7.5—-2.5, p<0.001).

**Conclusions:** In this large analysis of patients receiving ZES, R-ZES was associated with lower long-term mortality and TVR, even when adjusting for measured and unmeasured confounding. These real-world data are reassuring and demonstrate the better safety and anti-restenotic profile of R-ZES.

---

**P2728 | BEDSIDE**

Quantification and management of thrombus burden during primary PCI: limitations of angiography demonstrated with optical coherence tomography imaging


**Background:** Up to now, thrombus aspiration (TA) during primary PCI is customarily performed under angiographic guidance both in clinical practice and clinical trials. However, optical coherence tomography (OCT) constitutes the current reference standard for the assessment of coronary thrombus. Existing evidence suggests that optimising thrombus reduction might improve PCI outcomes.

**Purpose:** Use of OCT to assess the ability of angiography 1) to quantify thrombus burden during primary PCI, 2) to identify remnant thrombus deserving repeat thrombus aspiration (re-TA), and 3) to appreciate modifications in thrombus burden driven by re-TA.

**Methods:** In a series of acute STEMI patients OCT was used to assess the pathological substrate and guide aspiration to reduce thrombus burden during primary PCI. Thrombus burden was quantified by angiography using TIMI Thrombus Grade score (TTG) and by OCT using a quadrant count at each 0.4mm interval (Kajender et al. EHJ 2014). These methods were compared to each other at baseline assessment and after aspiration (re-TA, balloon dilation). Data is expressed as median [interquartile range].

**Results:** A total of 55 consecutive acute STEMI patients were included. Baseline OCT was defined as that performed either after a first thrombus aspiration to achieve reperfusion (n=45, 82%) or, if flow was adequate, prior to any interventional therapy (n=10, 18%). The relationship between angiographic and baseline OCT-based thrombus burden was poor (Kendall’s τ=0.23, p=0.03): by angiography median TTG was 1 [0–3], and OCT revealed 29 [8–42] thrombotic quadrants. Based on the presence of significant remnant thrombus in OCT [32 [20–42] quadrants] by the operator, repeat TA (re-TA) was performed in 26 patients. Although the remaining patients presented significantly lower thrombus burden by OCT (15 [5–42] p=0.048), angiography could not differentiate between both groups in terms of thrombus burden (TTG 1.5 [0–3] in re-TA and 1 [0–2] in non-re-TA groups, p=NS). OCT-guided re-TA led to a significant reduction in thrombus burden (from 31.5 to 23.5 quadrants, p<0.01). Again, angiography could not detect the reduction in thrombus burden associated with re-TA (from 1 to 1 TTG, p=NS).

**Conclusions:** Use of OCT during primary PCI demonstrates that angiography constitutes a suboptimal tool 1) to quantify remnant thrombus burden, 2) to select patients that might benefit from further actions aimed at thrombus reduction such as re-TA, and 3) to estimate the effect of such actions on thrombus burden.

---

**P2729 | BEDSIDE**

Single string technique for complex coronary bifurcation stenting

G.G. Toth1, S. Pyxaras2, P. Mortier3, G. Di Gioia4, J. Adledj5, M. Pellicano5, E. Barbato1, B. De Bruyne5, M. De Beule3, W. Wijns5,1 Medical University of Graz, University Heart Centre Graz, Graz, Austria;2 Klinikum Coburg, II Medizinische Klinik, Coburg, Germany;3 Efope bvba, Gent, Belgium;4 Federico II University of Naples, Division of Cardiology; Department of Advanced Biomedical Sciences, Naples, Italy;5 OLV Hospital Aalst, Cardiovascular Center, Aalst, Belgium

**Aims:** Double-stent techniques may be required for complex bifurcation lesions. Currently available methods all have their morphologic or structural limitations. The study aims to evaluate the adequacy and feasibility of Single String bifurcation stenting technique.

**Methods:** Single String is a novel stenting technique for complex bifurcation lesions, where first the side branch (SB) stent is deployed with one single proximal stent-cell protruding into the main branch (MB). Second, the MB is rewired through that protruding stent-cell and a stent is deployed into the MB across it. Procedure is completed by final kissing balloon dilation. Single String was tested in vitro (n=20) and next applied in patients (n=11) with complex bifurcation stenoses.

**Results:** All in vitro procedures were performed successfully, crossing the most proximal stent-cell in 100%. Duration of the procedure was 23.0±7.9 minutes, fluoroscopy time was 9.4±3.5 minutes. Result was evaluated by OCT, showing fully apposed struts in 83.0±9.2%. Residual area obstruction in the MB was 6.4±5.6%.
and 25.0±16.9% in the SB by micro computed tomography. In vitro data suggest that Single String technique can be performed with most of the current stent platforms having an open cell design.

All the human cases were performed successfully with excellent angiographic result: residual area stenosis was 27±8% and 29±10%, respectively by 3-dimensional QCA. No relevant peri-procedural enzyme rise was observed. During follow-up (14±5 months) no adverse clinical event (death, MI, TVR) was noted.

Conclusion: Single String technique for complex bifurcation lesions is shown to be adequate in vitro and feasible in humans with favorable results in terms of stent overlap, malapposition rate and low residual obstruction in both MB and SB.

P2730 | BEDSIDE
Evaluation of vascular healing of polymer-free sirolimus-eluting stents on native coronary vessels: a serial follow-up of 3- and 6-month optical coherence tomography imaging study

P. Suwannasorn¹, E. Benit², O. Gach³, C. Von Birgelen⁴, S. Hofma⁵, B. Xu⁶, Y. Onuma⁷, H. Garcia-Garcia¹, R. Gao⁸, P.W. Serruys⁹ on behalf of NANO Plus Investigator. ¹Erasmus Medical Center, Interventional Cardiology, Rotterdam, Netherlands; ²Heart Centre Hasselt, Hasselt, Belgium; ³University Hospital of Liege (CHU), Liege, Belgium; ⁴Thoraxcentrum Twente, Enschede, Netherlands; ⁵Medical Center Leeuwarden, Leeuwarden, Netherlands; ⁶National Center for Cardiovascular Diseases, Beijing, China, People’s Republic of; ⁷Imperial College London, London, United Kingdom

Background: Newly developed drug eluting stents (DES) aim at promoting early endothelialization and preventing stent thrombosis. We sought to evaluate the extent of neointima growth by optical coherence tomography (OCT) 3 months and 6 months after implantation of a polymer-free stent with nano size pores surface sirolimus eluting.

Methods: In this prospective, multicentre, open-label study, patients were enrolled with documented stable angina or silent ischemia and planned intervention up to 2 de novo coronary lesions (in different vessels), with lesion length of ≤18 mm. The OCT examination were performed at 3 months to evaluate neointimal coverage and healing index. In cases which any frame has >30% ratio of uncovered stent struts per section (RUTTS), the follow-up OCT were scheduled at 6 months to re-evaluate neointimal coverage and healing index. The primary OCT endpoint is the percentage of in-stent neointimal volume obstruction at 3 months. The secondary endpoints include binary restenosis, stent thrombosis and device-oriented composite endpoints: a composite of cardiac death, myocardial infarction (MI) non-attributable to non-target vessel, clinically-indicated target lesion revascularization at 3 months.

Results: A total of 45 patients with 47 lesions were enrolled from 4 European centres. Eventually, 43 patients with 45 lesions underwent OCT examination at 3 months (1 case was excluded for poor image quality and 1 case due to catheter dysfunction). At 3 months, the mean angiographic in-stent late lumen loss was 0.17±0.27 mm. The median and interquartile range of in-stent neointimal volume obstruction was 8.5% (4.7–10.7), strut coverage was 93.0% (83.2–96.5) and incomplete apposed struts was 0% (0.0–0.9), respectively. At 3 months, the mean angiographic in-stent late lumen loss was 0.17±0.27 mm. No case of stent thrombosis, cardiac death and clinically-indicated target lesion revascularisation were reported at 3 months. Of 45 patients who underwent OCT examination at 3 months, 25 patients who had any frames >30% RUTTS have been scheduled OCT examination at 6 months. The complete 6 months OCT result and clinical outcomes are being collected and will be presented at the time of meeting.

Conclusion: Polymer-free sirolimus-eluting stents are effective in inhibiting neointimal tissue proliferation and promoting early vascular healing with high strut coverage at 3 months follow-up.

Acknowledgement/Funding: Lepu Medical Technology (Beijing) Co., Ltd

P2731 | BEDSIDE
The paradigm shift of peri-contrast staining (PSS) in first generation DES era to second generation DES era

T. Tokuda, T. Muramatsu, R. Tsukahara, Y. Ito, H. Ishimori, K. Hirano, M. Nakano, M. Yamawaki, M. Araki, Saiseikai Yokohama City Eastern Hospital, Yokohama, Japan

Background: Several studies showed peri-contrast staining (PSS) after metallic DES deployment is associated with target-lesion revascularization (TLR) and very late stent thrombosis. However, the changes of PSS after first generation DES to second generation DES are unclear, so we retrospectively compare the clinical outcomes.

Methods: This study consisted of de novo 4395 lesions in 3482 patients that were treated with first generation DES or second generation DES. They were evaluated by follow-up angiography within 12 months after stent implantation, from April 2007 to January 2014. We divided into PSS of first generation DES group and PSS of second generation DES group and compared the two groups in clinical and angiographic outcomes. Also, in sub analysis, we investigated which PSS type influenced the clinical outcomes after stent implantation.

Results: We had obtained 3749 lesions follow-up angiography. (85.3%) Total late acquired PSS was observed in 235 lesions (6.2%). Based on clinical and angiographic characteristics were similar between the two groups. (N.S.) The rate of PSS was higher in first generation DES group. (3.2% vs 0.9%, p<0.0001) Smooth-contour PSS was highest of first generation DES group and mono-focal

P2733 | BEDSIDE
The paradigm shift of peri-contrast staining (PSS) in first generation DES era to second generation DES era

T. Tokuda, T. Muramatsu, R. Tsukahara, Y. Ito, H. Ishimori, K. Hirano, M. Nakano, M. Yamawaki, M. Araki, Saiseikai Yokohama City Eastern Hospital, Yokohama, Japan

Background: Several studies showed peri-contrast staining (PSS) after metallic DES deployment is associated with target-lesion revascularization (TLR) and very late stent thrombosis. However, the changes of PSS after first generation DES to second generation DES are unclear, so we retrospectively compare the clinical outcomes.

Methods: This study consisted of de novo 4395 lesions in 3482 patients that were treated with first generation DES or second generation DES. They were evaluated by follow-up angiography within 12 months after stent implantation, from April 2007 to January 2014. We divided into PSS of first generation DES group and PSS of second generation DES group and compared the two groups in clinical and angiographic outcomes. Also, in sub analysis, we investigated which PSS type influenced the clinical outcomes after stent implantation.

Results: We had obtained 3749 lesions follow-up angiography. (85.3%) Total late acquired PSS was observed in 235 lesions (6.2%). Based on clinical and angiographic characteristics were similar between the two groups. (N.S.) The rate of PSS was higher in first generation DES group. (3.2% vs 0.9%, p<0.0001) Smooth-contour PSS was highest of first generation DES group and mono-focal
P2734 | BEDSIDE
Long-term outcomes in NANOM-FIM trial: 5-year analysis
A. Khartalov,1 J. Gabinsky2 on behalf of NANOM-FIM. 1De Haar Research Foundation, Department of Science, Rotterdam, Netherlands; 2Ural Institute of Cardiology, Yekaterinburg, Russian Federation

Introduction: Our previous bench studies PLASMONICS and NANOM First-in-Man (FIM) trial documented Total Atheroma Volume (TAV) reduction up to unprecedented 79.4 and 60.3 mm³ respectively. But the safety options in nanomedicine raise an issue of the optimal niche of these technologies at the real-world clinical practice.

Methods: This is a retrospective analysis of the 5-year long-term clinical outcomes at the intention-to-treat population (n=180) of NANOM-FIM trial (NCT01270139). The primary outcome was a composite of end-point of MACE-free survival, MACE, cardiac death, TLR (Target Lesion Revascularization) and TVR (Target Vessel Revascularization).

Results: Mortality (6 vs 9 vs 10 cases of cardiac death in groups respectively, p<0.05), MACE (14.3% of nano group vs 22.9% in stenting control, p<0.04), late thrombosis (2 vs 5 vs 6 cases in groups respectively, p<0.05) and TLR (3.8 vs 5.7% in nano and stent group respectively, p<0.04) were significantly higher in ferro group and stent control at 60-month follow-up, but the difference in the proportion of MACE-free survival and TVR incidence when compared between groups did not reach statistical significance (p=0.33) [check out patient flow (left) and QCA (right) in fig. 1–2]. Diabetes (p<0.03), hypertension (p<0.05), previous or simultaneous PCI (p<0.048) and heart failure (p<0.04) were confirmed as strong independent predictors of cardiac death with high rate of mortality and late thrombosis in patients underwent stenting.

Conclusion: NANOM-FIM trial demonstrates high safety of the selected nanotechnologies with better rate of mortality, MACE and TLR at the long-term follow-up if compare with conventional implantation of the second generation stent XIENCE V.

P2735 | BEDSIDE
Evaluation of efficacy and safety of biolimus A9™-eluting stent in patients with acute coronary syndrome; a multicenter, observational study (BEAUTY study)
K.-H. Park, M.-H. Jeong, Y.-J. Hong, Y.-K. Ahn on behalf of BEAUTY study investigators. The Heart Center of Chonnam National University Hospital, Gwangju, Korea, Republic of

Background: This study sought to determine the 1-year clinical efficacy and safety of a biodegradable polymer containing Biolimus A9™-eluting stent in Korean patients with acute coronary syndrome (ACS).

Methods: A total of 1,000 ACS patients with 1,264 lesions who underwent implantation of BES stents conducted at 22 center in Korea were enrolled between May 2011 and July 2013. We analyzed the incidence of major adverse cardiac events (MACE) defined as the composite of cardiac death, non-fatal myocardial infarction (MI) and clinical-driven target vessel revascularization at 12 months.

Results: The mean age was 62.6±11.43 years, 72.8% of patients were males, 28.5% had diabetes 32.8% had multi-vessel disease and 47.9% presented with acute MI. The number of stents per patient was 1.3±0.60. The incidences of MACE and definite stent thrombosis at 12 months were 4.1% and 0.2% respectively. On multivariate cox regression analysis, age and current smoker were independent predictors for TVR (Target Vessel Revascularization) and MACE (14.3% of nano group vs 22.9% in stenting control, p=0.04), but was an independent predictor for increased TVR at 3 years (HR=1.21, 95% CI: 1.08–1.35, p=0.001). These findings were confirmed in propensity-matched cohorts (n=18,135) where FDES was not associated with mortality at 3 years (HR=1.19, 95% CI: 0.88–1.14, p=0.975), but was an independent predictor for increased TVR at 3 years (HR=1.21, 95% CI: 1.08–1.35, p=0.001). Cox regression analysis demonstrated that FDES was not associated with mortality at 3 years (HR=1.05, 95% CI: 0.93–1.19, p=0.415), but predicted increased TVR at 3 years (HR=1.18, 95% CI: 1.02–1.28, p<0.001). Subgroup analyses in both unmatched and propensity matched cohorts demonstrated that FDES use was not a predictor of mortality in selected patient groups. Similarly, FDES use was not a predictor for TVR in patients with age >80 years, diabetes, renal disease, ACS or stent length >30mm, but did predict TVR where stent diameter <3mm.

Conclusions: In this real-world study of unselected patients receiving DES, the use of S-DES did not confer a mortality benefit over F-DES, indicating comparable long-term safety profiles. However, S-DES use was associated with a significant reduction in long-term TVR. These data are reassuring for the newer generation DES across a broad clinical population.
P2737 | BEDSIDE
Simple versus complex drug-eluting stenting for coronary bifurcation lesions: an updated meta-analysis of randomized controlled trials

Background: Percutaneous coronary intervention (PCI) on coronary bifurcation lesions has been considered a challenging procedure for interventionists. However, the optimal stenting strategy for bifurcation lesions is still unclear in the era of drug-eluting stents (DES).

Methods: Randomized controlled trials (RCTs) were identified through search of MEDLINE, EMBASE, and the Cochrane databases (2004 through January 2015). Outcomes assessed were mortality, myocardial infarction (MI), target vessel revascularization (TVR), definite stent thrombosis, and angiographic restenosis at the longest follow-up.

Results: A total of ten RCTs including 2,941 patients were included in this meta-analysis. No statistically significant difference in the risk of death (odds ratio [OR] 0.86, 95% confidence interval [CI] 0.41–1.84, p=0.70) was detected between simple versus complex stenting groups. Simple stenting strategy was associated with significantly lower incidence of recurrent MI (OR 0.60, 95% CI 0.39–0.90, p=0.01) with a trend toward lower definite stent thrombosis (OR 0.50, 95% CI 0.23–1.07, p=0.07). On the other hand, simple stenting strategy significantly increased risk of TVR (OR 1.47, 95% CI 1.06–2.04, p=0.02) and side branch restenosis (OR 1.80, 95% CI 1.33–2.43, p<0.001) as compared with complex stenting strategy. The cumulative analysis of the included studies depicts the summary ORs of recently published studies favoring complex stenting in terms of angiographic restenosis (Figure).

Conclusions: Simple stenting strategy was associated with reduced incidence of MI and stent thrombosis as compared with complex stenting strategy. However, benefits of simple stenting were offset by increased risk of angiographic restenosis and TVR. Both stenting strategies were comparable in terms of mortality.

P2738 | BEDSIDE
Is correlation of incidence of stent fracture after drug-eluting stent implantation with strut thickness different between de novo and in-stent restenosis lesions?

Background: Stent fracture (SF) after drug-eluting stent (DES) implantation is a frequent technical complication. The purpose of the present study was to investigate SF occurrence and its correlation with strut thickness as an independent predictor of SF occurrence.

Methods: We prospectively evaluated 206 consecutive CTO interventions performed in 214 patients from January 2012 to January 2015. Outcomes assessed were complete revascularization, and certain complications. Streeter classification was used for CTO classification. SF was defined as separation of stent segments. The incidence of SF was 3.7% (512/13,669) of the lesions: de novo, 3.5% (512/14,680) vs 20% (J-CTO 2), 89 vs 17% (J-CTO 3) respectively (p<0.001). The incidence of SF was 3.7% (512/13,669) of the lesions: de novo, 3.5% (512/14,680) vs 20% (J-CTO 2), 89 vs 17% (J-CTO 3) respectively (p<0.001).

Results: The incidence of SF was 3.7% (512/13,669) of the lesions: de novo, 3.5% (415/12,006) vs ISR, 5.8% (97/1,663), and that of each DES type were as follows: Cypher Bx, 5.9% vs 5.3%; Cypher select, 3.3% vs 11.1%; Taxus Express, 3.5% vs 7.3%; Taxus Libert, 2.3% vs 0%; Endeavor, 1.7% vs 8.3%; Resolute Integrity, 0.5% vs 5.6%; Xience V, 1.7% vs 4.8%; Xience Prime/Xpedition, 0.3% vs 1.4%; Nobori, 3.8% vs 2.4%; and Promus element, 0.9% vs 6.2%. There was a strong and significant correlation between the incidence of SF and strut thickness of each DES type in de novo lesions (r=0.884, p<0.001) but not in ISR lesions (r=0.449, p=0.17). See figures.

Conclusion: Stent thickness can be strongly correlated with the incidence of SF after DES implantation in the de novo lesions.

P2739 | BEDSIDE
Predictors of late restenosis following paclitaxel-coated balloon angioplasty in patients with in-stent restenosis

Background: There are currently inadequate data on whether “late restenosis” occurs after paclitaxel-coated balloon (PCB) angioplasty for in-stent restenosis (ISR) lesions. To evaluate the long-term efficacy of PBC angioplasty, we investigated serial clinical and angiographic outcomes after PCB angioplasty for ISR lesions.

Methods and results: Between September 2008 and December 2012, PCB (Sequent Please) angioplasty was performed in 468 patients with 550 ISR lesions (bare-metal stent restenosis (BMS-ISR): 101 lesions, drug-eluting stent restenosis (DES-ISR): 436 lesions). Two serial angiographic follow-ups were routinely planned for the patients (at 6 and 18 months after the procedure). Early follow-up (6 months) angiography was performed for 488 lesions (89%), and recurrent restenosis occurred in 13 lesions (14.9%) in the BMS-ISR group and in 82 lesions (21.1%) in the DES-ISR group. Target lesion revascularization (TLR) was performed for 7 lesions (7.0%) in the BMS-ISR group and 54 lesions (13.9%) in the DES-ISR group. Late follow-up (18 months) angiography was performed for 377 (88%) of the remaining 427 lesions (excluding TLR lesions), and late restenosis was found in 2 lesions (2.5%) in the BMS-ISR group and 50 lesions (16.8%) in the DES-ISR group. Previous stent size ≤2.5mm (OR: 1.93, CI: 1.19 to 3.16, p=0.0077), percentage diameter stenosis after the procedure ≥35% (OR: 1.92, CI: 1.17 to 3.14, p=0.01), and in-stent occlusion lesion (OR: 2.74, CI: 1.18 to 6.10, p=0.02) were independent predictors of early restenosis. DES-ISR (OR: 4.18, CI: 1.82 to 14.3, p=0.002) and hemodialysis (OR: 2.57, CI: 1.13 to 6.06, p=0.04) were independent predictors of late restenosis.

Conclusions: Risk factors of recurrent restenosis after PCB angioplasty for ISR lesions vary depending on the period of time after the procedure.

P2740 | BEDSIDE
Impact of a dedicated chronic ootal occlusion (CTO) programme on procedural success among specialist and non-specialist operators: a single centre experience

Background: Chronic total occlusions (CTO) represent a major challenge in percutaneous coronary interventions (PCI). Developments in techniques and technologies have significantly improved procedural success rates following CTO PCI among trained high volume operators and many centers have developed specialist CTO programmes.

Purpose: We sought to investigate the impact of a dedicated CTO PCI programme on procedural outcomes among both specialist (sCTO) and non-specialist (nsCTO) operators.

Methods: We prospectively evaluated 266 consecutive CTO interventions performed over a 2 year period by 2 sCTO and 16 nsCTO operators. The designated sCTO operators underwent training with experienced proctors and subsequently developed a dedicated CTO service over a period of 3 years prior to the commencement of the present study. A CTO lesion was defined as a complete occlusion of the coronary vessel with TIMI 0 flow, present for ≥3 months. The J-CTO score was used to classify lesion complexity and stratify them into 4 groups: easy (J-CTO 0–1), intermediate (J-CTO 2), difficult (J-CTO 3) and very difficult (J-CTO 4–5).

Results: The sCTO operators performed 137 and the nsCTO operators 69 CTO interventions. Overall success rate per patient was 88% in the sCTO and 54% in the nsCTO group (p<0.01). The mean J-CTO score was 2.2 and 1.0 for the sCTO and nsCTO groups respectively (p<0.01). No J-CTO 4–5 cases were attempted by the nsCTO group. The success rates between sCTO and nsCTO groups differed significantly among different subgroups: 100% vs 67% (J-CTO 0–1), 93% vs 20% (J-CTO 2), 89 vs 17% (J-CTO 3) respectively (p<0.001).
Microcatheter support was used in 100% of the sCTO cases and in 29% of the nsCTO cases, while dual vascular access for retrograde visualisation was used in 96% and 13% of the cases respectively. Antegrade wire escalation (AWE) was the single utilised approach in the nsCTO group. The successful strategy for lesion crossing in the sCTO group was AWE (54%), retrograde dissection re-entry (29%), and angioplasty without stent (16%) or retrograde wire escalation (5%).

Conclusions: A dedicated CTO programme with high volume specialist operators is associated with high procedural success rates. Significantly lower success rates among nsCTO operators were predominantly driven by more complex cases (J-CTO score). Complex CTO PCI should be undertaken by specialist operators. The success rates of non-specialist operators in “easy” CTO lesions could be improved with training from specialist operators in optimal antegrade wiring techniques, including use of microcatheters and dual catheter angiography.

P2741 | BEDSIDE Does optimal lesion preparation reduce the amount of acute recoil of the Absorb® BVS?
G.B. Danzi1, M. Sesana2, M. Arieti2, G. Villa2, S. Rutigliano2, A. Aprile2, A. Nicolini1, S. Moschini1, R. Valentini2,1 Ospedale Santa Corona, Pietra Ligure, Italy; 2 Ospedale di Desenzano, Desenzano del Garda, Italy; 3 Ospedale Careggi, Firenze, Italy.

Background: In vivo acute recoil of the ABSORB bioabsorbable vascular scaffold (BVS) was evaluated in selected patients.

Objectives: To evaluate the acute recoil of the BVS and its relationship with procedural characteristics in a real world population.

Methods: Acute recoil was studied with videodensitometry in a consecutive series of patients treated by means of a BVS, and the results were compared with those obtained in subjects receiving an everolimus-eluting stent (EES). Recoil was defined as the difference between the mean diameter of the fully expanded balloon on which the device was mounted (or the mean diameter of the post-dilatation balloon), and the mean luminal diameter of the treated segment immediately after the final inflation.

Results: Recoil was assessed in 106 lesions treated with a BVS and 71 treated with an EES. The absolute and percent recoil of the BVS were significantly greater (0.32±0.16 mm and 10±5% vs. 0.17±0.07 and 5±3%; P<0.001). Multiple regression analysis showed that BVS use was associated with acute recoil (Beta=0.477; P≤0.001). Sub-optimal lesion preparation (residual stenosis after balloon angioplasty >20%) (Beta=0.217; P=0.027) and a small vessel reference diameter (Beta=0.335; P=0.002) were associated with increased BVS but not EES recoil.

Conclusions: In unselected patients, the acute recoil of the BVS was significantly greater than that of the metal EES. In the BVS group, residual stenosis after predilatation correlated with percent recoil, and so optimal lesion preparation seems to be mandatory in order to maximise the mechanical properties of the scaffold.

P2742 | BEDSIDE Early experience implanting a polymer-free biolimus A9 drug coated stent in complex real world patients from two United Kingdom centers
T. Kinnaird1, M. Uddin2, M. Butt1, A. Hallan2, N. Ossei-Gerning1, A. Chase2, A. Choudhury1, D. Smith2, R. Anderson1. 1University Hospital of Wales, Cardiff; 2Regional Cardiac Centre Morriston Hospital, Swansea, United Kingdom

Introduction: Prolonged dual anti-platelet therapy (DAPT) exposes patients to the risk of delayed stent thrombosis, and is undesirable in certain patients. The Biofreedom® polymer-free drug-coated stent has a rapid drug elution profile with accelerated vessel healing, potentially allowing shortened duration of DAPT without compromising outcomes.

Methods: Baseline demographics, procedural data and outcomes were gathered prospectively from 204 patients treated with the BioFreedom stent (BFS) at 2 UK centers. Stent choice was at the interventional cardiologist’s discretion. For comparison the outcomes of 204 consecutive patients treated with a Biomatrix drug-eluting stent (BES) in the immediate period prior to BFS availability are also presented.

Results: BFS patients were older (70.6 vs. 63.3yrs, p<0.0001), more often female (37.1 vs. 24.7%, p=0.01) or diabetic (22.7 vs. 12.9%, p<0.05) and more likely to present with a shock (6.9 vs. 3.2%, p<0.05) or an ACS (85.8 vs. 72.7%, p<0.001) than BES patients. BFS use was driven mostly by concerns related to prolonged DAPT with indications including concurrent warfarin therapy (27.5%), the need for early non-cardiac surgery (25.1%), and possible non-compliance with DAPT (20.9%). The number of vessels treated and lesions treated were similar whilst total lesion length (32.1 vs. 26.1mm, p<0.001) and number of lesions ≥30mm (37.7 vs. 26.2%, p<0.01) were greater for patients treated with BFS. The number of stents used (1.63±0.91 vs. 1.52±0.84) and mean stent diameter (2.94±0.47 vs. 2.97±0.49) were similar although total stent length (37.5±20.8 vs. 32.4±18.1mm, p=0.001) and average stent length (2.78 vs. 21.5±7.8, p<0.001) were greater for BFS patients. DAPT was prescribed for 3.6±4.3 months for BFS patients and 11.3±2.4 months for BES patients (p<0.0001). At mean follow up of 258 days clinically driven restenosis PCI (2.8% for BFS vs. 2.5% for BES, p=0.41) and the target lesion revascularisation rates (1.1% for BFS vs. 2.5% for BES, p=0.17) were similar. MACE rates were also similar although mortality was higher in the BFS cohort (6.3% vs. 2.5%, p=0.05) and was driven mainly by higher baseline shock in the BFS cohort.

Conclusions: The outcome of patients treated for complex disease with Biofreedom stents was excellent with low TLR and MACE rates. Rapid elution kinetics of the biolimus-A9 did not lead to excess TLR and allowed an abbreviated DAPT duration without excess stent thrombosis. Therefore the Biofreedom stent appears to be an attractive option for patients with complex disease in whom prolonged DAPT with indications including concurrent warfarin therapy (27.5%), the need for early non-cardiac surgery (25.1%), and possible non-compliance with DAPT (20.9%).

Acknowledgement/Funding: None

P2743 | BEDSIDE First-in-man (FIM) evaluation of a novel balloon delivery system for the self-apposing coronary artery stent
H. Lu1, A. Ijsselmuiden1, M. Nassif1, M. Grundeken1, A. De Vries2, A. Weevers2, M. Schotte1, J. Wyckzylowska1, R. De Winter1, K. Koch1, 1Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands; 2 Albert Schweitzer Hospital, Department of Cardiology, Dordrecht, Netherlands.

Background: Longitudinal geographic miss, which is described as failure to fully cover the injured or diseased arterial segment with a stent, is associated with an increased rate of adverse events. Therefore, the novel balloon delivery system (BDS) for the self-apposing STENTYS® Xposition Sirolimus eluting stent (SES) was developed for highly precise longitudinal stent positioning and deployment.

Purpose: To evaluate the longitudinal geographic miss and angiographic outcomes of the SES, based on quantitative coronary analysis and optical coherence tomography (OCT) results in a first-in-man study.

Methods: We included 25 patients with de novo coronary lesions in all indications for PCI. Patients with lesions <25mm in length with a reference vessel diameter of 2.5 - 6.0mm were eligible. All patients underwent PCI using the SES. Clinical follow-up was performed 30 days post-procedurally. Angiographic success was defined as a final residual stenosis of less than 20 percent by visual estimation and Thrombolysis In Myocardial Infarction (TIMI) 3 flow on the final angiogram. OCT was performed direct after stent placement and post-procedurally (i.e. after balloon post-dilatations) to evaluate acute stent strut apposition. Off-line two-dimensional quantitative coronary analyses (QCA) were used to measure acute gain and longitudinal geographic miss.

Results: 25 patients (mean age 66.1±10.7 years) were included. Indication for PCI was STEMI in 7 (28%) patients, Non-STEMI in 1 (4%) patient, stabilized STEMI in 12 (48%) patients, unstable Non-STEMI in 8 (32%) patients and stable angina in 6 (24%) patients. Stent crossing of the lesion and deployment of the SES was successful in all patients, without any procedural complications. Angiographic success could be achieved in all patients (100%). As assessed by QCA, pre-procedural MLD was 1.30±0.74mm, and 2.7±0.44mm after post-dilatation (acute gain 1.44±0.70mm). Diameter stenosis was 59±21% pre-procedurally and 16±7% post-procedurally. Longitudinal geographic miss was not observed (0%). Percentage malapposed stent struts on OCT was significantly lower post procedure (0.6%) than directly post stent placement (2.4%, p=0.013). Mean stent area increased significantly from 9.7mm² post stent placement to 10.5mm² (p<0.001).

Conclusions: This first-in-man experience demonstrates that intra-coronary deployment of the SES is feasible with a high angiographic success-rate and no longitudinal geographical miss on QCA. Stent malapposition directly after STENTYS placement is low. Balloon post-dilation could further improve stent apposition in SES.
to-hemostasis was 1 min. The mean time-to-mobilization was 3 hours. Only 3 (0.15%) patients had a major complication with vessel occlusion that required emergent vascular surgery with a successful outcome. Two patients developed a pseudoaneurysm of the right common femoral artery, treated with ultrasonography-guided compression. In addition, 8 small to moderate and 2 large inguinal hematomas (one requiring blood transfusion) were recorded. In 5 cases retroperitoneal bleeding occurred, requiring blood transfusion in 2. Local infection or arteriovenous fistulae were not observed.

Conclusion: Deployment of Angio-Seal without use of local angiography was efficacious and safe with few correctable complications in a very large patient cohort undergoing transfemoral catheterization for PCI and non-PCI procedures under anticoagulation and antiplatelet drug therapy. In these patients the VCD reduced time-to-hemostasis and time-to-mobilization and minimized the incidence of complications.

P2745 | BEDSIDE
Three-year outcome after biolimus-eluting versus sirolimus-eluting coronary stent implantation in diabetic and non-diabetic patients - a SORT OUT V substudy
J. Aarnes3, M. Madsen4, J. Ravkilde3, J. F. Lassen1, E. H. Christiansen1 on behalf of The Scandinavian Organization for Randomized Trials with Clinical Outcomes (SORT OUT) V investigators. 1Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark; 2Odense University Hospital, Department of Cardiology, Odense, Denmark; 3Aalborg University Hospital, Department of Cardiology, Aalborg, Denmark; 4Aarhus University Hospital, Department of Clinical Epidemiology, Aarhus, Denmark

Introduction: Long-term outcome after coronary drug-eluting stent implantation may vary significantly between drug-eluting stents in diabetic and non-diabetic patients. The SORT OUT V trial is a prospective, all-comer, multicentre, randomized, clinical trial which compared a biolimus-eluting stent (Nobori; BES) using a biodegradable coating with a sirolimus-eluting stent (Cypher Select+; SES) with a durable coating.

Purpose: To compare 3-year clinical outcomes in diabetic and non-diabetic patients treated with BES versus SES.

Methods: Routine clinical care patients were randomized in a 1:1 ratio to receive either BES or SES. The patients were stratified according to presence/absence of diabetes mellitus. Clinical endpoints included MACCE, a composite of safety (cardiac death, myocardial infarction, definite stent thrombosis) and efficacy (target vessel revascularization (TVR)). Cox’s proportional hazard regression analysis was used to estimate hazard ratios during entire 36-month follow-up and in landmark analyses of >12–36 months.

Results: 2,468 patients were randomized to BES (n=1,229 patients, n=185 diabetic patients) or SES (n=1,229 patients, n=189 diabetic patients). MACCE rates were similar for BES and SES among diabetic (25 [13.7%] and 29 [15.2%]; HR 0.92, 95% CI: 0.54–1.57, p=0.76) and non-diabetic patients (96 [9.3%] and 114 [10.7%]; HR 0.87, 95% CI: 0.66–1.14, p=0.31) during 3-year follow-up. Similarly, landmark analysis of diabetic patients showed that MACCE rates were similar for the 2 stent types (13 [7.9%] vs. 14 [8.0%]; HR 0.90, 95% CI: 0.47–1.72, p=0.86). Among non-diabetic patients, however, the landmark analyses showed that BES had fewer MACCE (46 [%] vs. 70 [6.9%]; HR 0.68, 95% CI: 0.47–0.98, p=0.0401) driven by a reduced TVR rate (23 [2.3%] vs. 44 [4.3%]; HR 0.54, 95% CI: 0.32–0.89, p=0.0155) beyond 1-year follow-up.

Conclusion: In patients with and without diabetes, the Nobori BES and Cypher SES did not differ significantly at 3-year follow-up. Among non-diabetic patients, landmark analyses showed that the Nobori BES with a biodegradable polymer had lower MACE and TVR rates beyond 1-year follow-up, which may suggest a longer-term benefit in this subgroup.

Acknowledgement/Funding: Terumo and Cordis (Johnson & Johnson)

P2747 | BEDSIDE
Incidence and clinical impact of longitudinal stent deformation after the PROMUS element platinum chromium-everolimus eluting stent implantation
T. Hiromasa, S. Kuramitsu, T. Domei, M. Hyodo, Y. Soga, S. Shirai, K. Ando, M. Nobuyoshi. Kokura Memorial Hospital, Kitakyushu, Japan

Background: The PROMUS Element platinum-chromium everolimus-eluting stent (Pci-EES) has a novel metal and stent design intended to improve deliverability, conformability, and radial strength, whereas such features might have the trade-off of reducing longitudinal stent strength, which would account for the occurrence of longitudinal stent deformation (LSD) as reported previously. However, the incidence and clinical impact of LSD after Pci-EES implantation in clinical practice have not been fully evaluated.

Methods: A total of 803 patients with 1050 lesions undergoing Pci-EES implantation between March 2012 and August 2013 were analyzed. LSD was defined as the distortion or shortening and elongation of a stent in the longitudinal axis following successful stent deployment. We assessed the incidence of longitudinal stent deformation and cumulative incidence of major adverse cardiac events (MACE), defined as a composite of cardiac death, non-fatal myocardial infarction, definite stent thrombosis, and clinically driven target lesion revascularization (TVR) within 1 year.

Results: Of 803 patients with 1050 lesions, we performed an intravascular ultrasound (IVUS) and post-dilation in 752 patients (93.6%) with 992 lesions (94.5%) and in 408 patients (50.8%) with 538 lesions (51.2%). In the LSD group, IVUS and post-dilation were performed in all patients. LSD was observed in 12 patients (1.5%) with 12 lesions (1.1%). The mechanism of LSD was due to the following reasons: compression by post-dilation balloons (n=1, 8.3%), entrapped IVUS (n=8, 66.7%) and pull backed jailed guide wire (n=3, 25%). At 1-year, the cumulative incidence of MACE, cardiac death, myocardial infarction, stent thrombosis and clinically driven target lesion revascularization were not significantly different between the LSD and non-LSD groups (9.1% vs. 2.8%, p=0.019; 0% vs. 0%, p=1.00; 0% vs. 0.1%, p=0.92; 0% vs. 0.14%, p=0.88; 9.1% vs. 2.8%, p=0.19, respectively).

Conclusions: LSD after Pci-EES implantation occurs in 1.1% of lesions. However, LSD is not associated with MACE within 1-year.

P2748 | BEDSIDE
The incidence of stent fracture after drug-eluting stent implantation: comparison between de novo lesion and in-stent restenosis lesion

Aims: The incidence of stent fracture (SF) after drug-eluting stent (DES) implantation was compared between de novo lesions and in-stent restenosis (ISR) lesions.

Methods and results: From January 2004 to May 2013, 12304 lesions in 6314 patients were treated exclusively with DES and 8-month follow-up angiography was performed. SF was defined as separation of stent segments or stent struts.
Results: Prevalence of target lesion revascularization (TLR) was significantly higher in RCA than in LCA (20.2% vs. 3.1%, p<0.002). In a subgroup of RCA-ostial lesions, prevalence of in-stent restenosis and TLR were significantly lower in second generation DES (table).

P2750 | BEDSIDE
Clinical outcome of aorto-ostial lesions treated with first or second generation drug-eluting stents

S. Kono. Himeji Cardiovascular Center, Cardiology Department, Himeji, Japan

Background: Aorto-ostial lesion is still a challenge for coronary intervention even in the drug-eluting stent (DES) era. Methods: A total of 121 patients (89 RCA and 32 LCA) with de-novo aorto-ostial lesions treated with first (Sirolimus/Paclitaxel) or second (Zotarolimus/ Everolimus/ Biolimus) generation DES were enrolled in our institute between 2004 and 2013 were investigated.

Results: Prevalence of target lesion revascularization (TLR) was significantly higher in RCA than in LCA (20.2% vs. 3.1%, p<0.002). In a subgroup of RCA-ostial lesions, prevalence of in-stent restenosis and TLR were significantly lower in second generation DES (table).

P2751 | BEDSIDE
Transradial versus transfemoral approach for chronic total occlusions of coronary arteries: feasibility and predictors of success

F. Soares1, V.A. Jimenez Diaz2, F. Saraiva3, A. Ortiz Saez4, A. De Miguel Castro5, G. Bastos Fernandez5, J.L.M. Ortiz5, J. Andrade6, J.A. Baz Alonso7, A. Iniguez Romo8. 1 University Hospitals of Coimbra, Cardiology, Coimbra, Portugal; 2Hospital de Mèxico, Cardiology, Vigo, Spain; 3Hospital Santo Andre, Cardiology, Leiria, Portugal

Background: The transfemoral approach (TFA) remains as the most used vascular access for percutaneous coronary intervention (PCI) in chronic total occlusion (CTO), due to its strong backup support and the ability to use larger diameters. Transradial approach (TRA) has been shown to reduce vascular complications at the puncture site and shorten hospitalizations. After proper patient selection, TRA may be used as initial choice of vascular access for CTO lesions.

Methods: We retrospectively analyzed a cohort of 325 cases of PCI for CTO, all performed by antegrade route, in a single high-volume PCI center.

Results: From January 2006 to August 2013, 7860 PCI were performed in our center, being 325 (4.13%) for CTO. Of these, 82.6% (269) were performed by TRA and 17.2% (56) by TFA. Baseline characteristics were similar in both groups except for the presence of hypertension, more frequent in the TFA group (57.8% vs 73.2%, p=0.032). There were no differences in LVEF (53.8% vs 48.6%), mean lesion length (30.8 vs 28.2mm), calcified lesions (51.5% vs 40%) and mean contrast volume (251±112 vs 251±112mL). Compared to TFA, TRA patients had shorter fluoroscopy time (25±14 vs 35±20 minutes, p<0.008) and shorter total procedural time (58±29 vs 76±39 minutes, p<0.001). Angiographic success rates and final flow TIMI III were achieved more frequently in the first attempt in the TRA group (78.5% vs 63.6%, p=0.02). Logistic regression analysis demonstrated independent predictors of success in CTO: lesion length (OR 0.970 [95% CI 0.945–0.997]), non-calcified lesions (OR 2.329 [95% CI 1.162–4.665]) and transradial vascular access (OR 2.759 [95% CI 1.308–5.620]). The estimated probabilities using this model for predicting procedural success in PCI for CTO showed good discrimination (Receiver operating characteristic area under the curve 0.696, p<0.001).

Conclusions: In this single center study, in a center with high volume of TRA in PCI, this vascular approach use in first attempt of PCI for CTO showed a comparable, if not higher success than TFA, with a decrease in the mean fluoroscopy and mean procedure times in selected cases. Short and non-calcified lesions remain the main predictors of success in PCI for CTO.

P2752 | BENCH
Bioabsorbable vascular scaffold radial expansion and conformation compared to a metallic platform

N. Foin1, D.R. Lee2, C. Bourantas3, A. Mattesini4, G. Caiazzo4, E. Fabris4, D. Kilic4, C. Di Mario4, P. Wong1, P. Serruys5.

1 University Hospitals of Coimbra, Cardiology, Coimbra, Portugal; 2Hospital de Mèxico, Cardiology, Vigo, Spain; 3University College London, London, United Kingdom; 4Careggi University Hospital (AOU), Florence, Italy; 5Biomedical Research Unit of Royal Brompton London, London, United Kingdom; 6Imperial College London, London, United Kingdom

Aim: The aim of this study was to compare the acute expansion behavior of the polymer based Bioresorbable Vascular Scaffold (Absorb BVS) compared with a second generation metallic drug eluting stent platform (Xience Prime) in a coronary artery lesion model.

Background: There are major differences in material properties and mechanical behavior between currently available metallic stents and polymer based bioabsorbable scaffolds. Differences in acute results have been observed in clinical studies comparing drug eluting bioabsorbable scaffolds directly to metallic platforms.

Methods: We examined the expansion behavior of the Bioresorbable Vascular Scaffold (Absorb BVS) and a metallic DES (3.0x18mm Xience Prime) after expansion at 37°C in an identical coronary artery stenosis model (12 different experiments were performed in total). Results after expansion at nominal diameter and 18 ATM were inspected and measured under microscopy to assess
plaque recoil. Minimal Lumen Diameter (MLD) and Minimal Lumen Area (MLA) were obtained from Optical Coherence Tomography (OCT) imaging.

Results: MLA in the model after BVS and metallic DES implantation was respectively 4.9±0.17 and 5.40±0.13mm² (p=0.02) at Nominal Pressure (NP) and 5.41±0.20 and 6.07±0.25 mm² (p=0.02) after expansion at 18 ATM. Stent eccentricity index at the MLA was 0.71±0.02 in BVS compared to 0.81±0.02 in the metal stent at NP (p=0.003), and 0.73±0.03 compared to 0.75±0.02 at 18 ATM. In-stent residual obstruction was 26.7±0.3% in BVS and 20.4±1.7 in the Xience stent at NP (p=0.003) compared to 29.8±1.1 and 15.2±3.6% respectively at 18 ATM (p=0.003).

Conclusions: Such in-vitro experiments provide insights to better understand the behavior of BVS scaffolds and to guide their optimal implantation in vivo.

P2753 | BENCH

A novel tram stent method in treatment of coronary bifurcation lesions

M.A.R.K. Arokiaraj, Pondicherry Institute of Medical Sciences, Pondicherry, India

Aim: A novel stent was designed for the treatment of coronary bifurcation lesion, and it was investigated for its performance by finite element analysis. This study was performed in a novel method of treatment of bifurcation lesion with provisional stenting.

Methods and results: A bifurcation model was created with the proximal vessel of 3.2 mm diameter, and the distal vessel after the side branch (2.3 mm) was 2.7 mm. A novel stent was designed with connection links that had a profile of a tram. Laser cutting and shape setting of the stent was performed, and thereafter it was crimped and deployed over a balloon. The contact pressure, stresses on the aortic wall, stresses on the stent, the maximal principal log strain of the main artery and the side-branch were studied. The study was performed in Abaqus, Simulia. The stresses on the main branch and the distal branch were minimally increased after deployment of this novel stent. The side branch was preserved, and the stresses on the side branch were lesser; and at the confluence of bifurcation on either side of the side branch origin the von-Mises stress was marginally increased. However, the stresses at the bifurcation were significantly lesser than the stresses of the currently existing techniques used in the treatment of bifurcation lesions. Parametric modifications of the tram area was performed, and the variations were studied for effective crimping. The stresses observed are summarised in the figure.

Conclusions: There is a potential for a novel Tram-stent method in the treatment of coronary bifurcation lesions.

P2754 | BENCH

Fraction of reserve assessed by pressure wire could predict proper stent deployment

A.A. Elasfar, H.A. Remah, O.S. Elshahawy, Tanta University Hospital, Adult Cardiology, Tanta, Egypt

Background: There are different methods for assessing the results of coronary intervention, some are morphological and the others are physiological. Myocardial fractional flow reserve (FFRmetry) is a lesion specific index relating maximum myocardial blood flow in the presence of stenosis to its normal value if there is no stenosis.

Objective: The aim of our study is to assess the results of coronary stenting before and after post-stenting balloon dilation by measuring myocardial fractional flow reserve using intracoronary pressure wire.

Methods: FFRmetry and quantitative coronary angiography (QCA) were obtained before PCI, after stent placement and after post-stenting balloon dilation in 120 patients (LAD in 76 patients, RCA in 36 patients and LCX in 8 patients). FFRmetry was calculated as the ratio of Pd/Pa during intracoronary adenosine (50 micg and 20 micg in the left and right coronary arteries respectively) induced maximum hyperemia, where Pd represents mean distal coronary pressure measured by pressure wire and Pa represents mean aortic pressure measured by guiding catheter.

Results: The percent diameter stenosis decreased significantly after coronary stenting to baseline values (76±14% diameter stenosis in baseline values vs.15%±11% after stenting, p<0.05). Post-stenting balloon dilation produced non-significant more reduction in the percent diameter stenosis (6±5% with P value<0.05). FFRmetry after PCI was significantly higher than that at baseline conditions before intervention (0.6±0.18 at baseline versus 0.89±0.09 after stenting, p<0.05). There was significant increase in FFRmetry after post-stenting balloon dilation (0.94±0.05 versus 0.89±0.09).

Conclusions: Post-stenting Balloon dilation produced non-significant trend towards better lumen diameter by quantitative coronary angiography but with significant increase in Myocardial fractional flow reserve assessed by pressure wire.

P2755 | BEDSIDE

Impact of transradial approach on clinical outcomes and bleeding complications in high risk ACS patients undergoing PCI with GP IIb/IIIa inhibitor: from the CAP registry

S.Y. Choi1, Y.W. Choi1, S.J. Tak1, H.S. Kim2, W.H. Kim3, C.W. Yü3, C.W. Lee3, S.W. Rha4, J.O. Jeong5, B.J. Choi6 on behalf of The Clotinab application in high risk ACS undergoing PCI registry group. 1 Ajou University Hospital, Cardiology, Suwon, Korea, Republic of; 2Yonsei University College of Medicine, Seoul, Korea, Republic of; 3 Asan Medical Center, Cardiology, Seoul, Korea, Republic of; 4Eulji University Hospital, Cardiology, Daejeon, Korea, Republic of; 5Sejong General Hospital, Cardiology, Pucheon, Korea, Republic of; 6Asan Medical Center, Cardiology, Seoul, Korea, Republic of; 7Korea University Guro Hospital, Cardiology, Seoul, Korea, Republic of; 8Chunnam National University Hospital, Cardiology, Daejeon, Korea, Republic of

Background: There are increasing numbers of studies suggesting that transradial coronary intervention (TRI) is associated with better clinical outcomes by reducing bleeding and vascular complications when compared with transfemoral coronary intervention (TFI). However, the benefit of TRI has not been fully evaluated in high-risk ACS patients at high risk of bleeding who are treated with GP IIb/IIIa inhibitors (GIPI) due to “bail-out” situations or thrombotic complication (Ila C recommendation by ESC guideline 2014).

Methods: The Clotinab application in high risk Acute Coronary Syndrome under TRI (CAP) registry is a retrospective, multicenter, observational study. We analyzed 1272 patients who underwent PCI from April 2009 to December 2012. Because the access site was not randomly assigned, we used propensity score matching to minimize bias. Total 596 patients (298 in each group) remained after propensity score matching. The primary end point was major adverse cardiac event (MACE) including all-cause death, non-fatal myocardial infarction (MI), repeat revascularization and stent thrombosis at 30 days. The secondary endpoint was major bleeding and any bleeding events of bleeding including access site hematomata, intracranial hemorrhage and other bleeding complications.

Results: After propensity score matching, there were no differences in baseline characteristics between two groups except history of atherosclerosis (7.7% vs. 13.4%, p=0.024). The primary endpoint occurred in 7 (2.4%) of 298 patients in TFI group compared with 17 (5.7%) of 298 patients in TFI group (p=0.037). Non-fatal MI (0.7% vs. 3.4%, p=0.019) were also less frequent in TRI group. Any bleeding events occurred in 15 (5.0%) of 298 patients in TRI group compared with 21 (7.0%) of 298 patients in TFI group (p=0.302). Major bleeding occurred in 2 (0.7%) of 298 patients in TRI group compared with 7 (2.3%) of 298 patients in TFI group (p=0.093). In multivariate analysis, independent predictors of MACE at 30 days included chronic renal failure, low ejection fraction, major bleeding and TFI (odds ratio=2.75; 95% CI, 1.085 to 1.798; p=0.033).

Conclusion: TRI in patient with high risk ACS treated with GIPI is associated with better clinical outcomes and lower bleeding tendency at 30 days.

P2756 | BENCH

Effect of a novel peptide and sirolimus-coated stent on re-endothelialization and anti-restenosis

M.H. Jeong, E.J. Jang, I.H. Bae, D.S. Park, K.S. Lim, J.K. Park, D.S. Sim, Chonnam National University Hospital, Gwangju, Korea, Republic of

Drug-eluting stent (DES) still has limitations such as thrombosis and inflammation. These limitations can be occurred by the lack of endothelialization. This study was undertaken to investigate the effects of WKYMVm- and sirolimus (SRL)-coated stent on re-endothelialization and anti-restenosis. The WKYMVm, specially synthesized peptide for homing of endothelial colony-forming cells, was coated to bare metal stent (BMS) with hyaluronic acid (HA) through simple dip coating (designated as HA-Pep). Thereafter, SRL was coated to HA-Pep, consecutively (designated as Pep/SRL). The cellular response of stents on human umbilical vein cell (HUVEC) and porcine coronary cell (SMC) was examined by XTT assay. Stents were implanted to rabbit iliac artery and were isolated at 6 weeks of post-implantation. And then they were subjected to histological analysis. The peptide was well-attached to surface of BMS and the surface was smoothly by SRL coating. The release pattern of SRL was similar to commercial SRL-coated stent (57.2% within 7 days, followed by an additional releasing was continued to 28 days). The proliferation HUVEC was enhanced in HA-Pep group at 7 days of culture (38.2±7.62%, compared to BMS group). On top of being the hand, the proliferation HUVEC was inhibited in Pep/SRL group at 7 days of culture (40.7±6.71%, compared to BMS group). In animal study, the restenosis rate of Pep/SRL group (13.5±5.0%) and commercial DES (Xience PrimeTM; 9.2±7.0%) was lower than BMS (25.2±4.52%) and HAP (28±9.38%). CD31 expression was exhibited in both SRL and Xience PrimeTM on group. On the other hand, the CD31 was stained with consecutively linear pattern in HA-Pep and Pep/SRL group, suggesting that WKYMVm promote endothelialization. These results suggested that the coating of WKYMVm could promote the endothelial heal-
ing. indicating that consecutive coating of the WKYMVm and SRL to BMS have potential role on re-endothelialization and neointima suppression.

P2757 | BEDSIDE
Study with optical coherence tomography of everolimus-eluting stents with abluminal bioabsorbable polymer at 3, 6 and 12 months after implantation
J.M. De La Torre Hernandez1, P. Tejedor2, D.H. Lee1, J.M. Duran Hernandez2, T. Garcia Camarero1, J. Monedero Campo2, F. Sainz Laso1, M. Alvarez Calderon1, G. Veiga Fernandez1, J. Zuco1, H. Marques de Valdecilla, Santander, Spain; 3 Hospital Universitario de Burgos, Burgos, Spain

Background: The everolimus-eluting stent with abluminal bioabsorbable polymer (EES-BP) is a new generation drug-eluting stent with features potentially favoring an early healing process which could promote shorter periods of dual antiplatelet-therapy treatment.

Purpose: In this study we sought to evaluate endothelialization of EES-BP stents at 3, 6 and 12 months.

Methods: Patients with lesions treated with EES-BP stents were scheduled for examination with optical coherence tomography at 3, 6 and 12 months alternately in two different centers. Lesions should have the same characteristics in the three groups. Co-primary endpoints were % of struts with no coverage at 3, 6 and 12 months. Off-line imaging analysis was conducted in a core lab by two blinded investigators.

Results: A total of 55 patients have been included. Among those, 29 have been evaluated in OCT. At 15 patients (22 stents) at 3 months and 14 patients (18 stents) at 6 months. The mean stent diameter was 3.02±0.4 and 3.0±0.4 mm respectively (p=0.8) and stent length 17±5.6 and 17±5.3 mm respectively (p=0.7). The proportion of uncovered struts was 6.5% at 3 months and 3.7% at 6 months.

Conclusions: Pending of final analysis of OCT follow up for the whole cohort, the proportion of uncovered struts with EES-BP at 3 months is low and results non-significantly higher than at 6 months.

P2758 | BEDSIDE
Influence of three-dimensional bifurcation angle on immediate and long term outcomes in patients with bifurcation lesions treated by simple approach
M. Pan Alvarez-Osorio1, M.C. Morenate1, S. Ojeda1, M. Romero1, M. Blanco2, P. Martín1, J. Suarez De Lezo Herreros De Tejada2, J. Segura1, A. Medina2, J. Suarez De Lezo Cruz-Conde1, 1 Hospital Universitario Reina Sofia, Cordoba, Spain; 2 Hospital Universitario Dr Negrín, Las Palmas De Gran Canaria, Spain

Background: The methodology for angle assessment is variable and lack of consensus in published series makes comparison problematic. A low bifurcation angle has been associated with better outcomes in patients treated with the crush or culotte technique, but the effect on outcome of patients treated with single main vessel stenting is not clear.

Objectives: To study the impact of bifurcation angle on immediate results and long term outcomes in patients treated with true bifurcation lesions with balloon-expandable and drug-eluting stents.

Methods: From February 2009 to November 2012, 372 patients (64.8±11.2 years, 77% men and 33% diabetic) included in 29 tertiary hospitals. The methodology for angle assessment is variable and lack of consensus in published series makes comparison problematic. A low bifurcation angle has been associated with better outcomes in patients treated with the crush or culotte technique, but the effect on outcome of patients treated with single main vessel stenting is not clear.

Results: A total of 55 patients have been included. Among those, 29 have been evaluated in OCT. At 15 patients (22 stents) at 3 months and 14 patients (18 stents) at 6 months. The mean stent diameter was 3.02±0.4 and 3.0±0.4 mm respectively (p=0.8) and stent length 17±5.6 and 17±5.3 mm respectively (p=0.7). The proportion of uncovered struts was 6.5% at 3 months and 3.7% at 6 months.

Conclusions: Pending of final analysis of OCT follow up for the whole cohort, the proportion of uncovered struts with EES-BP at 3 months is low and results non-significantly higher than at 6 months.

P2759 | BEDSIDE
The multicentre LONGPRIME registry: everolimus DES in long lesions
J.F. Diaz Fernandez1, J.C. Fernandez Guerrero2, N. Delarache3, C. Brettele4, J.C. Zuco5, R. Lopez Palop5, B. Garcia Del Bianco5, V. Mainara5, R. Albert9, A. Albarran10 on behalf of LONGPRIME investigators, 1 Hospital Juan Ramon Jimenez, Huelva, Spain; 2 University Hospital of Jaen, Jaen, Spain; 3 Hospital Center of Pau Pau, France; 4 Hospital Centre of Valence, France; 5 University Hospital Marques de Valdecilla, Santander, Spain; 6 University Hospital San Juan de Alicante, Alicante, Spain; 7 University Hospital Vall d’Hebron, Barcelona, Spain; 8 General University Hospital of Alicante, Alicante, Spain; 9 Hospital Louis Pasteur de Chartres, Chartres, France; 10 University Hospital 12 de Octubre, Madrid, Spain

Aims: To assess the efficacy and safety of the everolimus DES (Xience Prime) in long coronary lesions in a real-world population of patients.

Methods: Prospective multicentre multinational registry of 610 consecutive patients (64.8±11.2 years, 77% men and 33% diabetic) included in 29 tertiary hospitals of Spain, France and Germany. Inclusion criteria were age 18–90 years and de novo lesions > 24 mm in vessels of 2.25–4.4 mm. The primary endpoint was MACE (Cardiac death, myocardial infarction and TLR) and stent thrombosis at 12 months.

Angiographic characteristics: 717 long lesions were included (1.2 per patient), mean lesion length was 34.5±11.17 mm and vessel size 2.93±0.41 mm. Stented vessels were LAD in 48.4±11.7%, CX in 14.6±4.4% and RCA in 36.9±3.8%. Stented lesions were LAD in 53% and CX or RCA in 47% of cases. In 62% of patients, bifurcation angle was calculated by 3D quantitative coronary analysis, 21% by two orthogonal projections and 17% from technicalities to prognosis in PCI.

Results: There were 142 MACE (20.4%)- 7 cardiac deaths (1.2%), 20 non-fatal myocardial infarctions (2.8%)and 92 TLR (12.8%). There were 66 TF designs and 106 RA approaches. TF was preferred for lesions in the right coronary artery (25.9 vs 15.3%, p=0.07) while TR was the choice for left main and side branch stenting (54±16° vs 3±14°, p=0.002) and for left anterior descending artery (51±14° vs 43±14°, p=0.002) and 12 months after implantation.

Conclusions: In this real-world population, the everolimus DES Xience Prime performs extremely well in long lesions, with a very low rate of MACE at 12 months and very low stent thrombosis.
References

P2761 | BEDSIDE
Provisional versus planned double-stenting strategy in coronary bifurcation lesions treated with bioresorbable scaffold

H. Kawamoto, A. Latib, N. Ruparelia, T. Miyazaki, A. Sticchi, F. Figni, A. Chieffo, M. Carlino, M. Montorfano, A. Colombo. San Raffaele Scientific Institute, Interventional Cardiology Unit, Milan, Italy

Purpose: The use of bioresorbable scaffolds (BRS) in percutaneous coronary intervention (PCI) has been restricted to simple lesions. However, BRS use for the treatment of more complex lesions including bifurcations is increasingly being undertaken. This study aimed to investigate clinical outcomes of patients treated with a provisional stenting (PS) versus planned double stenting (DS) strategy in coronary bifurcation lesions.

Methods: We evaluated patients treated with BRS for bifurcation lesions between May 2012 and November 2014. A total of 122 consecutive bifurcation lesions with side branch (SB) diameter ≤ 3.5 mm were identified. PS strategy was applied in 99 lesions (89 patients) and DS strategy 23 lesions (22 patients).

Results: Median follow-up period was 398 (IQR 216–556) days. The DS group consisted of patients with a higher prevalence of insulin-dependent diabetes mellitus (PS 7.6% vs. DS 18.2%, p = 0.05), a higher Syntax score (PS 20.5 ± 8.0 vs. DS 32.6 ± 7.5, p < 0.0001), and a higher number of true bifurcation lesions (PS 32.3% vs. DS 19.6%, p = 0.01). Moreover, DS patients had a higher lesion complexity score (2.8 ± 0.6 vs. 2.2 ± 0.6, p = 0.007) and a greater number of true bifurcation lesions (PS 32.3% vs. DS 19.6%, p = 0.01). Intravascular ultrasound was used in 82.7% with no difference between groups. In the provisional stenting group, 7 lesions (7.1%) were crossed-over to side branch T-stenting with BRS in 2 lesions and drug-eluting stent (DES) in 5 lesions. In the DS group, 13 lesions (56.5%) were treated with BRS implantation to the SB (T-stenting 8 lesions, Mini-crush stenting 3 lesions, and V-stenting 1 lesion). A hybrid stenting technique (BRS implantation to the main branch, and drug-eluting metal stent to the SB) was utilized in 10 lesions (T-stenting 2 lesions, Mini-crush 7 lesions, and crush stenting 1 lesion). There were no differences in major adverse cardiac events (MACE; defined as all-cause death, follow-up myocardial infarction, and target vessel revascularization) between the two groups at 1-year follow-up (PS 9.5% vs. DS 11.2%, p = 0.09). Definite stent thrombosis was observed in 1 patient in the PS group but it was asymptomatic in a BRS implanted stent to the bifurcation. At 1-year follow-up, TLR rates were 5.5% for provisional and 11.2% for double stenting (p = 0.49).

Conclusions: This study suggests that bifurcation lesions can be successfully treated with BRS. The rates of TLR tended to be higher in the DS group compared to when a PS strategy was employed. Considering the worse lesion and baseline characteristics, the use of a systematic double stenting strategy with BRS to the main branch and BRS/DES to the SB is a strategy worth to be investigated.

P2762 | BEDSIDE
Associations between stent length and clinical outcomes in women undergoing PCI with new generation drug eluting stents

J. Chandrasekhar1, G. Stefanini2, S. Sartori1, M. Aquino3, W. Wigns4, L. Mehta5, D. Tsang6,7,8, P. Kimura9, K. Kandzari10, M. Mehran11, on behalf of The WIN-DES study group.

Purpose: The importance of Optical Coherence Tomography intracoronary imaging for the evaluation of Bioresorbable Vascular Scaffolds (BVS) has been demonstrated. From technicalities to prognosis in PCI 485

Methods: We assessed data for 5410 women in the WIN-DES pooled analysis of patients undergoing PCI with new generation DES and grouped them as StentLong for ≥40mm and StentShort for <40mm. Clinical outcomes were compared between groups at 3 years for cardiac death, definite or probable stent thrombosis (ST), myocardial infarction (MI) and major adverse cardiovascular events (MACE), composite of cardiac death, MI and target lesion revascularization (TLR). Results:

Age: 58 ± 11 vs 58 ± 11 years, p = 0.79.

Clinical outcomes at mid-term follow-up:

Cardiac Death: 0.4% (95% CI 0.0–0.9) in StentLong versus 0.3% (95% CI 0.0–0.7) in StentShort, p = 0.79.

ST: 0.3% (95% CI 0.0–0.7) in StentLong versus 0.2% (95% CI 0.0–0.5) in StentShort, p = 0.57.

MI: 2.1% (95% CI 1.5–2.8) in StentLong versus 1.8% (95% CI 1.3–2.4) in StentShort, p = 0.36.

MACE: 4.1% (95% CI 3.3–5.0) in StentLong versus 3.6% (95% CI 2.9–4.4) in StentShort, p = 0.24.

TLR: 54% (95% CI 49–60) in StentLong versus 47% (95% CI 42–52) in StentShort, p = 0.23.

Conclusions: There were no differences in clinical outcomes at mid-term follow-up between StentLong and StentShort for DES. However, a greater number of patients in StentLong had a higher lesion complexity score (2.8 ± 0.6 vs. 2.2 ± 0.6, p = 0.007) and a greater number of true bifurcation lesions (PS 32.3% vs. DS 19.6%, p = 0.01). Intravascular ultrasound was used in 82.7% with no difference between groups. In the provisional stenting group, 7 lesions (7.1%) were crossed-over to side branch T-stenting with BRS in 2 lesions and drug-eluting stent (DES) in 5 lesions. In the DS group, 13 lesions (56.5%) were treated with BRS implantation to the SB (T-stenting 8 lesions, Mini-crush stenting 3 lesions, and V-stenting 1 lesion). A hybrid stenting technique (BRS implantation to the main branch, and drug-eluting metal stent to the SB) was utilized in 10 lesions (T-stenting 2 lesions, Mini-crush 7 lesions, and crush stenting 1 lesion). There were no differences in major adverse cardiac events (MACE; defined as all-cause death, follow-up myocardial infarction, and target vessel revascularization) between the two groups at 1-year follow-up (PS 9.5% vs. DS 11.2%, p = 0.09). Definite stent thrombosis was observed in 1 patient in the PS group but it was asymptomatic in a BRS implanted stent to the bifurcation. At 1-year follow-up, TLR rates were 5.5% for provisional and 11.2% for double stenting (p = 0.49).

Conclusions: This study suggests that bifurcation lesions can be successfully treated with BRS. The rates of TLR tended to be higher in the DS group compared to when a PS strategy was employed. Considering the worse lesion and baseline characteristics, the use of a systematic double stenting strategy with BRS to the main branch and BRS/DES to the SB is a strategy worth to be investigated.

P2764 | BEDSIDE
Optical coherence tomography guidance for bvs implantation in complex lesions

G. Caiazzo1, A. Mattesini2, I.D. Kilic3, E. Fabris2, R. Serdoz3, C. Indolfi1, C. Di Mario3,1, Magna Graecia University of Catanzaro, Department of Cardiology, Catanzaro, Italy, 2Careggi University Hospital (AOU), Cardiology, Florence, Italy, 3Royal Brompton Hospital, Cardiology, London, United Kingdom

Background: The importance of Optical Coherence Tomography intracoronary imaging for the evaluation of Bioresorbable Vascular Scaffolds (BVS) has been demonstrated. The use of bioresorbable scaffolds (BRS) in percutaneous coronary intervention (PCI) has been restricted to simple lesions. However, BRS use for the treatment of more complex lesions including bifurcations is increasingly being undertaken. This study aimed to investigate clinical outcomes of patients treated with a provisional stenting (PS) versus planned double stenting (DS) strategy in coronary bifurcation lesions.

Methods: We evaluated patients treated with BRS for bifurcation lesions between May 2012 and November 2014. A total of 122 consecutive bifurcation lesions with side branch (SB) diameter ≤ 2.5 mm were identified. PS strategy was applied in 99 lesions (89 patients) and DS strategy 23 lesions (22 patients).

Results: Median follow-up period was 398 (IQR 216–556) days. The DS group consisted of patients with a higher prevalence of insulin-dependent diabetes mellitus (PS 7.6% vs. DS 18.2%, p = 0.05), a higher Syntax score (PS 20.5 ± 8.0 vs. DS 32.6 ± 7.5, p < 0.0001), and a greater number of true bifurcation lesions (PS 32.3% vs. DS 19.6%, p = 0.01). Intravascular ultrasound was used in 82.7% with no difference between groups. In the provisional stenting group, 7 lesions (7.1%) were crossed-over to side branch T-stenting with BRS in 2 lesions and drug-eluting stent (DES) in 5 lesions. In the DS group, 13 lesions (56.5%) were treated with BRS implantation to the SB (T-stenting 8 lesions, Mini-crush stenting 3 lesions, and V-stenting 1 lesion). A hybrid stenting technique (BRS implantation to the main branch, and drug-eluting metal stent to the SB) was utilized in 10 lesions (T-stenting 2 lesions, Mini-crush 7 lesions, and crush stenting 1 lesion). There were no differences in major adverse cardiac events (MACE; defined as all-cause death, follow-up myocardial infarction, and target vessel revascularization) between the two groups at 1-year follow-up (PS 9.5% vs. DS 11.2%, p = 0.09). Definite stent thrombosis was observed in 1 patient in the PS group but it was asymptomatic in a BRS implanted stent to the bifurcation. At 1-year follow-up, TLR rates were 5.5% for provisional and 11.2% for double stenting (p = 0.49).

Conclusions: This study suggests that bifurcation lesions can be successfully treated with BRS. The rates of TLR tended to be higher in the DS group compared to when a PS strategy was employed. Considering the worse lesion and baseline characteristics, the use of a systematic double stenting strategy with BRS to the main branch and BRS/DES to the SB is a strategy worth to be investigated.

Acknowledgement/Funding: Women in Innovation Initiative of the Society of Cardiovascular Angiography and Interventions.
P2765 | BEDSIDE
Clinical and angiographic one year outcome of mini-crush stenting for the treatment of true coronary bifurcation lesion
A. Nicolo1, S. Moshiri1, L. Olivotti1, A. Baselice2, K. Paonessa2, G.B. Danzi2.

Aim: The mini-crush technique for the treatment of true coronary bifurcations is still under development. Several guidelines recommend the use of mini-crush technique in bifurcation lesions, but data about outcomes for this technique are limited.

Purpose: To evaluate the clinical and angiographic outcome of mini-crush stenting for the treatment of true coronary bifurcation lesions.

Methods: We conducted a retrospective study between January 2006 and December 2013. All patients were consecutively treated with implantation of DES with mini-crush technique for the treatment of true CBL. Follow-up-in our outpatient clinic was performed at 1 year. For the first 50 patients an angiographic control was scheduled at 9 months. The measured end-points were cardiac death, follow-up myocardial infarction (MI), TLR, target- vessel revascularisation (TVR) and major adverse cardiac events (MACE) defined as combination of cardiac death, MI and TVR.

Results: In the study period, 110 were treated. Clinical presentation was an acute coronary syndrome (ACS) in 80% of the cases and acute myocardial infarction (STEMI) in 18% of the cases. Unprotected left main was treated in 21% of patients. Two-step kissing balloon inflation and final kissing balloon inflation was systematically performed. First-generation DES were used in 72% of patients and the same type of DES for the whole bifurcation was used in 41% of the patients. Immediate procedural success was obtained in all of the cases. One episode of definite stent thrombosis was documented 10 days after the index procedure (premature DAP discontinuation). No deaths were documented. The 1-year cumulative incidence of MACE was 5.5%: 4 episodes of myocardial infarction and 6 TLR were recorded and provides good angiographic and clinical outcomes at 1-year in a high-risk patients population.

Conclusions: Our results suggest that the treatment of bifurcation lesions by means of mini-crush stenting technique is associated with excellent immediate success rate and provides good angiographic and clinical outcomes at 1-year in high-risk patients population.

Acknowledgement/Funding: none

P2766 | BEDSIDE
Impact of different drug-eluting kinetics on 3-year clinical outcomes following first- or second-generation zotarolimus-eluting stent implantation: a propensity score-matched analysis
S.W. Rha, B.G. Choi, S.Y. Choi, J.K. Byun, C.U. Choi, E.J. Kim, C.G. Park, H.S. Seo, D.J. Oh. Korea University Guro Hospital, Seoul, Korea, Republic of

Background: The only difference between the first and second generation zotarolimus-eluting stent (ZES) is the coated polymer, which controls drug-eluting rates. Although the second generation, slow releasing ZES (SR-ZES, Endeavor Resolute), has been shown to be superior to the first generation, fast-releasing ZES (FR-ZES, Endeavor Sprint) in short term outcomes, there are no study comparing long-term clinical outcomes between the two stents.

Method: A total of 714 patients (pts) receiving FR-ZES or SR-ZES were pooled from our percutaneous coronary intervention (PCI) registry. To adjust potential confounders, a propensity score matched (PSM) analysis was performed, and clinical outcomes were compared between the two groups up to 3 years.

Results: After PSM analysis, 2 propensity-scored matched groups (214 pairs, n=428, C-statistic=0.767) were generated, and all baseline characteristics were well balanced. The SR-ZES were superior to FR-ZES for 6-month angiographic outcomes with reduction in in-stent restenosis (22 [15.1%] vs 6 [5.5%], p=0.015). The incidence of mortality, myocardial infarction and stent thrombosis was not different between the two groups; however, the incidence of target lesion revascularisation (TLR) and target vessel revascularisation (TVR) were lower in pts receiving SR-ZES up to 3 years (TLR: HR 0.342, 95% CI: 0.129–0.916, p=0.033; TVR: HR 0.413, 95% CI: 0.177–0.962, p=0.041). There was a trend toward lower incidence of TLR and TVR-major adverse cardiac events (MACE) in the SR-ZES group (Table).

Conclusion: As compared with FR-ZES, the use of SR-ZES was associated with lower rate of repeat revascularization than FR-ZES during 3-year follow-up, suggesting slow-releasing drug-eluting kinetics would be better for long-term clinical outcomes.

P2767 | BEDSIDE
Platelet related procedure activation in long lesions treated with bioresorbable vascular scaffold versus xience xpedition implantation (prospective trial)
M. Pellicano1, G. Di Gioia2, G. Thot3, A. Ferrara4, J. Adjedj1, L. Delreux1, J. Bartunek1, W. Wijns1, B. De Bruyne1, E. Barbato1. 1OLV Hospital Aalst, Cardiovascular Center, Aalst, Belgium; 2Federico II University of Naples, Division of Cardiology, Naples, Italy

Background: Significant procedure-related platelet activation and myonecrosis has been reported with increasing stent length due to dual anti-platelet therapy. Procedure-related platelet activation in long lesions was increased with everolimus-eluting bioresorbable vascular scaffold (BVS) versus everolimus-eluting stent (EES) implantation; and to investigate the related impact on microvascular function and possible myocardial damage.

Purpose: We sought (a) to compare in long lesions procedure-related platelet activation with everolimus-eluting bioresorbable vascular scaffold (BVS) versus everolimus-eluting stent (EES) implantation; and (b) to investigate the related impact on microvascular function and possible myocardial damage.

Methods: Between December 2013 and December 2014, 22 patients with stable coronary artery disease and long lesions (to be treated with ≥25 mm stent/scaffold) were randomized (1:1) into the open-label, non-inferiority pilot “Proactive” trial either to Absorb BVS (11 patients) or Xience Xpedition EES (11 patients). All patients with ACS, bifurcation lesions with a side branch ≥2.0 mm and severely calcified stenosis suitable for rotational atherectomy were excluded. All patients were loaded with 500 mg aspirin and 600 mg clopidogrel at least 12 hours before the procedure. The primary endpoint was the immediate procedural changes in the index of microvascular resistance (IMR post-PCI – IMR pre-PCI), peri-procedural myocardial injury as assessed by increase in high sensitivity troponin (hs-Tn) at 24 h, and changes at 30 days in hs-ADP within and between groups.

Results: Clinical and angiographic characteristics of the patients were not different in both groups. Scaffold/stent length was 36.5±12.2 in the BVS and 31.7±7.5 in the EES group (p=0.58). A significant periprocedural reduction of hs-ADP was observed in the BVS group (from 22.5±9.1 to 14.4±4.6, p=0.01), but not in the EES group (from 19.1±11.2 to 15.8±13.6; p=0.35). IMR did not significantly change in both groups (BVS, from 22.7±12.1 to 16.2±4.7, p=0.106; EES, from 18.7±6.6 to 18.8±10.3; p=0.52). A peri-procedural myocardial injury occurred in 3 (27%) patients of the BVS and 2 (18%) patients of the EES group (p=1.00). At 30 days, there was no difference in hs-ADP as compared to post-PCI between and among the 2 groups.

Conclusions: In long lesions, peri-procedural platelet reactivity was unchanged with EES and even decreased with BVS implantation with no further changes at 30 days. Peri-procedural myocardial infarction occurred in less than 30% of the patients similarly in both groups, without a significant impact on microvascular resistance.

P2768 | BEDSIDE
Acute performance of second generation everolimus-eluting bioresorbable vascular scaffolds for percutaneous treatment of chronic total coronary occlusion
A. La Manna, A. Chisari, G. Gioacchi, D. Capodanno, G. Longo, M. Di Silvestro, C. Tambarino. Ferrarotto Hospital - Institute for Cardiology, Department of Cardiovascular, Catania, Italy

Aim: There is a lack of knowledge regarding the use of bioresorbable scaffold (BRS) in chronic total occlusions (CTO). The aim of the present study was to evaluate the acute performance of systematic BRS use in CTO lesions.

Methods: Procedural device and periprocedural changes in the index of microvascular resistance (IMR) were recorded in 12 CTO lesions treated with 2 (18%) patients of the EES group (p=1.00). At 30 days, there was no difference in hs-ADP as compared to post-PCI between and among the 2 groups.

Conclusions: In long lesions, peri-procedural platelet reactivity was unchanged with EES and even decreased with BVS implantation with no further changes at 30 days. Peri-procedural myocardial infarction occurred in less than 30% of the patients similarly in both groups, without a significant impact on microvascular resistance.

P2768 | BEDSIDE
Acute performance of second generation everolimus-eluting bioresorbable vascular scaffolds for percutaneous treatment of chronic total coronary occlusions
A. La Manna, A. Chisari, G. Gioacchi, D. Capodanno, G. Longo, M. Di Silvestro, C. Tambarino. Ferrarotto Hospital - Institute for Cardiology, Department of Cardiovascular, Catania, Italy

Aim: There is a lack of knowledge regarding the use of bioresorbable scaffold (BRS) in chronic total occlusions (CTO). The aim of the present study was to evaluate the acute performance of systematic BRS use in CTO lesions.

Methods: Procedural device and periprocedural changes in the index of microvascular resistance (IMR) were recorded in 12 CTO lesions treated with 2 (18%) patients of the EES group (p=1.00). At 30 days, there was no difference in hs-ADP as compared to post-PCI between and among the 2 groups.

Conclusions: In long lesions, peri-procedural platelet reactivity was unchanged with EES and even decreased with BVS implantation with no further changes at 30 days. Peri-procedural myocardial infarction occurred in less than 30% of the patients similarly in both groups, without a significant impact on microvascular resistance.
culation involving a side branch ≥2 mm in diameter were intentionally excluded. Device acute success was defined as 1) successful BRS delivery and implantation 2) post-procedural residual diameter stenosis ≤30% within the treated segment; 3) restoration of Thrombolysis in Myocardial Infarction (TIMI) grade 3 antegrade flow. Procedural success was defined as device success with no in-hospital major adverse cardiovascular events (MACE).

**Results:** Between May 2013 and May 2014, 51 patients underwent intended CTO-PCI with BRS. Wire crossing of the CTO lesion was achieved successfully in 42 cases and the Absorb BRS implanted in 32 of them. At least one exclusion criteria was encountered in 10 patients. Most of the procedures (30/32) were performed via the default antegrade approach, whereas switching to a retrograde approach was needed in two cases (6.2%). A total of 90 BRS were successfully implanted with a mean weight per patient of 2.8±1.28 and a mean scaffold length (L) of 40±16.8 cm. Eight of 32 patients (25%) received both BRSs and drug eluting stents (due to shelf unavailability in seven cases and delivery failure in one case). Intravascular ultrasound evaluation was carried out in 21/32 patients (65.6%). Device and procedural success were 78.1% and 78.1% respectively. In 7 of 32 patients (21.9%) a maximum residual stenosis >30% persisted. In hospital stay was uneventful in all cases. OCT assessment was performed post-PCI in 26 of 32 patients (81.2%). Among 63 scaffold analyzed, under-expansion was noted in 14 (22%) while both sub-medial dissection and BRS fracture were observed in 2 cases (3% respectively). Mean scaffold area was 8.2±2.52 and 9.5±2.54 mm² in overlapping and non-overlapping segments respectively. No case of incomplete scaffold apposition was detected.

**Conclusions:** BRS use for CTO's recanalization appears to be affected by a non-negligible rate of device failure. Adequate lesion preparation together with expected device ameliorations will be key to enable routine use of BRS in the CTO setting.

---

**P2770 | SPOTLIGHT**

Temporal trend in the incidence of stent thrombosis—is it the impact of improved antiplatelet regimen and evolving coronary stent technology?


**Background:** The incidence of stent thrombosis (ST) may have declined over the last several years, perhaps due to a combination of continuously improving antiplatelet regimen (AR) and coronary stents. We studied the temporal change in the incidence of ST.

**Methods:** We retrospectively examined the percutaneous coronary intervention (PCI) database at our large academic medical center from 1/1/06 and 12/31/13. Patients with ST within 1 year of index PCI were identified (as per Academic Research Consortium definition). The AR and characteristics of CS at the time of index PCI were recorded for pts developing ST.

**Results:** The study sample included 4460 patients. Of those, 210 patients (4.7%) developed ST (71: definite, 22: probable, 117: possible). Patients with ST were older (68±13 vs 62±13, *p<0.0001), higher smoking rate (53% vs 32%, *p<0.0001), more diabetes (67% vs 28%, *p<0.0001), more STEMI (43% vs 33%, *p<0.005), higher stent/pt (1.6±0.9 vs 1.6±0.9, *p<0.0001), lesser drug eluting stent after index PCI (13% vs 22%, *p=0.006). Incidence of stent thrombosis, AR and stent type for patients with ST is described in Table 1.

**Conclusion:** We have noticed a steady decline in the incidence of ST from 2006 to 2013. This trend correlates with an increase in the use of prasugrel or ticagrelor as well as an increase in the use of second generation drug eluting stents.

---

**P2771 | BEDSIDE**

Anatomical and functional assessment of Tryon bifurcation stent before and after final kissing balloon dilation: evaluations by three-dimensional coronary angiography, optical coherence tomography

S. Pyxaras1, G.G. Toth2, G. Di-Gioia3, G.J. Ughi4, S. Tu5, D. Rusinaru1, T. Adriansens4, J.H.C. Reiber5, M.B. Leon6, W. Wijns1. 1 Klinikum Coburg, Institute of Cardiology, Germany; 2 University Heart Centre Graz, Austria; 3 Cardiovascular Center Aalst, Aalst, Belgium; 4 KU Leuven, Department of Cardiovascular Sciences, Leuven, Belgium; 5 Leiden University Medical Center, Division of Image Processing, Department of Radiology, Leiden, Netherlands; 6 Columbia University Medical Center, New York Presbyterian Hospital, Center for Interventional Vascular Therapy, New York, United States of America.

**Aims:** Current experience and retrospective analysis suggest clinical benefit of final kissing balloon dilation (FKB) in patients undergoing bifurcation dilation using the Tryon Side Branch Stent (Tryon-SBS), but the reasons for these observations remain speculative. In this study we sought to assess the anatomical and functional impact of FKB after implantation of this dedicated bifurcation stent system.

**Methods and results:** An unmatched group of 10 patients with complex bifurcation coronary lesions undergoing percutaneous coronary intervention (PCI) with Tryon-SBS underwent paired anatomical assessment with two- and three-dimensional quantitative coronary analysis (2D- and 3D-QCA), and optical coherence tomography (OCT), including 3D reconstruction with dedicated software, before and after FKB. Functional assessment was performed in the main branch (MB) and side branch (SB) before and after FKB using fractional flow reserve (FFR). At 2D-QCA, a significant decrease in SB diameter stenosis was observed after FKB (from 27.6±15.6 to 15.4±10.5, *p<0.045). At 3D-QCA, no significant variations were detected after FKB. By OCT imaging, FKB increased both the SB ostial area (>2.5±2.8 mm², *p<0.001) and the SB maximum diameter (>7.0±9 mm, *p<0.003). These findings were associated with a significant increase in FFR in the SB (delta FFR >0.04±0.13; *p=0.011), with no significant change in the MB (delta FFR >0.01±0.04; *p=0.470).

**Conclusions:** In patients with complex bifurcation stenosis undergoing PCI with a dedicated bifurcation stent, FKB is associated with improved procedural anatomical and functional results at the SB level, without compromising outcomes of the MB.

---

**Table 1**

<table>
<thead>
<tr>
<th>Year</th>
<th>Slent thrombosis incidence % (n/total pts)</th>
<th>Antiplaque regimen at the time of Index PCI (in addition to Aspirin)</th>
<th>Stent type**</th>
<th>Type of DES placed during initial PCI in patients presenting with stent thrombosis</th>
<th>First generation DES**</th>
<th>Second generation DES**</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n/total pts)</td>
<td>Urapidog</td>
<td>Prasugrel or Clopidogrel</td>
<td>BMS</td>
<td>DES</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>5.8% (35/599)</td>
<td>100 (35)</td>
<td>12 (4)</td>
<td>38 (11)</td>
<td>88 (31)</td>
<td>88 (31)</td>
</tr>
<tr>
<td>2007</td>
<td>6.3% (32/516)</td>
<td>94 (30)</td>
<td>10 (3)</td>
<td>30 (10)</td>
<td>50 (16)</td>
<td>41 (13)</td>
</tr>
<tr>
<td>2008</td>
<td>6.1% (36/586)</td>
<td>98 (35)</td>
<td>12 (4)</td>
<td>39 (13)</td>
<td>89 (31)</td>
<td>89 (31)</td>
</tr>
<tr>
<td>2009</td>
<td>4.7% (25/534)</td>
<td>96 (24)</td>
<td>4 (1)</td>
<td>52 (13)</td>
<td>48 (12)</td>
<td>20 (5)</td>
</tr>
<tr>
<td>2010</td>
<td>4.6% (24/518)</td>
<td>97 (18)</td>
<td>3 (1)</td>
<td>50 (12)</td>
<td>50 (12)</td>
<td>8 (2)</td>
</tr>
<tr>
<td>2011</td>
<td>4.6% (23/502)</td>
<td>95 (18)</td>
<td>3 (1)</td>
<td>50 (11)</td>
<td>50 (11)</td>
<td>25 (9)</td>
</tr>
<tr>
<td>2012</td>
<td>3.0% (15/500)</td>
<td>12 (10)</td>
<td>3 (1)</td>
<td>42 (14)</td>
<td>34 (12)</td>
<td>17 (6)</td>
</tr>
</tbody>
</table>

*ST, stent thrombosis; DES, drug eluting stent; BMS, bare metal stent; PCI, percutaneous coronary intervention; pts, patients. Aspirin use remained unchanged across the study population from 2006 to 2013. **n represents patients with stent thrombosis; ***denominator is number of patients with stent thrombosis. Average stent dimension: 3.1±0.2 (18.6±2.2) mm.
Introduction: The aim of this abstract is to report our experience using extracorporeal membrane oxygenation assistance (ECMO) in an effort to improve outcomes in high-risk patients undergoing percutaneous interventions in the catheterization laboratory.

Methods: Between October 2013 and December 2014, 10 adult patients were placed on veno-arterial (VA) ECMO (CardiohelpTM, Maquet Cardiopulmonary AB, Solna, Sweden) for 24 hours in 4 patients. VA-ECMO was placed as hemodynamic support during high-risk percutaneous interventions in the catheterization laboratory. Underlying diseases included high-risk angioplasty (3 patients) of unprotected left main or multiple vessel revascularization in the context of severe left ventricular (LV) dysfunction; and during aortic valveoplasty in a patient with severe aortic valve stenosis, two- vessel disease and very severe LV dysfunction with heart failure symptoms at rest. All 4 cases were discussed in the heart- team and were rejected for surgery. Interventional cardiology and cardiothoracic surgeons made the implantation of cannulas and a perfusionist assisted the VA-ECMO during percutaneous intervention. In two patients prior to percutaneous insertion of the arterial cannulas a Prostar XL device was implanted for achieving arterial haemostasis.

Results: All patients, except one, required invasive mechanical ventilation during intervention due to heart failure and shortness of breath. Arterial and venous access was performed percutaneously except for a patient with severe peripheral arterial disease to whom axillary artery was cannulated by surgery to complete the ECMO circuit. During the procedures pump flow was 2.5–3.0 l/min. ECMO was placed immediately before percutaneous interventions and implantation was performed immediately after finishing the intervention except for a patient who was supported for three days because weaning in the catheterization laboratory was not successful. None of the patients required blood transfusion or had complications such as stroke or limb ischemia. Arterial haemostasis with Prostar XL sutures at the end of the procedure was successful in both attempted patients.

Conclusions: We believe that ECMO support is a viable mode of hemodynamic support in high-risk percutaneous interventions. Percutaneous ECMO implantation in the catheterization laboratory and immediate implantation after percutaneous intervention is feasible and safe.

P2773 | BEDSIDE
Percutaneous coronary intervention during extracorporeal membrane oxygenation versus coronary artery bypass graft surgery in high-risk patients
N. Kochergin, V. Ganyukov, D. Shukevich. Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation

Introduction: There is not enough evidence regarding safety and efficacy of extracorporeal membrane oxygenation (ECMO) during percutaneous coronary intervention (PCI) amongst high-risk patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS).

Aim: To compare the results of PCI during ECMO and coronary artery bypass graft (CABG) surgery amongst patients with NSTE-ACS.

Methods: Prospective analysis of 30-day follow-up of high-risk patients with NSTE-ACS who underwent either PCI during ECMO or CABG surgery. Study sample included 69 patients, and all of them had significant comorbidity along with high risk according to EuroScore scale and with high SYN-TAX score. 16 patients underwent PCI during ECMO (PCI-ECMO), and other 53 patients underwent CABG surgery. PCI was carried out in patients who were restricted to CABG surgery. Average risk according to GRACE score did not differ significantly between these two groups (PCI-ECMO group 100±22.9, CABG surgery group 95.6±16.4, p=0.39). There was no statistically significant difference concerning clinicopathological features. Both groups did not differ significantly regarding EuroScore scale (PCI-ECMO group 12.2±19.9, CABG surgery group 7.5±5.2%, p=0.12) and SYNTAX score (PCI-ECMO group 30.5±9.3, CABG surgery group 30±8.2, p=0.8). However, PCI-ECMO group included significantly more patients with left main disease.

Study endpoints included successful intervention, death, myocardial infarction (MI), stroke, repeat revascularization, and bleeding. There was also combined endpoint which included death, MI, stroke, and repeated revascularization.

Results: Intervention was successful in all cases. During the 30-day period of follow-up, case fatality rate was 12.5% in PCI-ECMO group (2 patients) and 7.5% (4 patients) in CABG surgery group (p=0.53). There were two cases (3.8%) of MI and one (1.9%) MI-related death during postoperative period in CABG surgery group. In addition, 7 (13.2%) patients from CABG surgery group had heavy bleeding (according to TIMI classification) versus 1 (6.2%) patient in PCI-ECMO group (p=0.44). There were no statistically significant differences in prevalence of endpoints during the perioperative period of follow-up. The prevalence of combined endpoint did not differ significantly between groups (12.5% in PCI-ECMO group, 9.4% in CABG surgery, p=0.72).

Conclusion: PCI-ECMO may be an alternative technique of myocardial revascularization in high-risk patients with multivessel coronary artery disease and NSTE-ACS.

P2774 | BEDSIDE
Predictor of persistent slow/no-reflow after percutaneous coronary intervention with thrombus aspiration and distal protection for ST-elevation myocardial infarction

Background: Slow/no-reflow after percutaneous coronary intervention (PCI) for ST-elevation myocardial infarction (STEMI) leads to poor prognosis. PCI with thrombus aspiration (TA) and distal protection (DP) is not able to prevent slow/no-reflow completely.

Purpose: To clarify the predictors of persistent slow/no-reflow after PCI with TA and DP for STEMI.

Methods: From January 2006 to December 2013, 1790 patients underwent PCI for STEMI, of whom 358 patients underwent PCI with TA and DP for STEMI. Persistent slow/no-reflow was observed in 43 patients. We evaluated the predictors of persistent slow/no-reflow.

Results: In persistent slow/no-reflow group, the rate of congestive heart failure and mean age was significantly higher than without persistent slow/no-reflow group. The rate of diffuse lesion was significantly higher and the rate of the right coronary artery lesion was relatively higher than without persistent slow/no-reflow group. No difference was observed between the two groups regarding onset to balloon time, stent size, reference vessel diameter and minimal lumen diameter, before and after PCI. A multivariate analysis revealed that the independent predictor of persistent slow/no-reflow was a Killip class ≥2 before PCI (odds ratio 3.21, 95% confidence interval 1.42–7.06, p=0.01).

Multivariate analysis for predictors of persistent slow/no-reflow

<table>
<thead>
<tr>
<th>Variables</th>
<th>Multivariate OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Killip class ≥2</td>
<td>3.21 (1.42–7.07)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Lesion length ≥25 mm</td>
<td>1.89 (0.95–3.78)</td>
<td>0.07</td>
</tr>
<tr>
<td>RCA lesion</td>
<td>1.79 (0.83–4.11)</td>
<td>0.14</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.53 (0.74–3.30)</td>
<td>0.25</td>
</tr>
<tr>
<td>Age ≥70 years old</td>
<td>1.49 (0.71–3.17)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Conclusion: In patients treated with primary PCI with TA and DP for STEMI, the independent predictor of persistent slow/no-reflow was only a Killip class ≥2 before PCI.

P2775 | BEDSIDE
The effect of drug-eluting stent on mid-term epicardial and microvascular endothelial function: a coronary blood flow assessment with acetylcholine test
H. Tamura1, K. Fuji1, M. Shibuya1, T. Imanaka2, A. Sumiyoshi1, T. Saita1, M. Nishimura1, T. Horimatsu1, M. Ishihara2, T. Masuyama1, 1Hyogo College of Medicine, Cardiovascular Division, Nishinomiya, Japan; 2Hyogo College of Medicine, Division of Coronary Heart Disease, Nishinomiya, Japan

Background: Previous studies reported drug-eluting stent (DES) induced significant impairment of the coronary epicardial endothelium-dependent vasomotor function in the left anterior descending artery in patients with acute coronary syndrome. Coronary microangiograms with physiological studies were conducted at the end of the initial procedure and 9 months later. Coronary diameter and average peak velocity (APV) were measured at the segment 5 to 10 mm distal to the DES, and coronary blood flow (CBF) was measured by the Doppler-derived time-velocity integral, calculated as CBF = (coronary diameter/2)π×APV/2. The percentage change of CBF in response to acetylcholine (Ach) and adenosine tri-phosphate (ATP) was evaluated as an index of microvascular endothelial function. The percent change in coronary diameter was measured in response to Ach and isosorbide dinitrate was also analyzed as an index of epicardial endothelial function.

Purpose: To compare the results of PCI during ECMO and coronary artery bypass graft surgery in high-risk patients with NSTE-ACS.

Methods: Consecutive 11 patients who were scheduled for DES implantation in the left anterior descending artery were prospectively enrolled. Coronary angiograms with physiological studies were conducted at the end of the initial procedure and 9 months later. Coronary diameter and average peak velocity (APV) were measured at the segment 5 to 10 mm distal to the DES, and coronary blood flow (CBF) was measured by the Doppler-derived time-velocity integral, calculated as CBF = (coronary diameter/2)π×APV/2. The percentage change of CBF in response to Ach was evaluated as an index of epicardial endothelial function.

Results: Microvascular endothelial function measured at follow-up was significantly impaired severely than that measured at the baseline study, but their epicardial endothelial function was preserved during the follow-up period (Figure).
Conclusion: DES impaired microvascular endothelial function rather than epicardial endothelial function of coronary artery distal to the DES. Our results support a long-term worsening of microvascular function by DES implantation.

P2776 | BEDSIDE
Modified stent platform favorably affects longitudinal stent strength and stent deformation of the platinum chromium everolimus-eluting stent: an in vivo frequency domain optical coherence tomography (FD-OCT) in vivo.

Methods: Fifty-two lesions treated with Ptcr-EES (Promus Element: n=29, Promus Premier: n=23) were studied. After successful stent implantation, FD-OCT was performed to measure actual stent length in vivo. Percent longitudinal stent shortening (%SS) was defined as % (the actual stent length divided by nominal stent length). Longitudinal stent deformation was defined as % SS > 10.

Results: Results and procedure: Cardiac catheterization was conducted in the cath lab using FD-OCT. As a new stent was deployed, coronary artery blood flow was measured bilaterally for 2 hours. Cyclical flow variation and inter-stent variation were measured with FD-OCT. The study group had a mean %SS of 11.8% and the control group had a mean %SS of 21.3%. %SS was significantly lower in the group with stent platform innovations compared to the group without innovations.

Conclusion: The study demonstrated that the modified version of the Ptcr-EES reduces stent deformation and is a promising platform for improving cardiac outcomes.

P2777 | BEDSIDE
Use of protective ballooning technique with provisional stenting for treatment of non-left main coronary bifurcation lesions

Methods: The study included 100 patients with non-left main coronary bifurcation lesions. The lesions were categorized into two groups: Group A (n=50) received protective ballooning followed by provisional stenting, and Group B (n=50) received stenting alone. The primary endpoint was the rate of in-stent restenosis at 6 months.

Results: The rate of in-stent restenosis was significantly lower in Group A (8.2%) compared to Group B (16.4%). No significant differences were observed in terms of procedural success or major adverse cardiac events. The study concluded that the use of protective ballooning followed by provisional stenting is an effective strategy to reduce in-stent restenosis in non-left main coronary bifurcation lesions.

P2778 | BENCH
A rabbit iliac model for testing the acute thrombogenicity and long-term biocompatibility of novel coronary stents and scaffolds

Methods and results: The study involved the use of a rabbit iliac model to assess the acute thrombogenicity and long-term biocompatibility of novel coronary stents and scaffolds. The model was designed to mimic the human arterial system and allow for detailed evaluation of stent performance under in vivo conditions.

Results: The rabbit iliac model proved to be a reproducible method for assessing the acute thrombogenicity and long-term biocompatibility of novel coronary stents and scaffolds.

Conclusion: The rabbit iliac model has been proven to be a reproducible method for assessing the acute thrombogenicity and long-term biocompatibility of novel coronary stents and scaffolds.
P2780 | BEDSIDE
Longitudinal neointimal distribution after drug-eluting stent implantation: an optical coherence tomography study
S. Otuku, S. Brugaletta, Y. Shiratori, G. Scalone, O. Gomez-Montesinos, S. Romero-Villafane, X. Freixa, V. Martin-Yuste, M. Masotti, M. Sabate. Hospital Clinic, University of Barcelona, Department of Cardiology. Thorax Institute, Barcelona, Spain

Background: Healing process following drug-eluting stent (DES) implantation is well-known. However, little is known about the longitudinal in-stent neointimal distribution and its predictors. We sought to evaluate the longitudinal in-stent neointimal distribution after DES implantation by optical coherence tomography (OCT).

Methods: All consecutive patients, who had an OCT analysis from 6 to 20 months after the DES implantation in our institution, were included into the present analysis. Lesions treated with overlapping stenting were excluded. Neointima thickness (NIT) was calculated per cross-section. Each stented lesion was divided into three equal parts with same numbers of cross-sections and each segment was defined as proximal, medial and distal. In order to estimate the predictors of NIT, univariate and multivariable (with all variables showing a P-value of <0.1 at univariate analysis) generalized estimating equations approaches, was also applied, correcting for repeated observations.

Results: From July 2010 to January 2013, a total 41 patients with 44 lesions, which have received either Xience™ (n=35) or NEVO™ stent (n=9), were analysed. Mean NIT was 140.0±174.7 µm. In the multivariate analysis, the independent predictors of NIT were male sex (p=0.001), time of OCT evaluation (≥180 days, [≥180 and <365 days] or >365 days; p=0.004), stent position within the vessel or distal coronary segment; p=0.018) and stent diameter (<3.0 mm or ≥3.0 mm; p=0.007). NIT of instent segments were not different between three groups (p=0.677).

Conclusions: NIT after DES implantation may depend from some clinical and angiographic factors. In particular it seems that it is homogenously distributed within the stent segment.

P2781 | BEDSIDE
Dedicated side branch stent versus mini-crushing stenting: comparison between two techniques in the true treatment of coronary bifurcation. The procedural outcome
A. Nicolino1, R. Rosso2, S. Moshiri3, A. Fogogni3, A. Lupi2, A.S. Bongó2, G.B. Danzi3. 1S.C. Cardiologia; Ospedale Santa Corona, Pietra Ligure, Italy; 2Hospital Maggiore della Carità, Cardiologia, Novara, Italy; 3Interventional Cardiovascular Unit; Santa Corona General Hospital, Pietra Ligure, Italy

Purpose: Introduction: True coronary bifurcation lesions (CBL) defined as Medina classification 1, 1, 1; 1, 1, 0; or 0, 1, 1; account for approximately 15% of all treated lesions and are associated with a lower procedural and long term success when compared with non-bifurcation lesions. Therefore, several dedicated bifurcation stents and devices have been developed to improve clinical outcomes in this setting.

Methods: The aim of this study was to compare the procedural outcomes associated with the Tryton Side Branch Stent™ (Tryton Medical, Durham, NC, USA) versus the “mini-crushing stenting” technique (MCT) for the treatment of CBL.

Results: We performed a retrospective analysis of patients with a true CBL who underwent PCI in two different centers between January 2008 and December 2012. We compared 30 CBL in 30 Patient treated with the Tryton (TR-group) in 36 CBL in 30 Patient treated with MCT (MCT-group). Patients were matched for age, risk factors and baseline characteristics. The measured end-points were: procedural time, fluoroscopy time, contrast medium, angiographic success, periprocudural MI.

Results: Two-step kissing balloon inflation and final kissing balloon inflation was systematically performed. Immediate procedural success was obtained in all of the cases. Non major complication during the procedure. The procedural time was 82±21 min in the TR-group vs 84±10 in the MCT-group (p=ns); the fluoroscopy time was 21±10 vs 28±7.7,4 (p=0.003); contrast medium was 235±45 vs 248±62 ml (p=ns); procedural MI was absent in both group.

Conclusions: Tryton Side branch stent and mini-crushing technique provides excellent angiographic and procedural success. Procedural time and contrast dose are acceptable for both; fluoroscopy time is higher for MCT.

P2782 | BEDSIDE
Favorable clinical long-term follow-up of mini-crushing technique for treatment of true bifurcations
A. Nicolino1, S. Moshiri2, L. Olivotti2, K. Paonessa1, A. Basilece1, G.B. Danzi1. 1S.C. Cardiologia; Ospedale Santa Corona, Pietra Ligure, Italy; 2Interventional Cardiovascular Unit; Santa Corona General Hospital, Pietra Ligure, Italy

Background: Percutaneous treatment of coronary bifurcations lesions (CBL) is associated with a low procedural success rate and high incidence of target lesion revascularization (TLR) and stent thrombosis in both branches of the bifurcations is still required in 15%-30% of cases. The “mini-crush” technique (MCT) is one of the techniques used to implant stents on both branches of a CBL and provides complete coverage of the ostium of the side branch, while minimizing the length of the crushed stent.

Purpose: The aim of this study is to evaluate the long-term clinical outcomes associated with the treatment of CBL with MCT.

Methods: Between January 2006 and December 2011, all consecutive patients who underwent mini-crushing (MCT) treatment for the treatment of true CBL were admitted to this observational study. The measured end-points were cardiac death, follow-up myocardial infarction (MI), TLR, target-vessel revascularization (TVR) and major adverse cardiac events (MACE) defined as combination of cardiac death, MI and TVR. Three-year follow-up was obtained in all of the cases by means of telephone interview or visit at our out-patient clinic.

Results: In the study period we treated 90 CBL in 90 patients with “mini-crush” technique. Clinical presentation was ACS-NSTEMI in 40% and STEMI in 16%. Unprotected left main lesions were identified in 19.3% of patients. True bifurcation lesions accounted for (Medina classification [1,1,1], [1,0,1], [0,0,1], [0,1,1]) were observed in 81 lesions. Two-step kissing balloon inflation and final kissing balloon inflation was systematically performed. Second generation DES was used in 7% of the patients. Immediate procedural success was obtained in all of the cases. One episode of definite stent thrombosis was documented 10 days after the index procedure (DAPT discontinuation). The 3-year cumulative incidence of MACE was 11.1%. 2 deaths, 6 cases of myocardial infarction, 9 TLR and 4 TVR.

Conclusions: Our results suggest that the treatment of CBL by means of mini-crush technique and provides acceptable long-term outcomes in a high-risk patients population.

P2783 | BEDSIDE
Anti-CD34 capturing in coronary stenting leads to improved endothelial coverage: COMBO vs. Xience Prime
G.H.J.M. Ellenbroek1, E. Ligtengberg2, S. Rowland2, J.A. Post3, G. Pasterkamp4, I.E. Hoeter1. 1University Medical Center Utrecht, Experimental Cardiology, Utrecht, Netherlands; 2O Orus Neich Medical, Hoewelaken, Netherlands; 3H University of Applied Sciences of Utrecht, Biomolecular imaging, Utrecht, Netherlands

Introduction: Drug-eluting stents (DES) reduce neointimal hyperplasia (NIH) by inhibition of vascular smooth muscle cell (VSMC) proliferation. Because of their non-selective anti-proliferative effect, stent re-endothelialization is also inhibited, which may increase the risk for stent thrombosis. The COMBO stent combines an abluminal sirolimus-eluting coating with endothelial progenitor cell (EPC) capturing technology to combine intimal hyperplasia reduction with improved re-endothelialization.

Purpose: The aim of our study was to compare the novel COMBO stent with current standard treatment.

Methods: Twelve New-Zealand White (NZW) rabbits were subjected to iliac artery stent placement. Twenty-eight days after implantation, optical coherence tomography (OCT) was performed (n=4) and tissue was harvested from the animals (n=6). Late lumen loss ratio was defined as angiographic stent diameter directly after implantation/stent diameter at twenty-eight days of follow-up. Intimal hyperplasia was assessed by both histology and OCT. Additionally, scanning electron microscopy (sEM) was performed to evaluate stent coverage.

Results: Compared to EES, strut coverage was significantly higher in the COMBO stent (78.5±6.8% vs. 96.6±3.5%; p=0.043). Intimal hyperplasia did not differ between the EES and COMBO stent as assessed by OCT (0.227±0.025 mm² vs. 0.188±0.044 mm²; p=NS) or histology (0.823±0.200 mm² vs. 0.891±0.312 mm²; p=NS). No differences were observed in late lumen loss ratio between both EES and COMBO stent (0.952±0.027 vs. 0.94±0.024; p=NS).

Conclusion: Re-endothelialization was significantly improved in the COMBO stent as compared to EES with equal inhibition of intimal hyperplasia. As stent endothelialization is a major determinant of stent thrombosis, this may reduce thrombotic events after DES implantation.

Acknowledgement/Funding: Project CIRCULATING CELLS (grant 01C-102) and support by the Dutch Heart Foundation

P2784 | BEDSIDE
Takotsubo cardiomyopathy in regional Australia
R.J. MacFadyen1, S. Lovibond2, K. Rajah1, A. Antonov2, J. Martin2, A. Sharma1, C. Lengel1, F. Charchar4, E. Oqueci2, 1Ballarat Base Hospital, Cardiology, Ballarat, Australia; 2Deakin University, Cardiology, Geelong, Australia; 3The Alfred Hospital, Cardiology, Melbourne, Australia; 4Federation University Australia, Ballarat, Australia

Background: Takotsubo cardiomyopathy (TCM) is prevalent, under recognized and often miss diagnosed. Detection rates reflect index of suspicion over a broad range of presentations and spectrum of ventricular injury. We highlight a sample of presentations over 23 months from regional Australia where coronary disease is excluded and ventricular injury defined at onset and recovery. Within this prevalence we propose genome wide screening for mechanisms of recovery is feasible.
Methods: Discharges were retrospectively audited to extract clinical demographic information; patient CV risk factors and ventricular injury (by rest TTE). Coronary angiography at presentation was reviewed in all cases.

Results: From a period where we managed 167 STEMI and 490 NSTEMI admissions, 23 index cases (20 d; 70±14 yr (range 40–94 yr)); current smoking (11/23,48%); ALC excess (3/20,13%); with SR in 20/23 (87%) or AF 3/23 (13%), were classed as new onset TCM. Of these 6/23 (26%) had suggested IHD; 20/23 (86%) had HBP. 15/23 (65%) had DM. 4/23 (17%) had a FH of CAD. Depression was present in 12/23 (52%), anxiety 4/23 (18%), hypertension 14/23 (60%) with non obstructive plaque not regarded as relevant (discordant anatomy and function). Mid left ventricular EF at presentation was 34±15%. Apical ballooning was present in 22/23 (91%); 1/23 (6%) showed RV involvement and 1/23 (6%) mitral valve dysfunction. By re-assessment at 24±26d, LV EF rose to 56±17%. None had persistent apical ballooning; basal hypokinesis or significant RV involvement in the context of standard therapies (Loop diuretic 14/23 (64%); MACE 5/23 (23%); ACEI/ARB 19/23 (87%) and BB in 20/23 (91%).

Conclusion: In regional Australia in line with urban reports there is a major prevalence of TCM. While tight diagnostic criteria are evolving the clinical course of these patients is distinct, definable and potentially holds clues to mediators of ventricular recovery as well as reversible injury. While past genomic screens have focused on the susceptibility to injury, future work should target mediators of recovery comparing more common forms of LVSD such as ischaemic or toxic CM. They are feasible in regional centres.

P2785  |  BEDSIDE
Demographic and clinical characteristics of male and female patients with preserved ejection fraction in a large health organization.

L Bash1, D Weitzenz2, O Sharon3, M Aviram-Paz4, G Chodick2, V Shalev5, A Merk and Company, Inc., Rahway, NJ, United States of America, 2Maccabi Healthcare Services, Tel Aviv, Israel, 3MSD Israel, Hod Hasharon, Israel, 4Tel Aviv University, Tel Aviv, Israel

Introduction: Congestive heart failure (CHF) with preserved ejection fraction (EF) has been reported to be more common in females than in males. However, the characteristics of those with a history of demographic and clinical characteristics to this difference has rarely been analyzed in real-world settings.

Purpose: The study aim was to characterize male and female CHF patients according to their EF level at diagnosis.

Methods: Included in the study were adult members of a public health organization who were diagnosed with CHF between January 2006 and December 2012 and had an available EF measurement in their medical records. MHS databases were used to collect data on other demographic and clinical characteristics.

Results: A total of 3076 patients were eligible for analysis (62.3% males). Although males had a higher EF overall as well as reversible in males. While past genomic screens have focused on the susceptibility to injury, future work should target mediators of recovery comparing more common forms of LVSD such as ischaemic or toxic CM. They are feasible in regional centres.

Conclusions: Male and female CHF patients are clinically and statistically significantly different in important clinical characteristics that may affect survival. While ischemia is more common in male CHF patients, female CHF patients substantially more often have preserved ejection fraction. Whether and how clinical characteristics of gender determinants may drive disease etiology and prognosis should be further assessed.

Acknowledgement/Funding: Work was funded by Merck & Co., Inc.

P2786  |  BEDSIDE
The impact of iron deficiency and anaemia on exercise capacity and outcomes in patients with chronic heart failure

N. Ebner1, E.A. Jankowska2, V. Sliziuk1, S. Elsner1, L. Steinbeck1, J. Kubel1, A. Sandek1, W. Doehner3, S.D. Anker1, S. Von Haehling1.

1Karolinska Institute, Danderyd Hospital, Department of Cardiology, Stockholm, Sweden, 2Karolinska University Hospital, Department of Cardiology, Stockholm, Sweden

Aim: To study predictors and characteristics of patients with in-hospital and late onset post-AMIs. Background: Few data are available on determinants of in-hospital and late-onset HF after AMI. Methods: SWEDEHEART records baseline characteristics, treatments and outcomes of consecutive patients with AMI admitted to all hospitals in Sweden. In-hospital HF was defined as presence of cracks, use of diuretics or use of IV inotropic drugs. Late-onset HF was defined as readmission within 2 years cause of HF in patients without prior HF and no in-hospital HF. (n=230,408).

Results: The incidence of in-hospital HF and late-onset HF decreased from 48% to 26% (p<0.001) and from 15% to 13% (p<0.001), respectively. Changes in baseline characteristics are shown in Table 1. In multivariable analyses, female gender (OR 95% CI), 1.14 (1.1–1.2), diabetes mellitus 1.3 (1.25–1.3), STEMI 1.5 (1.4–1.5) and prior HF (2.1 (2.0–2.2) were strongest associated with in-hospital HF, whereas diabetes (OR 95% CI), 1.5 (1.4–1.7), prior AMI 1.4 (1.1–1.8) and periferal arterial disease 1.3 (1.1–1.7) were strongest associated with late-onset HF. Calendar-year reduced the odds of in-hospital HF (OR 95% CI), 0.85 (0.8–0.9) as well as late-onset HF 0.8 (0.6–0.9).

Table 1. Changes in baseline characteristics of patients with in-hospital and late-onset HF after an index AMI

In-hospital HF Late-onset HF (at 2 years)

1996-97 1999-06 2008-09

Age (mean) 73.8 76.1 74.3 76.7
Female (%) 39.5 43.1 41 42
Diabetes (n=93, 19%) 25.4 31 28.4 29.1
Hypertension (%) 34.6 53.3 38.7 52.8
Prior MI (%) 23.1 31.4 20.2 13.2
Prior PCI (%) 17.6 17.6 18.2 18.2
Prior Stroke (%) 13.2 15.7 13.4 13.3
PAD (%) 7.4 7.3 7.5 8.0
Renal failure (%) 5.0 6.9 5.1 3.9
STEMI/LBBB (%) 5.6 6.3 5.6 4.1

Conclusion: Characteristics of patients with post-AMI HF have changed. The predictors of in-hospital and late-onset HF differ. Both in-hospital and late-onset HF after AMI are decreasing.
B. Sredniawa1, A. Lekston1, M. Zembala1, L. Polonski1, M. Gasior1.

10.8% in 2003 to 10.0% in 2012. However, the mean age of mortality increased due to cardiovascular disease (23% of all hospital discharges for cardiovascular heart failure from 2003 to 2012).

**Purpose:** This study aims to analyze the evolution of incidence and mortality of heart failure from 2003 to 2012.

**Methods:** Retrospective analysis of all hospitalizations due to cardiovascular disease in the National Health Service for the years 2003 through 2012 (N=3 667 066). The analyses focused on patients with HF as primary diagnosis (N=847 539). The association of the mortality with age, gender and etiological factors was determined.

**Results:** Over 10-year period, HF was the most common cause of hospitalization due to cardiovascular disease (23% of all hospital discharges for cardiovascular disease). The incidence rate increased significantly by 50% over the study period. The risk adjusted in-hospital mortality rate due to HF decreased slightly from 10.8% in 2003 to 10.0% in 2012. However, the mean age of mortality increased significantly by 7.7 years to 80.1 years. Our findings showed that those patients at highest mortality risk in HF patients was age-dependent (<0.05) during all study period. Male gender was associated with higher mortality for the whole sample of the study. However, gender ceased to be a significant contributor to the mortality risk in 2012.

**Conclusion:** HF is the most common cause of hospitalization due to cardiovascular disease. The progress in treatment of HF has achieved to lengthen the life of expectancy of HF patients but the mortality rate still remains high. Female HF incidence rates have increased recently.

**Acknowledgement/Funding:** This study was supported by an unconditional grant from Menarini.

---

**P2789 | BEDSIDE**

**Comorbidities and factors associated with reduced (<40%) left ventricle ejection fraction at discharge from acute myocardial infarction (results from the PL-ACS registry)**

M. Gierlotka1, M. Hawranek1, M. Tajstra1, K. Wilczek1, M. Janion2, B. Sredniawa1, A. Lekston1, M. Zembala1, L. Polonski1, M. Gasior1, Silesian Center for Heart Diseases, Zabrze, Poland; University of Humanities and Science in Kielce, Cardiology Center, Kielce, Poland

Left ventricle ejection fraction (EF) <40% at discharge from acute myocardial infarction (AMI) is a well-known major factor of poor long-term outcome. Therefore we assessed a relative impact of comorbidities and factors associated with acute phase of AMI on discharge EF <40%.

**Methods:** All patients who survived in-hospital phase with NSTEMI (N=86793) and STEMI (N=84925) with known EF at discharge registered in the prospective Polish Registry of Acute Coronary Syndromes (PL-ACS) from 2008 to 2013 were included. 12-months mortality was obtained from the government database.

**Results:** The percentage of patients with EF <40% at discharge was 28% (n=38918). Comorbidities and factors associated with reduced EF at discharge are presented in the table. Both acute heart failure during AMI and the history of heart failure or myocardial infarction before admission were the strongest predictors of EF <40% at discharge. Invasive treatment with PCI was associated with higher EF. 12-month mortality after discharge was significantly higher in patients with EF <40% (24.3% vs. 6.4%; p<0.0001), and after adjustment in multivariate analysis HR=1.81; 95% CI: 1.75–1.87; p<0.001.

**Conclusion:** Apart from the factors related to acute phase of AMI, most of the comorbidities of AMI patients is associated with reduced EF at discharge and they all contribute to high 12-month mortality.

---

**P2790 | BEDSIDE**

Outpatient consultation supporting post-discharge heart failure patients reduces 30-day re-hospitalization rate

C. Pacho, M. Domingo, R. Nunez, M. Rodriguez, R. Cabanes, B. Gonzalez, C. Rios, P. Barroso, J. lupon, A. Bayes-Genis. Germans Trias i Pujol Hospital, Badalona, Spain

**Introduction:** Heart failure (HF) is the main cause of hospital admissions in patients over 85 years in developed countries. The incidence of re-admissions in the first 30 days after being discharged with the diagnosis of HF is 20–30%, which accounts for a significant increase in healthcare costs. Several hospital strategies to lower re-admission rates have been developed. However, the magnitude of these strategies has been rather modest, with an absolute reduction around 2–3% (relative 10–15%). Moreover, those patients routinely not attended in the Cardiology Department and followed in specific Units show the highest rate of re-admissions.

**Purpose:** To reduce 30-day readmission rate in those patients not routinely attended in the Cardiology Department. 2) To facilitate the transition from hospital care to Primary Care physicians (GPs).

**Methods:** 88 years-old; 58.2% women). Mean calculated readmission risk was 26.3% ± 5.1 and 28% of them had a risk >30%. Mean time to first visit from discharge was 4.9±4.8 days. Mean number of performed visits was 3.9±2. HF 30-day readmission rate was 9.9% (6.4% through the Emergency Department and 3.5% directly from the consult). All-cause readmission rate was 16.3%. That represents a relative reduction of 38% and an absolute reduction of 10% on what was estimated with the CORE score.

**Conclusions:** A specific consultation that supports post-discharge HF patients achieved around 40% relative reduction of all-cause readmissions at 30 days in an elderly population. Readmission due to HF was only 9.9%.

---

**P2791 | BEDSIDE**

Incidence and prognostic impact of acute respiratory distress as a trigger for takotsubo cardiomyopathy - Results from the International Takotsubo Registry (InterTAKRegistry)

L.C. Napp1, V.L. Cammann2, J. Diekmann2, J.R. Ghadri2, T.F. Luescher2, J. Bauersachs1, C. Templin2 on behalf of InterTAKRegistry.

1 Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany; 2 University Hospital Zurich, University Heart Center, Zurich, Switzerland

**Introduction:** Takotsubo cardiomyopathy (TTC) represents an acute heart failure syndrome, which mimics acute coronary syndrome in the acute phase. It is characterized by a strongly but transiently impaired left ventricular function. TTC is often preceded by a trigger, such as emotional or physical stress. However, evidence on factors triggering TTC was derived from rather small studies and is therefore weak. From several single cases we suspected that acute respiratory distress (ARD) is a relevant triggering factor for the onset of TTC.

**Methods and results:** We screened 1639 patients from the International Takotsubo Registry (InterTAKRegistry), the largest collection of TTC patients worldwide, for emotional triggers such as grief or fear and physical triggers such as surgery or trauma, we identified acute respiratory distress as one of the major triggers preceding the onset of TTC. Acute respiratory distress (ARD) comprised acute exacerbation of COPD or asthma, pneumonia, pneumothorax, aspiration and acute respiratory failure from other pulmonary conditions. ARD triggers were present in N=112 patients (6.8%). We next compared these patients with the remaining patients from the registry (N=1527). While both groups were comparable regarding age (67.6±8.6 vs. 66.5±13.1; p=0.40), female gender (87.5% vs. 90.4%; p=0.32) and heart rhythm on admission (sinus rhythm: 92.9% vs. 92.0%; p=0.73), patients with ARD triggers required significantly more acute cardiac and intensive care (44.1% vs. 18.5%; p<0.001), with higher rates of catecholamine use (20.7% vs. 10.9%; p=0.002), cardiacolog infection (17.2% vs. 6.1%; p=0.009) and invasive mechanical ventilation (14.8% vs. p<0.001). ARD patients presented with a more severely reduced LVEF on admission (38.2±12.1 vs. 41.5±11.8; p=0.007) and higher heart rates (86.2±22.2 vs. 86.7±21.6; p<0.001). A five year survival analysis revealed increased MACCE.
Methods and materials: Heart transplantation (HTX) is an established therapy in for end-Union Medical College, Heart Failure Center, Beijing, China, People's Republic showed intravascular CD68 positive macrophages aggregation in 5 biopsies and severe rejection (3R) was found in this group. Antibody-mediated rejection (AMR) of 706 EMBs were performed in 240 patients. Among 703 biopsies with my-Results: From February 2014 to October 2014 we analyzed received telephone calls (TC) from family members and patients followed-up in our HFU. TC were re- and decreased to 17.8±12.1 events/h in semi-recumbent position (p<0.0001), pH from 7.20±5.11 to 7.40±0.97 (p<0.001), pO2 from 50±14 to 99±9 (p<0.001) as well, while pCO2 decreased from 72±12 to 42±24 (p=0.02).Significant variations of sys-tolic and diastolic blood pressure where not reported.

Conclusions: In very old patients with ACPE, NIV reduces the need for intuba-tion and induces a more rapid improvement in respiratory distress and metabolic disturbance than does standard oxygen therapy. Has no effect on short-term mor-tality. The choice of NIV aims to avoid complications, particularly in fragile patients as “very old patients”.

P2794 | BEDSIDE Is noninvasive ventilation effective and safe in cardiogenic pulmonary edema in very old patients? M. Poll1, P. Trambaido2, V. Basso1, M. Penco2, G. Ferriuolo1, 1 Sandro Pertini Hospital, Intensive Care Medical Unit, Rome, Italy; 2University of L’Aquila, Cardiology Department, L’Aquila, Italy

Background: The use of noninvasive ventilation (NIV) as first-line supportive therapy for acute respiratory failure (ARF) is frequently used for the management of acute cardiogenic pulmonary edema (ACPE) in very old patients (>80 years).

Aim: Aim of this retrospective study was to evaluate the safety of NIV in very old patients with ACPE hospitalized in ICU

Methods: From September 2013 to December 2014, 153 very old patients were admitted to the ICU, among them, 27 patients (18%) received ventilatory support and 2 additional very old patients (1.3%) received NIV after extubation.

Results: Failure to improve ABG values was the reason for ETI in 5 patients (3.2%). Four patients died during treatment (2.6%). Five patients did not tolerate the helmet (3.2%). No complications developed for the use of facemask. The average duration of NIPPV was 30±12 h. After 12 hours of the NIV in these patients has determined an improvement of the cardiac frequency from 121±8 to 79±9 (p<0.001), respiratory frequency from 39±7 to 19±2 (p<0.002). Arte-blood saturation increased from 72%±11 to 95%±4 (p<0.0001), pH from 7.20±5.11 to 7.40±0.97 (p<0.001), pO2 from 50±14 to 99±9 (p<0.001) as well, while pCO2 decreased from 72±12 to 42±24 (p=0.02).Significant variations of sys-tolic and diastolic blood pressure where not reported.

Conclusions: In very old patients with ACPE, NIV reduces the need for intubation and induces a more rapid improvement in respiratory distress and metabolic disturbance than does standard oxygen therapy. Has no effect on short-term mor-tality. The choice of NIV aims to avoid complications, particularly in fragile patients as “very old patients”.
P2796 Ferric carboxymaltose in iron deficient heart failure patients: a meta-analysis on individual patient data
1University Medical Centre Göttingen, Göttingen, Germany; 2Hospital del Mar Medical Research Institute (IMIM), Barcelona, Spain; 3Athens University Hospital Attikon, Athens, Greece; 4University Hospital Zurich, Zurich, Switzerland; 5State Medical University of Federal Agency of Social Policy and Health, Moscow, Russian Federation; 6Chain SHEBA Medical Center, Tel Hashomer, Israel; 7Vitor Pharma, Glattingbrugg, Switzerland; 8London School of Hygiene and Tropical Medicine, London, United Kingdom; 9University Medical Center Groningen, Groningen, Netherlands; 10Wroclaw Medical University, Wroclaw, Poland

Background and aim: Despite recent developments in heart failure (HF) management, the morbidity and mortality in this clinical syndrome remain unacceptable. Though iron deficiency is a frequent comorbidity in stable HF patients, thus, correction of ID itself can be considered an attractive therapeutic target in HF, and this has been recently tested in a few clinical studies. The aim of this meta-analysis on individual patient data is to pool all double-blind, randomized, placebo-controlled trials in patients with symptomatic chronic (CHF) and ID treated with intravenous (iv) ferric carboxymaltose (FCM) and assess the efficacy and safety of iv iron therapy with FCM.

Methods: This meta-analysis on individual patient data was performed using all available completed trials conducted in systolic CHF patients with ID (FER-CARDS-01 and FER-CARDS-02) comparin iv iron therapy with placebo (saline). All trials were designed as double-blind, multi-centre, prospective, randomized trials and enrolled ambulatory patients with symptomatic CHF (NYHA class III/II) with LVEF ≤ 45% and with presence of ID (defined as transferrin saturation (TSAT) <10%, ferritin <100 ng/dl, or ferritin 100–300 ng/dl if transferrin saturation (TSAT) <20%). FER-CARDS-01 and FAIR-HF were randomized 2:1, EFFICACY-HF and CONFIRM-HF 1:1 to treatment with FCM or placebo. CONFIRM-HF lasted 22 weeks and during the correction phase, FCM-treated patients received a cumulative dose of 300 mg of iv iron up to 1000mg as injection at baseline and Week 6 depending on their screening weight and screening haemoglobin measurements. Patients received a 500 mg maintenance dose during the maintenance period at Week 12, 24 and 36 if ID still present. FAIR-HF and EFFICACY-HF lasted 24 weeks, FER-CARDS-01 12 weeks, respectively. During the correction phase of the trials patients received iv injection of 200 mg until the individually required their quality of life. Cardiovascular and non-cardiovascular co-morbidities often complicate the natural course of HF with deleterious impact on clinical status, symptoms, and HF progression. Iron deficiency (ID) has also been reported as a frequent co-morbidity in stable HF patients. Thus, correction of ID itself can be considered an attractive therapeutic target in HF, and this has been recently tested in a few clinical studies. The aim of this meta-analysis on individual patient data is to pool all double-blind, randomized, placebo-controlled trials in patients with symptomatic chronic (CHF) and ID treated with intravenous (iv) ferric carboxymaltose (FCM) and assess the efficacy and safety of iv iron therapy with FCM.

Results: Overall, 839 evaluable patients were randomized and treated in 138 centres across 19 countries. The FCM group consists of 504 patients, the placebo group of 335 patients, respectively.

Conclusion: This meta-analysis on individual patient data will provide further information on the efficacy and safety of iron therapy with iv FCM in CHF patients with ID in regards to these clinically primordial and important endpoints. Results of will be available by end of June.

NON-PHARMACOLOGICAL THERAPY IN HEART FAILURE EXERCISE, VENTILATION

P2797 | BEDSIDE
Effects of positive airway pressure therapy on nocturnal oxygen saturation in heart failure patients with sleep-disordered breathing
A. Tueroff, H. Fox, T. Bitter, B. Wellmann, D. Horstkotte, O. Oldenburg, Department of Cardiology, Heart and Diabetes Centre North Rhine-Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany

Background: Nocturnal oxygen desaturations and hypoxemia are discussed to be one of the most robust and independent parameters to determine prognosis in heart failure (HF) patients with sleep-disordered breathing (SDB). Positive airway pressure (PAP) therapy is considered the gold standard to treat SDB in these patients.

Purpose: The present study investigates the effects of various types of PAP therapy on oxygen saturation, desaturations and hypoxemia within the first night of usage.

Methods: Inclusion criteria were chronic stable HF (NYHA ≥ II, LVEF ≤ 45%) treated according to current guidelines and moderate to severe SDB (apnoea-hypopnoea index, AHI >15/h), determined by full polysomnography (PSG). Obstructive sleep apnoea (OSAS) and central sleep apnoea (CSA) were treated by adaptive servosaturation (ASV).

Results: A total of 232 patients (25 female, 68±10 years, BMI 29.7±5.1, NYHA 3±2.5, NT-proBNP 2774±761 pg/ml, LVEF 34±9%) were enrolled. PAP therapy resulted in a substantial reduction of the number of respiratory events during the first night of therapy (AHI: 33.3±15.9 to 7.9±7.4/h, p < 0.001). More important, markers of hypoxic burden like time spent with oxygen saturation below 90% (T < 90%), as well as lowest or mean oxygen saturation (SaO2) and number of oxygen desaturations of at least 3% were reduced by either therapy (table; *p < 0.05).

Conclusion: PAP therapy of SDB is able to significantly reduce nocturnal hypoxia in HF patients. Important and robust outcome parameters like T < 90% improved markedly with PAP therapy.

P2798 | BEDSIDE
Exercise cardiac power and the risk of heart failure in men
S. Kuri1, S.Y. Jae2, F. Zaccardi3, J. Kauhanen4, K. Ronkainen4, J.A. Laukkanen4
1University of Eastern Finland, Institute of Public Health and Clinical Nutrition, Kuopio, Finland; 2University of Seoul, Seoul, Korea, Republic of; 3Catholic University of the Sacred Heart, Internal Medicine and Diabetes Care Unit, Policlinico Gemelli Hospital, Catholic University of Sac, Rome, Italy

Background: Heart failure (HF) is among the most common causes of death in developed countries.

Purpose: The aim of this study was to examine the relationship of exercise cardiac power (ECP), defined as a ratio of directly measured maximal oxygen uptake with peak systolic blood pressure during exercise, with the risk for heart failure in general population.

Design: Population-based cohort study with an average follow-up of 20 years from eastern Finland. Among 2357 men with no history of HF at baseline participated in exercise stress test 313 cases of HF occurred.

Results: Men with low ECP (<9.8 mL/min/m², lowest quartile) had a 2.36-fold (95% CI 1.7–3.3, p < 0.0001) risk of HF as compared with men with high ECP (>13.9 mL/min/m², highest quartile) after adjusting for age and examination year. Hazard ratio was also elevated in men with a 1.84-fold risk of HF after additional adjustment for conventional risk factors. After further adjustment for left ventricular hypertrophy, men with low ECP had markedly increased risk of HF (hazard ratio 1.7, 95% CI 1.17–2.57, p = 0.006) and adjustment for resting systolic blood pressure, the respective HF risk among men with low ECP was 1.6 (95% CI 1.12–2.37, p = 0.011).

Conclusion: ECP provides non-invasive and easily available measure for the prediction of HF. One of the most potential explanation for the association between ECP, and the risk of HF is an elevated afterload and peripheral resistance indicated by elevated systolic blood pressure.
Methods: After the initial improvement of ADHF, we performed overnight full polysomnography on consecutive patients whose left ventricular (LV) ejection fraction <45%, and who were hospitalized due to ADHF between May 2012 and December 2014. SDB was defined as an apnea-hypopnea index ≥15 per hour of sleep. Patients with SDB were subdivided as those with or without PAP treatment (former included those who could optimally use PAP <1 month). As an indicator of poor prognosis, the risk for composite endpoint including all-cause mortality and rehospitalization were assessed by stepwise multivariable Cox proportional model including other variables showing P < 0.15 in univariate analyses.

Results: Overall, 114 patients including 76 SDB (30 with PAP treatment) and 38 without SDB were enrolled. At a median follow-up of 6.8 months, 44 patients had clinical events (39%). In the stepwise multivariable analysis including age, etiology of LV dysfunction, NYHA class, cardiac resynchronization therapy (CRT), use of beta blockers, hemoglobin, serum sodium, creatinine, estimated glomerular filtration rate (eGFR), plasma B-type natriuretic peptide (BNP) level, percentage of REM sleep and slow wave sleep, mean and lowest SO2 and SDB as independent variables, was associated with increased risk of clinical events (hazard ratio [HR], 3.41; P=0.005). Among SDB patients, stepwise multivariable analysis including CRT, hemoglobin, serum sodium, eGFR, plasma BNP level and PAP as independent variables showed that PAP treatment was associated with reduced risk of clinical events (HR 0.37; P=0.027).

Conclusion: In hospitalized patients with LV systolic dysfunction following ADHF, patients with SDB were associated with increased risk of poor prognosis, regardless of PAP treatment.

Overall, 114 patients including 76 with SDB (30 with PAP treatment) and 38 without SDB were enrolled. At a median follow-up of 6.8 months, 44 patients had clinical events (39%). In the stepwise multivariable analysis including age, etiology of LV dysfunction, NYHA class, cardiac resynchronization therapy (CRT), use of beta blockers, hemoglobin, serum sodium, creatinine, estimated glomerular filtration rate (eGFR), plasma B-type natriuretic peptide (BNP) level, percentage of REM sleep and slow wave sleep, mean and lowest SO2 and SDB as independent variables, was associated with increased risk of clinical events (hazard ratio [HR], 3.41; P=0.005). Among SDB patients, stepwise multivariable analysis including CRT, hemoglobin, serum sodium, eGFR, plasma BNP level and PAP as independent variables showed that PAP treatment was associated with reduced risk of clinical events (HR 0.37; P=0.027).

Table 1. Analysis of % change in characteristics between the two points of PFT for HF admission

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coefficient (SE)</td>
<td>Coefficient (SE)</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.97 (0.94–1.01)</td>
<td>0.9 (0.93–1.01)</td>
</tr>
<tr>
<td>Estimated GFR</td>
<td>0.99 (0.97–1.01)</td>
<td>0.99 (0.97–1.02)</td>
</tr>
<tr>
<td>Log BNP</td>
<td>1.03 (1.04–1.06)</td>
<td>1.02* (1.09–1.06)</td>
</tr>
<tr>
<td>% VC</td>
<td>0.98 (0.94–1.02)</td>
<td>1.00 (0.94–1.05)</td>
</tr>
<tr>
<td>FEV1.0%</td>
<td>1.06 (0.99–1.14)</td>
<td>1.02 (0.93–1.11)</td>
</tr>
<tr>
<td>% DLCO</td>
<td>0.96 (0.92–0.99)</td>
<td>0.95 (0.90–0.99)</td>
</tr>
<tr>
<td>VC, vital capacity</td>
<td>FEV1.0, forced expiratory volume in one second; DLCO, diffusing capacity for carbon monoxide.</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: DLCO is decreased following decompensated HF. Pulmonary congestion resulting requirement of hospitalization may cause irreversible reduction of DLCO.

Abstract P2801 – Table 1. Safety of exercise training in CHF patients

<table>
<thead>
<tr>
<th>Author</th>
<th>All-cause mortality</th>
<th>Cardiac death</th>
<th>Hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ex</td>
<td>Control</td>
<td>Ex</td>
</tr>
<tr>
<td>Belardinelli</td>
<td>1/1 (100%)</td>
<td>1/1 (100%)</td>
<td>1/1 (100%)</td>
</tr>
<tr>
<td>Hambrecht</td>
<td>1/1 (100%)</td>
<td>1/1 (100%)</td>
<td>1/1 (100%)</td>
</tr>
<tr>
<td>Winkler</td>
<td>1/3 (100%)</td>
<td>1/3 (100%)</td>
<td>1/3 (100%)</td>
</tr>
<tr>
<td>Werenbommer</td>
<td>2/10 (20%)</td>
<td>2/10 (20%)</td>
<td>2/10 (20%)</td>
</tr>
<tr>
<td>AF action</td>
<td>5/9 (56%)</td>
<td>5/9 (56%)</td>
<td>5/9 (56%)</td>
</tr>
</tbody>
</table>

P2801 BEDSIDE
Exercise therapy in heart failure with reduced ejection fraction is safe but did not improve mortality, cardiac death or hospitalisation - a meta-analysis

S. Sze, V. Algar, K.Y.K. Wong. Castle Hill Hospital, Hull, United Kingdom

Background: European and American guidelines recommend exercise training to improve the quality of life in stable heart failure patients. However, there is conflicting evidence regarding whether exercise reduces mortality and hospitalisation in patients suffering from heart failure.

Methods: We conducted a systematic review and meta-analysis of prospective studies which investigated the efficacy and safety of exercise therapy in stable chronic heart failure patients with reduced ejection fraction. Using a defined research strategy, electronic databases (MEDLINE and Embase) were searched for randomised controlled trials (RCTs) published between 1946 and 2013. Five eligible studies which investigated the relationship between exercise therapy and all-cause mortality, cardiac mortality and all-cause hospitalisation were identified and appraised using set criteria. Heterogeneity test was considered significant if p < 0.10. If significant, random effect model was used to allow generalisation of the results and sources of heterogeneity were investigated. If there is no significant heterogeneity, then the fixed effect model would be used.

Results: Combined, these 5 RCTs recruited a total of 2581 patients (Table 1). Compared with usual care, the pooled risk ratio of all-cause mortality, cardiac mortality and all-cause hospitalisation after exercise therapy in chronic HF patients was 0.85 (95% CI = 0.80–1.14, p=0.61) (Figure 1); 0.68 (95% CI = 0.34–1.42, p=0.20) (Figure not shown) and 0.95 (95% CI = 0.90–1.01, p=0.13) (Figure 2) respectively.

Conclusions: Exercise training in patients with stable chronic heart failure due to left ventricular systolic dysfunction is safe, but there is no evidence that exercise training improves all-cause mortality, cardiac mortality or all-cause hospitalisation.

Abstract P2802 – Table 1. Safety of exercise training in CHF patients

<table>
<thead>
<tr>
<th>Author</th>
<th>Ex</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>T. Kato1, N. Takama2, K. Aihara, Y. Sugito1, Y. Seta1, K. Kaneko1, M. Kurabayashi3, 1 Public Tomioka General Hospital, Division of Cardiology, Tomioka, Japan; 2 Gunma University School of Medicine, Department of Cardiovascular Medicine, Maebashi, Japan</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P2802 BEDSIDE
Impact of adaptive servo ventilation therapy on cardiovascular event free survival in heart failure patients

T. Kato1, N. Takama2, K. Aihara, Y. Sugito1, Y. Seta1, K. Kaneko1, M. Kurabayashi3. 1 Public Tomioka General Hospital, Division of Cardiology, Tomioka, Japan; 2 Gunma University School of Medicine, Department of Cardiovascular Medicine, Maebashi, Japan

Background: Adaptive Servo Ventilation (ASV) is considered beneficial to heart failure patients with respiratory insufficiency, in particular those with severe obstructive sleep apnea syndrome (SAOS). However, the benefits of exercise training in chronic heart failure patients with ASV received mixed evidence. The purpose of this study is to evaluate the impact of ASV on cardiovascular mortality and hospitalisation in chronic heart failure patients with reduced systolic function.

Methods: We studied 220 SAS patients, all underwent polysomnography in our institutes. Subjects were divided into 2 groups based on cardiac function (Ejection fraction 40% below or not) (HF group#1 vs. NonHF group#2). Daytime sleepiness was assessed by the Epworth Sleepiness Scale (ESS) and overnight urinary catecholamines were measured.

Results: HF group was less sleepy compared with NonHF group (ESS score 6 ±1.7 vs. 12 ±7.5; p=0.004). HF group had significantly increased overnight urinary adrenaline, dopamine and dopamine levels compared to NonHF group. Sleepiness was inversely correlated to urinary catecholamine levels.

Conclusions: In SAS patients with HF, daytime sleepiness was inversely correlated to urinary catecholamine levels. This may help to explain the lack of daytime sleepiness in SAS patients with HF.
group. We are anxious ASV poor responder might have an inappropriate influence on HF.

**Purpose:** It is reported that the improvement of cumulative percent of time at oxygen saturation below 90% (CT90%) after 3 months of ASV therapy is associated with event free survival. We estimate the value of CT90% which predict good response to ASV therapy and evaluate the effectiveness of ASV therapy.

**Methods:** The study group consisted of 71 HF patients. According to receiver operating characteristic curve analyzing cardiovascular event, cut off point of CT90% after 3months of ASV therapy was 0.1%. Patients were divided into those whose CT90%≤0.1% or >0.1% (good response group, n=34, and poor response group, n=37), and ASV cessation group (n=10). No significant differences were observed among these groups with respect to age, sex, New York Heart Association class, brain natriuretic peptide level, left ventricular ejection fraction, apex hypogonadal index. They were followed for two years and cardiovascular event free survival was compared among these three groups.

**Results:** Kaplan Meier survival plots demonstrated that compared with poor response group, good response group significantly improved cardiovascular event free survival (p=0.027). However, compared with cessation group, poor response group also improved cardiovascular event free survival (p=0.048) (Figure 1).

**Conclusion:** These results suggest that ASV is effective in not only good response group but also poor response group.

---

**P2804 | BEDSIDE**

Rapid introduction of adaptive servo-ventilation in the emergency room reduces the rate of endotracheal intubation and hospitalization in patients with acute cardiogenic pulmonary edema

M. Kinoshita, H. Okayama, T. Miyoshi, A. Higaki, K. Hara, Y. Kawata, G. Hiasa, T. Yamada, Y. Kazatani. Ehime Prefectural Central Hospital, Cardiology, Matsuyama, Japan

**Background:** Adaptive servo-ventilation (ASV) has been used for chronic heart failure or sleep-disordered breathing in patients at home. However, its effect in acute cardiogenic pulmonary edema (ACPE) is not clear.

**Purpose:** To elucidate the effect of ASV on patients with ACPE.

**Methods:** We enrolled 205 consecutive acute HF patients (122 men, mean age: 74±12 years). Eighty-four received standard therapy such as oxygen inhalation and vasodilators (control group) and 121 received ASV in addition to standard therapy (ASV group). ASV was initiated in the emergency room as soon as a diagnosis was made. The initial settings for ASV were an end-expiratory pressure of 5–10 cmH2O, a minimum pressure support (PS) of 3 cmH2O and a maximum PS of 10 cmH2O. Oxygen inhalation of 10–15 L/min was used. Exchange from ASV to endotracheal intubation (ETI) was performed according to the attending physician’s judgment when oxygenation was insufficient. Exclusion criteria included cardiogenic shock, disturbance of consciousness, fatal arrhythmia, right-sided heart failure, infection, past history of noninvasive positive pressure ventilation and DNR.

**Results:** There were no significant between-group differences in sex, age, background disease, vital signs, medications, ejection fraction, brain natriuretic peptide and NYHA class IV. The mean duration of ASV was 9.8 hours. The ETI rate was significantly lower in the ASV group than the control group (3% vs 21%, P<0.01). The intensive care unit (ICU)/high care unit (HCU) length of stay was also significantly less in the ASV group than the control group (1.9±2.0 vs 5.3±6.8 days, P<0.01). Consequently, the hospitalization period was significantly lower in the ASV group than the control group (19.3±11.0 vs 26.3±16.6 days, P<0.01). Thirty-day mortality was not different between the two groups.

**Conclusion:** In patients with ACPE, rapid introduction of ASV in the emergency room reduces the hospitalization period and the need for ETI.

---

**P2808 | BEDSIDE**

Device-measured rapid shallow breathing with exertion worsens prior to heart failure decompensation

S. Rial1, B. Merkely2, R. Gardner3, V. Averina1, R. Sweeney4, Y. Zhang4, Q. An5, J. Boehmer6,1 Grant Medical Center, OhioHealth, Columbus, United States of America; 1Semmelweis University Heart Center, Budapest, Hungary; 2Golden Jubilee National Hospital, Glasgow, United Kingdom; 4Boston Scientific, St. Paul, United States of America; 5Penn State Milton S. Hershey Medical Center, Hershey, United States of America

**Introduction:** Respiratory complaints are common prior to heart failure events (HF) and may present as an elevated respiratory rate (RR) or decreased tidal volume (TV). We hypothesized that the changes in device-based respiratory measures in the week leading up to HF would be larger with exertion than at rest.

**Purpose:** To elucidate the effect of ASV on patients with ACPE.

**Methods:** The study group consisted of 122 men, mean age: 58±17 years) underwent standard transthoracic 2D and 3D full-volumes acquisitions in the week leading up to HFE, when used by trainees with different levels of expertise.

**Results:** Of the 532 patients, 58 had 3D HF with sufficient data. ASV showed largest change during both rest (4%) and Act (6.9%), with RR being larger than at rest. RR showed significant change during both rest (2.1%) and Act (2%) with no difference between activity levels. TV showed significantly larger change with Act (~3.7%) when compared to rest. MV did not change.

**Conclusion:** Rapid shallow breathing with exertion measured by RR, TV, and RSBI changes prior to HFES and may be a useful device-based measure of impending HF decompensation.

---

**P2809 | BEDSIDE**

Is 3D interchangeable with 2D echocardiography for the initiation of device therapy in patients with heart failure with reduced ejection fraction?

S. Mihaila1, A. Velocea2, A. A. Andronic2, S. I. Calin2, L. L. Matei2, R. C. Rimbas1, D. Muraru1, L. P. Badano3, D. Vinerearu1, 1University of Medicine and Pharmacy Carol Davila, Bucharest, Romania; 2University Emergency Hospital, Bucharest, Romania; 3University of Padova, Department of Cardiothoracic and Vascular Sciences, Padua, Italy

**Background:** Left ventricular ejection fraction (LVEF) is a key element for the initiation of different therapeutic strategies in patients with heart failure with reduced ejection fraction (HF) and the cutoff limit of 35%, recommended by the current guidelines, is based on 2D echo, but it is accepted that 2D and 3D echo provide similar results for the LVEF.

**Purpose:** To establish if 3D echo can be interchangeable with 2D echo for the initiation of device therapy in HF and when used by trainees with different levels of expertise.

**Methods:** We enrolled 51 patients with symptomatic HF and sinus rhythm (46 males, age ≥58 ±17 years) underwent standard transthoracic 2D and 3D full-volume acquisitions of the LV. One expert observer with more than 2 years of training in both 2D and 3D echo (Expert), and 3 trainees with different levels of expertise in 2D and one month training in 3D echo (Beginner, Medium, and Advanced) measured the 2D and 3D LV volumes and LVEF of the same already-acquired images.

**Results:** Mean LVEF was 35±10% with 2D, and 33±10% with 3D echo. There was a good agreement between 2D and 3D echo classification of the LVEF (greater than 35% and lower than 35%), for all levels of training (all kappa >0.60, but below 0.80). However, using 3D echo, the expert observer did not re-classify any patient into having a LVEF more than 35%, but re-classified more than 10% of the patients into having a LVEF below 35% and, therefore, indication for device implantation.

**Conclusion:** Regardless of the level of training in echocardiography, 3D has a good agreement with 2D for measuring LVEF in patients with HF. However, more than 10% of the patients are reclassified into having indication for device therapy even using 3D. Further studies are necessary to assess if new cutoff limits need to be defined, when using 3D assessment of the LVEF in patients with HF.
Effect of heart rate on the response to cardiac resynchronization therapy

H. Mohamed Foreig Hamed1, A.M. Hamdy1, M.A. Nabib2, N.A. Agiba1.
1Al-Azhar University, Cairo, Egypt; 2 Ain Shams University, Cairo, Egypt

Background: Elevated resting heart rate (HR) is associated with worse outcomes in patients with heart failure (HF) and reduced left ventricular ejection fraction (LVEF). The purpose of this study was to evaluate the impact of HR on the clinical and hemodynamics of patients (pts) under cardiac resynchronization therapy (CRT).

Patients and methods: This study comprised 45 HF pts under CRT who were subjected to clinical assessment for NYHA functional class and echo-Doppler examination for determination of LVEF, mtral & aortic velocity time integral (VTI) & Ao-VTI), filling & ejection times (FT & ET), and systolic arterial pressure (SPAP). Tissue Doppler imaging (TDI) was performed to calculate dysynchrony index (TS-SD) from 6 basal LV segments. Average HR was assessed using 24 hour Holter monitoring. Patients were classified according to their average HR into Group 1 (17 pts) with average HR >75 bpm and Group 2 (28 pts) with average HR <75 bpm.

Results: Group 1 (patients with lower HR) had significantly lower mean NYHA functional class & SPAP, significantly higher LVEF, M-VTI, Ao-VTI, FT and ET compared to Group 2 (patients with higher HR). There was no significant difference between Group 1 and Group 2 regarding TS-SD (Table 1).

Variable Group 1 (HR >75 bpm) n=17 Group 2 (HR <75 bpm) n=28 p value
Mean NYHA class 2.1±0.7 2.7±0.6 0.013
SPAP (mmHg) 40.1±10 48.1±12 0.022
LVEF (%) 40.1±9.4 34.0±5.3 0.026
M-VTI (cm) 21.9±4.1 17.5±3.9 0.000
FT (ms) 480±100 342±96 0.000
Ao-VTI (cm) 291.3 23.1±17.2 0.005
ET (ms) 270±29 244±26 0.004
TS-SD (ms) 17.4±1.8 19.4±1.61 NS

Conclusion: Lower average HR (<75 bpm) is associated with better clinical and hemodynamic response to CRT.

Basic mechanisms in heart failure

P2808 | BENCH
Apocynin attenuates systolic dysfunction and decreases superoxide generation in soleus muscle of heart failure rats
1 Universidade Estadual de Campinas, Sao Paulo, Brazil; 2 Federal University of Mato Grosso do Sul, Campo Grande, Brazil; 3 Heart Institute (InCor) - HC-FMUSP, Vascular Biology Laboratory, Sao Paulo, Brazil

Oxidative stress is increased in cardiac and skeletal muscles during heart failure. In this study we evaluated the effects of the antioxidant apocynin on cardiac remodeling and oxidative stress in soleus muscle of rats with aortic stenosis (AS)-induced heart failure.

Methods: Twenty weeks after AS induction or sham surgery (n=11), rats were assigned to non-treatment (NT, n=11) or treatment with apocynin (AS, 16 mg/kg/day in drinking water, n=9) for 8 weeks. Echocardiogram and tissue Doppler imaging were performed before and after treatment. Antioxidant enzymes activity was assessed by spectrophotometry. Total production of reactive oxygen species was evaluated by muscle quantifying two dihydroethidium (DHE) oxidation-derived fluorescent compounds, 2-hydroxyethidium (EOH) and ethidium, using high performance liquid chromatography (HPLC). Soleus trophism was assessed by measurement of muscle, using high performance liquid chromatography (HPLC). Soleus trophism was assessed by measurement of muscle, using high performance liquid chromatography (HPLC). Soleus trophism was assessed by measurement of muscle, using high performance liquid chromatography (HPLC).

Results: Before treatment, both AS groups presented left cardiac chambers dilatation. Mean mtral annular systolic velocity (Sham 3.15±0.51; AS 2.32±0.38; AS-A 2.71±0.41 mm/s; p=0.01) was decreased in AS than Sham; in AS-A, it was between that in the Sham and AS. Endoglin was depleted in adult Rosa26-Cre-ERT2;Engfl/fl mice to generate "ubiquitous" endoglin knockout (Eng-iKOu) mice, and we used a transgenic model (Eng-iKOe) mice. Cardiac malondialdehyde (MDA) levels were measured at baseline and after treatment. Cardiac MDA levels were significantly lower in Eng-iKOe mice compared to Eng-iKOu mice (p<0.05).

Conclusions: These data show that the acute salutary actions of A1R on atrial chronotropy and inotropy are preserved in PAH animals. The A2BR may contribute to decrease RV contractility, since its blockade uncovered a positive inotropic effect of the adenosine analogue, NECa, in PAH animals. Intestinal infiltration with A2BR-positive fibroblasts and macrophages in the RV myocardium suggest that adenosine may control the release of pro-fibrotic inhibitory mediators and contribute to mechanical adaptation of RV to pressure overload in PAH patients.

Introduction: Endoglin, a co-receptor for ligands of the transforming growth factor-beta (TGFß) superfamily, can promote signalling through the ACVR1 receptor. The importance of endoglin in regulating haematopoiesis, angiogenesis and cardiovascular development is well established, and endoglin mutations are associated with the vascular disorder hereditary haemorrhagic telangiectasia, a disease characterized by localised arteriovenous malformations (AVMs), fragile vessels and bleeding.

Purpose: Given the central role of the TGFß superfamily in cardiovascular conditions, we used mouse models to determine endoglin’s role during adult life and assess its effect on cardiac function.

Methods: Eng-depleted mice were bred in both wild-type and endoglin−/− backgrounds. The Eng−/− and Eng−/−/− mice were generated by intercrossing Eng+/− males and females. The Eng−/−/− mice were then bred with hypertrophic transgenic mice to generate hypertrophic Eng−/−/−/− mice. In addition, endoglin−/−/− mice were crossed with mice expressing a dominant-negative form of endoglin (Eng-iKOe) to generate endoglin−/−/−/−/Eng-iKOe mice. Using these models, we studied the effect of endoglin deletion on cardiac function and morphology.

Results: Endoglin−/−/−/−/Eng-iKOe mice exhibited increased cardiac output, reduced cardiac hypertrophy, and improved heart function compared to wild-type mice. Cardiac performance was assessed by echocardiography, and cardiac morphology was evaluated by histology. These findings suggest that endoglin deletion can improve cardiac function and reduce cardiac hypertrophy in response to pressure overload.

Conclusions: Endoglin−/−/−/−/Eng-iKOe mice exhibit improved cardiac function and reduced cardiac hypertrophy, suggesting a potential role for endoglin in regulating cardiac remodeling and function.
the pulmonary distal vassalature consistent with a defect in regulating vascular architecture or vasomotor tone. We assessed vasomotor function in the aorta and found an increased contraction response to phenylephrine in Eng-koE mice compared to controls, suggesting that endoglin is important in controlling the vasomotor response.

Conclusion: We have identified a major role for endoglin in regulating normal cardiovascular function and highlight the importance of endoglin in adult life for maintenance of cardiac structure and function.

P2811 | BEDSIDE Clinical correlates of soluble nephrin in concentrations in patients with acute heart failure


Background: Nephrin (NEP) is a neutral endopeptidase that degrades natriuretic and other vasoactive peptides. A recent trial, the PARADIGM-HF, has shown that inhibition of NEP in patients with chronic heart failure (HF) and left ventricular systolic dysfunction is associated with better prognosis. However, no data are available about NEP significance in patients with acute HF (AHF). The aim of this study was to investigate soluble NEP concentrations and their clinical correlates in patients with AHF at admission and discharge.

Methods:

Results: Soluble NEP levels (ng/ml) at admission showed a skewed distribution (median 0.67 [Q1-Q3 0.36-1.4]). At discharge, levels of NEP showed a trend to be lower (median 0.52 [0.35 to 1.15]; p=0.05). We found a significant correlation of NEP and NT-proBNP concentrations at admission (rs=0.25; p=0.009), Creatinine and BUN were also significantly correlated to NEP levels at admission (rs=0.28; p=0.002 and rs=0.26; p=0.004 respectively). In addition, patients who were already receiving ACEi/ARB had a trend to higher levels of NEP at admission (median 0.72 vs 0.58; p=0.069), as well as those who were on beta-blockers (rs=0.28; p=0.002 and rs=0.26; p=0.004 respectively). In addition, patients who presented lower creatinine and BUN were also correlated with changes of NEP concentrations at discharge.

Conclusions: Patients with AHF, soluble NEP concentrations at admission are elevated and decreased after clinical stabilization at discharge. NEP levels at admission (median 0.72 vs 0.58; p=0.069), as well as those who were on beta-blockers (rs=0.28; p=0.002 and rs=0.26; p=0.004 respectively). In addition, patients who were already receiving ACEi/ARB had a trend to higher levels of NEP at admission (median 0.72 vs 0.58; p=0.069), as well as those who were on beta-blockers (rs=0.28; p=0.002 and rs=0.26; p=0.004 respectively). In addition, patients who presented lower creatinine and BUN were also correlated with changes of NEP concentrations at discharge.

P2812 | BEDSIDE Distribution of leukocyte populations is affected by cardiac resynchronisation therapy

K. Kaminski1, K. Ptaszynska Kopczynska2, M. Marcinkiewicz Siemon3, P. Paghi4, U. Thiel1, M. Rusak1, A. Lisowska1, W.J. Mussial1, M. Moniuszko2.

Background: The study enrolled 50 stable CHF-REF patients, NYHA class II-III, EF 40-50% who underwent CRT implantation and a clinical follow-up of 6 months after the CRT device implantation. We aimed to investigate the specific characteristics of patients with sarcopenia with acute decompensated heart failure (ADHF).

Methods:

Results: Sarcopenia was observed in 80 patients (59%). Of these, 55 patients were male (69%). The BNP levels on admission for the patients with sarcopenia with acute decompensated heart failure were 1093.6±547.2–1659.7 vs. 718.2 [514.0–1081.6] pg/ml, p<0.01. Further, the BNP levels in the compensated phase for both patient groups were similar (584.0±979.8 vs. 490.9±32.8 pg/ml) after decongestion treatment. The ratio of ECW-to-TBF was lower in these patients (0.95±0.2 vs. 0.89±0.12; p<0.01). In addition, the ratio of ECW-to-TBF was lower in patients with sarcopenia with ADHF (0.95±0.2 vs. 0.89±0.12; p<0.01). In the compensated phase, the BUN levels of these patients were higher (33.7±17.4 vs. 27.3±10.1 mg/dl) and Na levels were lower (136.6±3.4 vs. 139.1±3.1mEq/l).

Conclusions: Sarcopenia was observed in 80 patients (59%). Of these, 55 patients were male (69%). The BNP levels on admission for the patients with sarcopenia with acute decompensated heart failure were 1093.6±547.2–1659.7 vs. 718.2 [514.0–1081.6] pg/ml, p<0.01. Further, the BNP levels in the compensated phase for both patient groups were similar (584.0±979.8 vs. 490.9±32.8 pg/ml) after decongestion treatment. The ratio of ECW-to-TBF was lower in these patients (0.95±0.2 vs. 0.89±0.12; p<0.01). In addition, the ratio of ECW-to-TBF was lower in patients with sarcopenia with ADHF (0.95±0.2 vs. 0.89±0.12; p<0.01). In the compensated phase, the BUN levels of these patients were higher (33.7±17.4 vs. 27.3±10.1 mg/dl) and Na levels were lower (136.6±3.4 vs. 139.1±3.1mEq/l).

P2813 | BEDSIDE Hepatocyte growth factor in patients with acute heart failure


Background: Experimental models have shown that hepatocyte growth factor (HGF) plays an important role in the improvement of cardiac function and remodeling in a variety of cardiovascular diseases. Data about its prognostic value are scarce, but this marker could reflect changes in the treatment of patients with established prognosticators as natriuretic peptides. In particular, its role in acute heart failure (AHF) patients has not been evaluated.

Methods: We aimed to evaluate the complementary prognostic role of HGF in a consecutive series of 373 patients with AHF admitted to our university hospitals, of which 135 were admitted with AHF in three university hospitals. Blood samples were obtained at admission, and clinical and echocardiographic data were recorded during the hospitalization. Patients were followed at 1 year.

Results: HGF concentrations were 2323±1659 pg/ml, which significantly correlated with NT-proBNP (p=0.001), cystatin (p=0.006) and eGFR (KoKD-EPI, MDRD, cyst or Hoek-13 based, p<0.01). However, no correlations were found with echocardiographic parameters (LVEF, LV mass index, and left atrium diameter), serum sodium or BUN. Moreover, the changes in HGF were associated with mortality of patients admitted with AHF in 1000 patients and one year. HGF showed a significant interaction and added complementary prognostic information to NT-proBNP concentrations: mortality risk increased 1.6 fold per 100 pg/mL increase in HGF. Moreover, the changes in HGF were associated with mortality of patients admitted with AHF in 1000 patients and one year. HGF showed a significant interaction and added complementary prognostic information to NT-proBNP concentrations: mortality risk increased 1.6 fold per 100 pg/mL increase in HGF.

Conclusions: HGF concentrations correlate with those of natriuretic peptides and measures of renal function in patients with AHF, but not with echocardiographic parameters of cardiac remodeling. HGF provided significant prognostic information and added complementary information over natriuretic peptides.
state, rendering them resistant to further diuretic therapy. Thus, clinically indicated compensated status of patients with sarcopenia is not sufficiently compensated as well as their hypovolemic state, which is contradictory, clinicians misread the fluid status at the chronic phase of heart failure management. This shows why clinicians face difficulty managing the health condition of such patients compared with patients without sarcopenia and why the prognosis of such patients is uncertain.

P281 | BEDSIDE
Procalcitonin is a marker of infection in patients with heart failure and a strong predictor of mortality: a systematic review and meta-analysis
C. Meune, L. Aissou, E. Sorbets, F.X. Goudot, N. Pop, L. Benouda. Hospital Avicenne of Bobigny, Cardiology, Bobigny, France

Background: Procalcitonin (PCT), a marker of bacterial infection, has recently been studied in patients with congestive heart failure (CHF). While PCT concentrations seem to be increased in patients with coexisting infection and CHF versus CHF alone, its prognostic significance remains uncertain. Thus, we performed a systematic review and meta-analysis of studies that aimed at determining the prognosis of PCT in CHF.

Methods: MEDLINE/PubMed and Cochrane CENTRAL were searched for studies assessing PCT in patients with CHF using the term “procalcitonin” and “heart failure”, with/without “infection”, “mortality”, “prognostic”. Following data extraction, fixed-effects methods were used to compare the data for PCT.

Results: From a total of 52 references found, 43 were excluded by title and abstract. 9 articles were examined for more details, and 5 were included in the present analysis, corresponding to a total of 5123 patients (mean age 71±10 years, male 2588). Patients with infection coexisting with CHF tended to have higher PCT concentration versus those with CHF alone (0.230±0.15ng/l versus 0.19±0.03 ng/l, p=0.145). Follow-up ranged from 22 days to 180 days among the studies. Cut-off values for PCT ranged from 0.1 ng/l to 2.525ng/l; when compared to patients with low PCT concentrations, patients above the cut-off value PCT had increased mortality (RR 1.82; 95% CI [0.1.33–2.49], p<0.001)

Conclusions: PCT allows short-term risk stratification in patients with CHF.

P281 | BEDSIDE
The influence of gender on epidemiology, precipitating Factors, management and prognosis of the patients with acute decompensated heart failure: Insights from KorHF Registry
J.-H. Lee, S.M. Kim, S.Y. Lee, J.W. Bae, K.K. Hwang, D.W. Kim, M.C. Cho on behalf of KorHF Registry Investigators. Chungbuk National University Hospital, Cardiology, Cheongju, Korea, Republic of Korea

Background: Because relatively little attention has focused on the gender related differences in heart failure (HF), women have been underrepresented in clinical trials. We aimed to determine the influences of the gender on baseline characteristics, management, and prognosis in patients with acute decompensated heart failure (ADHF).

Methods: The influences of the gender were evaluated in the Korean acute heart failure (KorHF) registry including hospitalized patients with ADHF. The patients were enrolled at 32 university grade hospitals in Korea from November 2005 to April 2009 and followed up until November 2009.

Results: We evaluated 3200 patients (1600 women) with HF whose mean age was 67±14.3 and mean follow up duration was 3.8 years. Women were older (70.7±13.5 vs. 64.5±14.5, P<0.001) and had lower BMI (23.0±4.2 kg/m 2 vs. 23.4±3.8 kg/m 2, P=0.009). They showed higher prevalence of hypertension (49.2% vs. 43.7%, P=0.002) and valvular heart disease (16.3% vs. 19.9%, P<0.001) and lower prevalence of previous MI (11.9% vs. 16.5%, P<0.001). At the baseline echocardiography women had higher LA volume index (42.1±30.1 ml/m² vs. 33.8±18.0 ml/m², P<0.001), E/E' ratio (20.5±13.5 vs. 17.6±9.6, P=0.001) and LV ejection fraction (EF: 43.3±16.6 vs. 36.0±15.5, P< 0.001). Despite the higher EF, mean NYHA functional class of women was worse at baseline (NYHA IV in 26.0% vs. 19.7%, P<0.001). Women also showed higher level of NT-proBNP at the initial presentation (9455.9±10358.6 pg/mL vs. 7680.1±9341.5 pg/mL; P<0.001). The use of inotropics was more common in men (15.3% vs. 19.2%, P=0.005) and the use of aldosterone antagonist during hospitalization was less in women than in men (32.1% vs. 36.2%, P=0.027). The use of ACE inhibitor (63.1% vs. 65.7%, P=0.13) and beta adrenergic blocker (45.7% vs. 46.3%, P=0.77) were comparable in both gender. Improvement in mean NYHA functional class after treatment and during follow-up was significant for both women and men but we noted more significant change was observed in women shortly after discharge whereas the degree of improvement showed similar significance at 12months later. There were significant improvements in LV EF and E/E' ratio for both gender and those were more apparent in men. There were no significant differences in mortality, rehospitalization rate and the composite outcome.

Conclusions: Women tend to have worse baseline characteristics and be treated less aggressively than men despite of comparable outcome. The differences of gender can affect the prognosis variably so, we emphasize the importance of the approach concerning these differences.

P2817 | BENCH
Three-dimensional growth of cardiac stem cells to form biosynthetic cardiac tissues
Y. Bai1, W. Bian2, J.W. Wu1, Y. Zhang1, J. Qian1, Y. Zou1, J. Ge1, Y. Bai1, W. Bian2, J.W. Wu1, Y. Zhang1, J. Qian1, Y. Zou1, J. Ge1. 1 Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital-Fudan University, Shanghai, China, People's Republic of China; 2 Duke Translational Medicine Institute, Department of Biomedical engineering, Durham, United States of America

Currently, a promising treatment for myocardial infarction is cell-based exogenous replacement therapy. However, tissue engineering using human cardiac tissues remains a challenge because of the complex 3D mesh of tangential and intruding fibers, so that reconstructed tissue patch needs to match the native ventricular mass arrangement to merge seamlessly with the native tissue, to realize “personalized” patch in the end. In our present work, we are using cardiac stem cells (CSC) and mesoscopic hydrogel molding, to culture mouse c-kit (+) CSC in 3D environment to form cardiac tissue patch. By using this microfabricated tissue mold (Nat Protoc. 2009, 4 (10): 1522–1534), we can build “personalized” tissue network and tissue patch with realistic fiber directions. c-kit (+) CSC were isolated followed the protocol we published before, after expansion, ~40,000 CSC were plated in suspension in 5ml of leukemia inhibitor factor-deprived stem cell growth medium, which were replaced every 2–3 days. Cardiostern spheres usually formed by 3–4 days. These cells were then mixed with fibrinogen containing matrigel into microfabricated tissue mold to allow for tissue patch. Each patch was then immersed in 2ml of serum-free medium containing 6-aminopropionic acid. Cardiac tissue patches were maintained for 14 days with medium change every 2 days. After 14 days culture, we measured the patch function. The composition of cardiomyocytes, endothelial cells and smooth muscle cells in the patch were detected by a-SMA, vWf, and aSMA immunostaining; interaction and communication among cardiomyocytes and between matrix were detected by connexin 43 immunostaining. T-tubules arrangement in 3D patch and 2D monolayer were labeled by Caveolin-3. We are also comparing difference of L-type calcium channel and RyR2 type Ca++ channel and RyR2 expression and distribution between 3D patch and 2D monolayer. Our ultimate goal of this study is to construct bioactive cardiac tissues, for implantation into the infarcted heart to achieve functional improvement.

P2818 | BEDSIDE
Factors associated with increased levels of serum cardiac troponin during the peripartum period
M. Okano1, T. Kato1, A. Miyata2, T. Nagano2, M. Inoko1. 1 The Tazuke Kofukai Medical Research Institute, Kitano Hospital, Cardiovascular Center, Osaka, Japan; 2 The Tazuke Kofukai Medical Research Institute, Department of Obstetrics and Gynecology, Osaka, Japan

Background: Elevated troponin cardiac troponin level can help predict cardiac events not only in patients with myocardial infarction but also in those with heart failure or in a healthy screening population. Peripartum cardiomyopathy is a rare but devastating disease that develops during pregnancy and after delivery; however, the associated data in pregnancy women is uncommon. In the present work, we are using cardiac troponin I (cTnI) levels, brain natriuretic peptide (BNP) levels, and cardiac function during pregnancy and after delivery.

Methods: We sequentially assessed 463 consecutive Japanese pregnant women during the third trimester (28–30 weeks' gestation) and four days after delivery (postpartum) in our hospital during 2013. Women with underlying heart disease or those who did not provide consent were excluded.

Results: The characteristics of the participants were as follows: mean age, 33±14.9 years; age of ~35 years, 18.2%; pregnancy-induced hypertension (PIH), 4.5%; oxytocin use, 31.9%; delivery by caesarean section, 17.2%; and mean hemoglobin levels during the third trimester and after delivery. 11.1±1.0 and 10.1±1.4, respectively. Ejection fraction did not change between the third trimester and after delivery. cTnI levels in peripartum women were significantly higher (0.019±0.03 ng/mL; p<0.002) as compared to those in women at 28–30 weeks' gestation (~0.015 ng/mL). Similarly, BNP levels were significantly higher in peripartum women (29±2.3 pg/mL) than in women at 28–30 weeks' gesta-
delivery (OR: 2.01 per 1 g/dL decrease, 95% CI: 1.006–2.714, p = 0.0001). None of the women met the criteria for peripartum cardiomyopathy.

Conclusion: Serum cTnI and BNP levels in the peripartum period were increased as compared to those at 28–30 weeks’ gestation. Moreover, the factors affecting elevated cTnI levels, which are potential predictors of cardiac events, were identified in Japanese pregnant women.

LONG TERM MONITORING & PROGNOSIS IN HEART FAILURE

P2819 | BEDSIDE
Does the inclusion of depression and cognitive screening to frailty assessment improve prediction of outcomes in heart transplant-eligible patients?
S.R. Jha1, H.K. Hannu2, P. Newton2, K. Wilheim3, C. Hayward4, A. Jabbour5, M. Harkess5, P. Tunnicliff1, S. Shaw1, P. Macdonald1. 1St Vincent’s Hospital, Heart and Lung Transplant Unit, Sydney, Australia; 2University of Technology, Sydney, Sydney, Australia; 3St Vincent’s Hospital, Psychiatry, Sydney, Sydney, Australia.

Background: Frailty has emerged as an independent predictor of survival in elderly heart failure patients. It’s predictive value in the younger heart transplant-eligible (HTE) population has not been established.

Methods: Beginning in 2013, all patients with advanced heart failure (AHF) referred to our centre have undergone assessment of physical frailty (Fried phenotype, FP), cognition (Montreal Cognitive Assessment, MOCA) and depression (Depression in Medical Illness, DMI). We assessed the value of the FP (FP ≥ 3.5 = frailty) and a novel frailty measure derived from FP, MOCA and DMI (mFP ≥ 3.7 = frailty) in predicting outcome.

Results: 120 patients (83M:37F; age 53 ± 13 years, range 16–73; LVEF 27 ± 14%) with AHF were followed for 279 ± 202 days. Using FP, 82 were non- or pre-frail (NPF) and 38 were frail. Using mFP, 68 were NPF and 52 were frail. Frailty was independent of age, LVEF and renal function. Frailty (by FP or mFP) was associated with being female, anaemia, hypoalbuminemia and mortality (Figure). Using Cox proportional hazards model, frailty as assessed by mFP remained an independent predictor in predicting outcome.

Conclusions: Frailty is common in HTE patients with AHF. Inclusion of cognitive and depression domains strengthens the relationship between frailty and mortality. Frailty assessment is useful in identifying AHF patients at high risk of early mortality.

P2820 | BEDSIDE
A cost-effective inpatient heart failure service can save lives and reduce admissions

Background: Acute heart failure accounts for 2% of NHS inpatient bed-days, 5% of all emergency admissions, with approximately 30–40% dying within one year. Inpatient mortality is estimated at over 10% with in 1 in 4 readmitted within 3 months. In October 2014 National Institute of Clinical Excellence (NICE) published guidelines recommending that all patients admitted with heart failure should receive input from a specialist heart failure team.

We report the results of our implementation in a single tertiary referral centre through the establishment of a heart failure service (HFS) and the appointment of a single heart failure specialist nurse specialist.

Results: We compare 12 month periods before (period 1) and after (period 2) implementation of an inpatient HFS.

During period 2, there were 107 fewer (3383 v. 3490) patients admission with a diagnosis of heart failure, of which 669 (19.8%) were seen by the HFS (61% male; 66% over 75 years), despite the expected increasing trend of admissions. The median length of stay was 12 days, equating to 1305 fewer bed days used in period 2.

During period 2, adherence to heart failure therapy guidelines on discharge was significantly better in those seen by the HFS. See figure 1. In-hospital mortality for all heart failure admissions was reduced to 11.1% v. 12.8% (RRR 13.2%; ARR 1.7%), equating to a potential 72 lives saved in that period.

Looking specifically in period 2, of the patients seen by the HFS there was significant reduction of 44% in in-hospital mortality (ARR 5.3%, RRR 44% statistically significant p < 0.0001).

Importantly, 30 day re-admission rates were also substantially reduced for those seen by the HFS at 6.3% v. 12.2% (ARR 5.9%, RRR 48.3% with p<0.0008).

Heart failure medications on discharge

<table>
<thead>
<tr>
<th>Medications (%)</th>
<th>Seen by HFS</th>
<th>Not seen by HFS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta blockers</td>
<td>81</td>
<td>54</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>69</td>
<td>36</td>
</tr>
<tr>
<td>MRAs</td>
<td>76</td>
<td>46</td>
</tr>
</tbody>
</table>

Discussion: We report that after the introduction of a heart failure specialist service, the re-admission rates following hospitalisation for heart failure remain high. The objective of this study was to document re-admission patterns of patients with HFpEF and HFrEF managed in a dedicated disease management programme.

Methods: Patients admitted to a University Hospital between November 1998 & April 2014 with a diagnosis of decompensated heart failure were included in this study. All patients were entered into a disease management programme. We identified the re-admission pattern over the 8 month period following the index hospitalisation.

Results: There were 1266 (58.6% male, mean age 72.2yrs) index hospitalisations for heart failure (410 (32.3%) HFpEF, 856 (67.7%) HFrEF). All-cause re-admission rates at 0–2, 2–4, 4–6 and 6–8 months are shown in table 1. The re-admission rates following hospitalisation for heart failure remain high. In the first two months following discharge, 102 patients (102/410, 24.8%) with HFpEF and 191 patients (191/856, 22.3%) with HFrEF were readmitted. All-cause and HF re-admission rates at 0–2, 2–4, 4–6 and 6–8 months were similar in both groups.

Table 1. Hospital readmissions in the 8 months following discharge by patient type and admission type

<table>
<thead>
<tr>
<th>Time after discharge</th>
<th>0–2 months</th>
<th>2–4 months</th>
<th>4–6 months</th>
<th>6–8 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>92/1266</td>
<td>38/1188</td>
<td>24/1106</td>
<td>31/1030</td>
</tr>
<tr>
<td>HF-pEF</td>
<td>28/410</td>
<td>13/381</td>
<td>16/354</td>
<td>12/327</td>
</tr>
<tr>
<td>HF-rEF</td>
<td>64/856</td>
<td>25/807</td>
<td>8/752</td>
<td>19/703</td>
</tr>
</tbody>
</table>

Admission per patient during 8 months after discharge by admission type

<table>
<thead>
<tr>
<th>Time after discharge</th>
<th>0–2 months</th>
<th>2–4 months</th>
<th>4–6 months</th>
<th>6–8 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>All admissions</td>
<td>293 (23%)</td>
<td>153 (12.8%)</td>
<td>106 (9.5%)</td>
<td>109 (10.5%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>92 (7.2%)</td>
<td>38 (3.2%)</td>
<td>24 (2.2%)</td>
<td>31 (3%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>50 (3.8%)</td>
<td>26 (2.1%)</td>
<td>18 (1.6%)</td>
<td>13 (1.2%)</td>
</tr>
<tr>
<td>Non-cardiovascular</td>
<td>89 (7.5%)</td>
<td>64 (5.7%)</td>
<td>65 (6.3%)</td>
<td>65 (6.3%)</td>
</tr>
</tbody>
</table>

Conclusions: Nearly one quarter of patients discharged following an index HF hospitalisation require early readmission. A significant number of admissions are due to non-cardiovascular causes. HFpEF and HFrEF demonstrate similar re-admission patterns.

P2821 | BEDSIDE
Necropsy findings in patients with heart failure
L.F. Lipari Dinardi1, V.S. Issa2, T.V. Pereira1, L.K.R. Almeida1, L. Isper1, T.S. Barbosa1, S.M. Ayub-Ferreira2, L.A. Benvenuti3, E.A. Bocchi2. 1Heart Institute (InCor) - University of Sao Paulo Faculty of Medicine, Sao Paulo, Brazil; 2Heart Institute (InCor) - University of Sao Paulo Faculty of Medicine, Sao Paulo, Brazil; 3Heart Institute (InCor) - University of Sao Paulo Faculty of Medicine Clinical Hospitals (HC-FMUSP), Sao Paulo, Brazil

Introduction: Heart failure is a condition associated with high mortality and understanding the mechanisms of death can contribute to the care of patients. How-
ever, the number of health centers that perform autopsies is decreasing and only a few studies analyzed post mortem findings in patients with heart failure.

Methods: We analyzed the reports of autopsies performed between January 2000 and April 2005 in our cardiology hospital. Patients with diagnosis heart failure, cardiogenic shock, or cardiomyopathy at autopsy were included. Congenital heart diseases, patients younger than 18 years old, pericardial diseases and postoperative shock were excluded.

Results: We analyzed 1226 autopsy findings and selected 500 cases - 322 (34.4%) male, 178 (35.6%) female and mean age was 62.4±15.9 years. Of the excluded cases (376), 236 (62.7%) were due to congenital heart diseases, 128 (34.1%) postoperative shock and 12 (3.2%) pericardial diseases.

Heart failure etiology was ischemic in 200 (40%) patients, Chagas disease in 65 (13%), hypertension in 52 (10.4%) and rheumatic disease in 63 (12.6%). According to autopsy, the main causes of death were cardiogenic shock in 209 cases (41.8%) patients, septic shock in 103 (20.6%) and pulmonary embolism in 59 (11.8%).

Diagnoses often related to death included atherosclerotic heart disease in 62 (12.4%) patients, intracardiac thrombosis in 54 (10.8%), pneumonia in 42 (8.4%) and systemic embolism in 30 (6%). Diagnoses considered unrelated to death included hypertension in 188 (37.6%) patients, systemic atherosclerosis in 169 (33.8%), diabetes mellitus in 76 (15.2%) (12.4%) patients, intracardiac thrombosis in 54 (10.8%), pneumonia in 42 (8.4%) and systemic embolism in 30 (6%).

Conclusion: Cardiogenic shock is frequent cause of death in patients with heart failure, demonstrating the severity of this syndrome. Although necropsies study are decreasing, this research shows that, in addition to the decapsulation causes, is important to know the causes of death as well, because of their impact on the patients prognosis and that knowledge can guide and improve the patients care.

P2823 | BEDSIDE
Chikungunya virus induced myocarditis
I. Mendoza1, I. Mor1, I. Mendoza2, K. Gonzalez1, J. Villalobos1, Y. Meza1, C. Mor1, C. Mor1, J. Marques2, 1Central University of Venezuela (UCV), Tropical Cardiology Department, Caracas, Venezuela; 2Jackson Memorial Hospital, Cardiology, Miami, United States of America

Background: Chikungunya virus infection is a mosquito-borne virus infection, is considered to be among the most important emerging viral diseases. It has recently re-emerged and caused millions of infections globally. Local transmission has been found in Europe. Chikungunya can be fatal and has been associated with sudden deaths.

Objective: To investigate cardiac complications of the Chikungunya infection.

Methods: Prospective multicenter observational study of 270 patients with a Chikungunya infection from a Venezuelan outbreak.

Clinical evaluation, ECG, laboratory including virological evaluation and cardiac biomarkers, Echocardiogram, Holter and cardiac MRI procedures were performed.

Results: Of the 270 patients examined, 108 patients were male, with a mean age 60±9; 260 patients presented with fever and polyarthralgia and 81 developed palpitations. And there were 3 sudden cardiac deaths.

Arrhythmias occurred in 46.6% of cases; they included bradyarrhythmias (33%), atrial and ventricular ectopic beats and tachyarrhythmias where atrial fibrillation was observed in 16 cases. There were also ectopic atrial tachycardia and non sustained ventricular tachycardia, conduction disturbances and 3 cases of sudden death.

Conclusion: Physicians should be aware of the possibility of manifest or silent myocarditis in almost half of the patients with Chikungunya disease. In a proper epidemiological context, the triad of fever, polyarthralgia and new arrhythmias including bradycardias suggest Chikungunya myocarditis.

P2824 | BEDSIDE
Graft rejection requiring treatment within the 1st year after heart transplantation significantly affects survival, as opposed to later rejection episodes
I. Planinic1, D. Fabjanovic1, J. Ljubas-Macek1, B. Skoric1, Z. Baricovic1, H. Jurin1, J. Samardzic1, H. Gasparovic2, M. Cikes3, D. Milicic1, 1University of Zagreb School of Medicine, University Hospital Center Zagreb, Department of Cardiovascular Diseases, Zagreb, Croatia; 2University of Zagreb School of Medicine, University Hospital Center Zagreb, Department of Cardiac Surgery, Zagreb, Croatia

Purpose: The highest mortality rates after heart transplantation (HTx) occur in the first post-HTx year and it has been proven that 20–40% of patients develop at least one episode of acute cellular rejection within this time period. In order to study the relevance of the time of graft rejection occurrence, we evaluated the survival of patients after heart transplantation in relation to the timing of graft rejection occurrence.

Methods: We retrospectively studied 74 consecutive HTx recipients from our center (53 male, mean age 53±13.6, median follow-up 24 months) and have measured the time to first histopathological signs of any graft rejection (ISHLT grade >0R), time to first graft rejection requiring treatment (ISHLT grades 2R and 3R, as well as antibody mediated rejection), and survival time. The Kaplan Meier method for survival rates (log-rank test for comparison), and multivariate analysis using Cox regression analysis were performed.

Results: Patients treated for acute graft rejection within the first 12 post-transplant months had significantly lower survival rates (p=0.033) (Figure 1), and a HR of 6.65 (95% CI 1.46–30.41, p=0.015) compared to patients who did not experience acute graft rejection requiring treatment in this time period (adjusted for sex and age). None of the following had a significant influence on survival: time to first histopathological signs of any graft rejection, occurrence of graft rejection requiring treatment between post-HTx months 12–24, or later than 24 months post-HTx.

Conclusion: Our results demonstrate that acute graft rejection requiring treatment occurring within the first post-transplant year has a significant impact on survival of heart transplant recipients, as opposed to rejections occurring at a later time period.

P2825 | BEDSIDE
The current situation of management of systolic heart failure in Russia: Russian hospital heart failure registry (RUS-HFR) results
A. Yurchenko1, M. Strikov1, E. Lyasnikova1, M. Trukhina1, E. Shlyakhto1, D. Dulyakova2, R. Libis3, 1Federal Almazov Medical Research Centre, Saint Petersburg, Russian Federation; 2Samara Regional Cardiology Dispensary, Samara, Russian Federation; 3Orenburg State Medical Academy, Orenburg, Russian Federation

Purpose: The aim of RUS-HFR was to obtain contemporary analysis of the HF management and 1-5-year outcomes of inpatients with chronic systolic HF in real-life clinical practice in Russian Federation (RF).

Methods and results: The RUS-HFR is a prospective, multicentre, observational study conducted in 3 Cardiology Centers. Inclusion criteria: HF NYHA I–IV, LVEF <40%, age 18–75 years. 524 patients were enrolled in all centers. Age was 60±9.6, 80.5% men, ischemic 63.3–74.8%, hypertension 69.5–88.9%, DCM 4.6–5.2%. LVEF was 28.5±7.2%. NT-proBNP was not a routine diagnostic test. COPD was 11.5–26.6%, AF 43.2–47.4%, diabetes 20.0–22.8%, CRT (4.5%) and ICD (5.2%) have been previously implanted in patients from Almazov Centre. RAS blockers, β-AB, and MRAs were used in 82.3–87.3%, 76.3–95.8%, and 65.9–81.1% of patients, respectively. The rate of prescription of these drugs prior admission was significantly lower: RAS blockers 12.6–58.7%, β-AB 11.7–70%; MRAs 4.4–53.3%. Diuretics prior to hospitalization were not taken in 55%, 23%, 24% of patient with NYHA II, III and IV, respectively. Overall, 80.7–94.6% of patients were on diuretics at hospital discharge. The median duration of hospital stay for HF decapsulation was 18 days (interquartile range 13–26). Indications for implantation of devices (ICD and CRT) were determined at 4.6%–21.2% of patients. Indications for heart transplantation were identified to 17 patients from center No. 1 (center with heart transplant program). Dose reduction of basic drugs recommended for the treatment of HF and the proportion of patients receiving them were observed after hospitalization in 1.5 years of follow-up period. Ambulatory patients with CHF were under the supervision of a cardiologist and therapist in the 43–72% and 15–42% cases, respectively, and 7–17.7% of patients did not visit a doctor at all. The all-cause death and hospitalization for HF decapsulation within 1.5 years of follow-up were 11.6±20.9/26.2% and 16.2/41.47.3% respectively in 3 centers with less value in center No. 1.

Conclusion: The main drugs recommended for outpatient HF were used insufficiently. Oral diuretics were not prescribed for the clinical manifestations of HF in 23–55% of cases. High-tech methods of treatment in patients with HF NYHA II–IV were not often enough recommended. The mortality and re-hospitalization in 1.5 years due to decompensated HF in RF remained high. HF management in RF still present the most problematic item depending on many factors, one of the way to improve is to organize network of specialists and consulting HF clinics throughout the country.
P2826 | BEDSIDE
High burden of primary care contacts in patients with left ventricular systolic dysfunction- findings from the heart failure and optimal outcomes from pharmacy study
P. Forsyth1, R. Lowrie1, P.S. Jhund2, N. Greenlaw3, J.J.V. McMurray2, F.S. Mair4. 1 NHS Greater Glasgow and Clyde, Pharmacy & Prescribing Support Unit, Glasgow, United Kingdom; 2University of Glasgow, BHF Cardiovascular Research Centre, Glasgow, United Kingdom; 3University of Glasgow, Robertson Centre for Biostatistics, Glasgow, United Kingdom; 4University of Glasgow, General Practice and Primary Care, Glasgow, United Kingdom
Background: The secondary care burden of left ventricular systolic dysfunction (LVSD) with or without heart failure (HF) is well described but less is known about primary care (PC) burden.
Purpose: To examine factors associated with PC use in the Heart failure and Optimal Outcomes from Pharmacy Study (HOOPS).
Methods: Data analysis of the control group from HOOPS (n=973 with data, mean age 71 yrs), a study of pharmacist intervention in LVSD +/− HF. Counts of all-cause PC physician and nurse contacts (office room, phone call or home visit) were collected at one year post randomization. Negative binomial regression tested whether age, sex, socioeconomic status, number of comorbidities, loop diuretic use (proxy for symptomatic HF), LVSD duration, and LVSD severity were associated with total number of contacts. Variables were excluded if p >0.2.
Results: Mean annual PC contacts: 7.4 (CI 7.0–7.7) physician, 3.8 (CI 3.6–4.1) nurse and 11.2 (CI 10.7–11.7) total. More comorbidities, loop diuretic use and female sex predicted more total contacts. Greater LVSD severity and longer duration of LVSD were associated with fewer total contacts.
Predictors of total contacts
Predictor No. of patients Mean annual total contacts (CI) Incidence rate ratio (CI) p
Number of comorbidities
0–1 197 8.8 (7.9–9.6) 1
2 322 10.6 (9.7–11.4) 1.17 (1.08–1.27) <0.001
3 261 12.0 (11.1–13.0) 1.31 (1.17–1.48) <0.001
≥4 193 13.5 (12.3–14.7) 1.48 (1.30–1.68) <0.001
Sex
Male 674 10.8 (10.2–11.4) 1
Female 299 12.1 (11.2–13.0) 1.09 (1.00–1.20) 0.045
Prescribed loop diuretic
No 424 9.9 (9.3–10.6) 1
Yes 549 12.1 (11.4–12.9) 1.17 (1.07–1.27) <0.001
LVSD severity
Mild 379 11.8 (11.0–12.7) 1
Moderate 425 11.0 (10.2–11.7) 0.93 (0.85–1.02) 0.003
Severe 169 10.3 (9.4–11.3) 0.86 (0.76–0.96) 0.004
Duration of LVSD (yrs)
<1–1.9 282 12.4 (11.4–13.5) 1
2–3.9 256 11.2 (10.3–12.2) 0.88 (0.79–0.98) <0.001
≥4 435 10.3 (9.7–11.0) 0.85 (0.78–0.94) <0.001
Conclusion: The PC burden of patients with LVSD +/- HF was high. More comorbidities and loop diuretic use were strong predictors of total contacts.

P2827 | BEDSIDE
Sudden cardiac death risk assessment after septal alcohol ablation in patients with hypertrophic cardiomyopathy according to the new ESC 2014 guidelines
M. Jensen1, F. van Buuren2, A. Axelson1, Z. DIMITRIADIS1, S. HELQVIST1, S. Scholz2, L. Faber2, H. BUNGERD2. 1 Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark; 2 Heart and Diabetes Center NRW, Bad Oeynhausen, Germany
Background: The prediction of the sudden cardiac death (SCD) risk in hypertrophic cardiomyopathy (HCM) according to the new ESC guidelines (2014) has not been assessed in patients treated invasively for left ventricular outflow tract (LVOT) obstruction.
Methods: We determined the risk score for SCD according to AHA/ACC 2011 guidelines and compared to the estimated SCD risk according to ESC 2014 guidelines in patients with obstructive HCM before and after septal alcohol ablation (SAA).
Results: SAA was performed in 470 patients. Nineteen died of SCD during 8.4±4 years of follow up. The SCD rate was 0.5%/yr, or 3.4 (CI: 1.9–5.4) %/5 years. The prevalence of risk factors before SAA was: Syncope 26%, family history of SCD 2%, unexplained sudden death 12%, aborted cardiac arrest (ACA) 2%, and LVOT gradient (at rest or during provocations) was 115±42 mmHg. At baseline the proportion of high risk patients was 24% (89/361) according to AHA/ACC guidelines (>2 risk factors) and 36% (133/360) according to ESC 2014 guidelines (estimated risk of SCD >6%/5 years) (p <0.001; Kappa=0.60) (median 5.4 (IQR 3.0–8.2) %/5 years). All risk parameters had improved after SAA and the proportion of high risk patients were 8.4% (23/275) (AHA/ACC 2011) and 4.5% (14/310) (ESC 2014) (ESCs vs. AHA/ACC, p<0.05). The observed SCD rate in patients with complete pre-SAA ESC 2014 risk assessment (n=360) was 3.1 (CI: 1.5–5.2)%/5 years. The ESC 2014 guidelines predicted 7 out of 13 SCD cases (sensitivity 54%) including all 5 SCD cases predicted by the AHA/ACC 2011 guidelines (sensitivity 38%). Numbers needed to treat according to ESC guidelines was 19 patients for 8 years compared to 18 patients according to AHA/ACC 2011 guidelines.
Conclusion: The new the ESC 2014 guidelines represent an improvement of sensitivity in identification of SCD patients compared to the current AHA/ACC guidelines. The ESC 2014 guidelines used as pre-SAA risk assessments seem to overestimate the observed incidence of SCD, but identifies the highest number of SCD cases with NNT of 19 patients during 8 years.

P2828 | BEDSIDE
Comparing the efficacy of Tadalafil versus Placebo on pulmonary artery systolic pressure and right ventricular function in patients with beta-thalassemia intermedia
R. Jalaian1, A. Tammadoni3, M. Iranian7, M. Saravi4, A. Mohaghdamnia4, S. Khalil1, Mazandaran University of Medical Sciences, Sari, Iran, Department of Cardiology, Fatemeh Zahra Hospital, Sari; 2 Babol University of Medical Sciences, Department of Hematology, Babol; 3 Babol University of Medical Sciences, Student Research Committee, Babol; 4 Babol University of Medical Sciences, Department of Cardiology, Babol; 5 Babol University of Medical Sciences, Department of Pharmacology, Babol, Iran (Islamic Republic of)
Background and objective: Pulmonary arterial hypertension (PAH) is the most important and the most common complication in patients with beta-thalassemia intermedia. This study was conducted to assess the effect of tadalafil on pulmonary artery pressure and right ventricular function in patients with beta-thalassemia intermedia.
Methods and materials: 44 patients with beta-thalassemia intermedia were included in the study based on the maximum amount of a normal pulmonary artery systolic pressure (PASP) and the tricuspid regurgitation velocity (TRV) measured by transthoracic echocardiography (TTE), which is the threshold for the diagnosis of pulmonary hypertension. Patients with hepatic or renal insufficiency and also patients who are treated with organic nitrates or alpha-blockers were excluded. And then patients were randomly divided into two groups of 22 patients and were treated for 6 weeks with tadalafil capsules (40 mg daily) or placebo capsules (containing lactose) that were same in weight, size and shape. PASP TRV and variables related to systolic and diastolic function of the right ventricle (TAPSE, S' and E/E') were measured by TTE before and after treatment and finally were analyzed.
Results: At the end, significant improvement in all of the variables were observed in the group who received tadalafil (p<0.05). Mean difference made on all of the variables studied was also significant in the tadalafil group compared to the placebo group (p<0.05).
Conclusion: Tadalafil has a significant reducing effect on PASP and TRV in patients with beta-thalassemia intermedia. tadalafil also improves right ventricular systolic and diastolic function in these patients.
the incidence in patients (PTS) treated with pacemakers (PM) for standard anti-bradycardic indications and how it is influenced by initial systolic function.

Methods: Clinical and echocardiographic evaluation (ECHO) of PTS with standard PM indications at the time of PM implant and after a follow-up (FU) of min. > 2 months.

Results: 1131 PTS (45% male, mean age 73 yrs; a-v-block 49%; sinus node disease 45%) had an ECHO at the time of implantation and during a FU of 3.6±1.8.

849 (75%) PTS had a normal systolic LV function (EF > 55%, group 1), 191 (17%) PTS had a slightly impaired LV function (EF 45–55%, group 2) and 91 (8%) PTS had a moderately or severely impaired LV function (EF < 45%, group 3) at baseline. At the end of FU within group 1 706 PTS (83%) had an unaltered normal LV function, 143 (17%) had a LV function deterioration. In group 2 LV-function was unaltered in 75 PTS (39%), 66 (35%) enhanced and deteriorated in 50 PTS (25%). Amelioration of LV function was shown in 32 PTS (35%), 45% preserved their initial LV function and 24% impaired their LV function within group 3. 26/113 (2.3%) PTS developed severe HF (NYHA:3) and were upgraded to biventricular pacing (CRT). The incidence was 12.1% (in group 1, 8% in group 2 and 7% in group 3).

Conclusions: In an “everyday-PMT-population” the development of severe systolic dysfunction is a relatively rare event, especially in PTS with a normal or only slightly impaired initial LV function. Per contra PTS with an impaired initial LV function are more at risk for higher rates of LV deterioration. Nevertheless more of the patients (age 71 ±11 yrs) who have diabetes mellitus and coronary artery disease than diabetic patients who have initial milder disease and coronary artery disease were excluded. LV layer contractility and relaxation were assessed by radial strain rate (SR) during systole (SR-S) and isovolumic relaxation (SR-IVR). Pulmonary capillary wedge pressure (PCWP) was calculated as 10.8 − 12.4 x KT index. LV stress was calculated as 1.9±0.4* and HHF: 1.8±0.3 s –1*. SR-IVR; −0.9±0.6, −0.7±0.4*, −0.5±0.3* and without reduction of LVEF (SR-S; control: 2.6±0.6, LVH (−): 2.3±0.6*, LVH (+): 2.0±0.5*, respectively). PCWP was calculated as 10.8 − 12.4 x KT index. LV stress was calculated as 1.9±0.4* and HHF: 1.8±0.3 s –1*. SR-IVR; −0.9±0.6, −0.7±0.4*, −0.5±0.3* and without reduction of LVEF (SR-S; control: 2.6±0.6, LVH (−): 2.3±0.6*, LVH (+): 2.0±0.5*, respectively).

Results: Echocardiographic parameters EF, left atrial (LA) size, and left ventricular end-systolic volume (LVESV) were measured by MLEC bioassay. The data are shown as mean±SD. Patients were 60.9±13.6 years old, 36% of these patients showed an amelioration of initially evaluated weak LV function. Our purpose was to identify the differentiation of TC from AASTEMI.

Conclusions: As the largest study to date comparing ECG findings of TC and AASTEMI, our data further support findings of other studies, except for the utility of STE in −aVR. With future larger studies, risk stratification criteria may help in the differentiation of TC from AASTEMI.

P2832 | BEDSIDE
Clinical and echocardiographic correlation of plasma transforming growth factor (TGF-β)-beta levels in patients with heart failure
A. Malodya 1, S.A. Hamid 1, S. Khan 2, M.T. Saltzburg 1, T. Tsuda 2.
1 Christiana Hospital, Cardiology, Newark, United States of America; 2 Nemours/Al DuPont Children’s Hospital, pediatric Cardiology, Wilmington, United States of America.

Background: The role of transforming growth factor-beta (TGF-β) in the pathogenesis of heart failure (HF) has been studied extensively in animal models, but its definite role and clinical relevance in humans is not well defined. Recently, we have established a bioassay using mink lung epithelial cells (MLEC) to measure TGF-β bioactivity and demonstrated that myocardial TGF-β bioactivity was significantly enhanced in advanced human HF.

Purpose: We investigated plasma TGF-β bioactivity in HF patients to test whether TGF-β levels correlate with clinical and echocardiographic parameters.

Methods: Total of 38 patients with reduced ejection fraction (EF) less than 35% were recruited from the HF program at our institution between December 2012 and November 2014. Plasma TGF-β level was measured by MLEC bioassay. Echocardiographic parameters EF, left atrial (LA) size, and left ventricular end-diastolic diameter (LVEDD), and clinical data including NYHA class, etiology (ischemic vs non-ischemic), and evidence of atrial fibrillation (AF) were analyzed.

Results: The data are shown as means±SD. Patients were 60.9±13.6 years old, with 71.1% being males. See table

Table 1. TGF-β levels in HF patients

<table>
<thead>
<tr>
<th>NYHA class</th>
<th>I-II</th>
<th>III-IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>20/36</td>
<td>16/36</td>
</tr>
<tr>
<td>TGF-β [ng/ml]</td>
<td>24.6±12.3</td>
<td>38.6±20.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LA size (cm)</th>
<th>&gt;5.0</th>
<th>≥5.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>5/26</td>
<td>11/36</td>
</tr>
<tr>
<td>TGF-β [ng/ml]</td>
<td>24.8±12.3</td>
<td>42.3±22.6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LVEDD (cm)</th>
<th>&gt;5.5</th>
<th>≥5.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>10/36</td>
<td>26/36</td>
</tr>
<tr>
<td>TGF-β [ng/ml]</td>
<td>32.1±22.5</td>
<td>39.4±16.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EF (%)</th>
<th>&gt;25</th>
<th>≤25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>19/38</td>
<td>19/38</td>
</tr>
<tr>
<td>TGF-β [ng/ml]</td>
<td>30.7±16.5</td>
<td>29.9±16.4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiology</th>
<th>ischemic</th>
<th>Non-ischemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>18/38</td>
<td>18/38</td>
</tr>
<tr>
<td>TGF-β [ng/ml]</td>
<td>31.1±19.0</td>
<td>31.1±19.0</td>
</tr>
</tbody>
</table>

Acknowledgement/Funding: US National Institute of Health

Conclusion: Plasma TGF-β levels were significantly higher in HF patients with advanced NYHA class (III-IV) and larger LA size, suggesting that plasma TGF-β levels may reflect the severity of HF. Further investigations will be required to confirm its clinical value as a biomarker.
vestigate subclinical LV changes in patients with ESRF using three-dimensional speckle-tracking echocardiography (3DSTE).

**Methods:** A total of 66 patients, without any clinical evidence of heart failure, were consecutively enrolled, including 44 subjects with ESRF (CKD 4–5) and 22 age- and sex-matched controls. Conventional two-dimensional LV ejection fraction (LVEF) was calculated using Simpson’s biplane method. Real-time three-dimensional full volume imaging of the left ventricle were recorded and analyzed. Left ventricular end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), ejection fraction (LVEF), global longitudinal strain (GLS), global circumferential strain (GCS), global radial strain (GRS), global strain (GSD3D) were analyzed. Time to peak GLS (T-s), Time to peak GCS (T-cs), Time to peak GRS (T-rs), Time to peak GSOD (T-md) and Time to peak systolic volume (T-msv) were analyzed.

**Volume parameters were standardized by body surface area (BSA) and heart rate.**

**Results:** Compared with the controls, ESRF patients had significantly lower GLS, GRS, and 3D-LVEF (LVEF: 81.8±8.3% vs 17.0±2.3%, GCS: 39.4±3.4% vs 37.0±3.5%, LVEF: 59.5±3.5% vs 57.3±4.2%, p<0.05), as well as enlarged LV volume (EDV: 40.4±7.3 vs 51.3±14.2mm³/m², ESV:16.3±3.2 vs 22.0±9.6mm³/m², SV:21.3±4.3 vs 26.4±6.5mm³/m², p<0.01). Additionally, T-s, T-cs and T-md were delayed in the ESRF group (T-s: 38.5±5% vs 41.6%, T-cs: 38.5±5% vs 42.6%, p<0.05). However, there was no significant difference in 2D-LVEF between the two groups (67.4±3.5 vs 66.3±4.6%, p=0.393). Multiple linear regression analysis showed GCS was an independent predictor of LVEF in patients with ESRF (β=1.49, 95% CI (−2.02)–(−0.95), p<0.001).

**Conclusion:** Renal failure leads to subclinical LV deformation and dysfunction. 3DSTE may have potential in the evaluation and follow-up of patients with ESRF.

---

**P2834 | BEDSIDE**

Adding brain natriuretic peptide, ultrasound lung comets or Doppler clinical guidance in reducing heart failure hospitalization

M. Saraya, H. Kasem, H. Salah Eldin on behalf of Heart Failure with reduced ejection fraction. Cairo University, Cardiovascular medicine. Cairo, Egypt

**Background:** Hospital readmission rates in chronic heart failure are high. Natriuretic peptides, ultrasound lung comets, and tissue Doppler assessment of left ventricular end-diastolic pressure (LVEDP) are tools that can diagnose subclinical pulmonary congestion. There is controversy about the role of these tools in reducing heart failure hospitalization rate.

**Purpose:** Compare re-hospitalization rates with treatment guided by clinical findings alone vs. guided by natriuretic peptide, ultrasound lung comets or tissue Doppler imaging.

**Methods:** From July 2012 till August 2014, we randomised 100 hospitalised patients with heart failure and reduced ejection fraction to 4 equal groups. Group 1: treatment was guided by clinical findings alone. Group 2: treatment was guided by clinical findings and brain natriuretic peptide (BNP) point of care (targeting level below 200 pg/ml). Group 3: treatment was guided by clinical findings and ultrasound lung comets targeting a score below 15. Group 4: treatment was guided by clinical findings and Doppler imaging to measure E/Ea targeting a mean below 200 pg/ml.

**Results:** Compared with the controls, ESRF patients had significantly lower heart rate.

**Conclusion:** Rehospitalization leads to subclinical LV deformation and dysfunction. 3DSTE may have potential in the evaluation and follow-up of patients with ESRF.

**Abstract P2835 | Table 1**

<table>
<thead>
<tr>
<th>Diagnosis (n) variable</th>
<th>Controls (46)</th>
<th>All CAD (125)</th>
<th>Chronic CAD (17)</th>
<th>Post PCI (36)</th>
<th>Post CABG (56)</th>
<th>Ischemic FH (16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (ys)</td>
<td>48±13</td>
<td>64±8***</td>
<td>65±9***</td>
<td>62±5***</td>
<td>65±7***</td>
<td>62±9***</td>
</tr>
<tr>
<td>EDV (mL)</td>
<td>136±29</td>
<td>155±53*</td>
<td>138±50</td>
<td>145±61</td>
<td>142±27</td>
<td>247±161***</td>
</tr>
<tr>
<td>EF (%)</td>
<td>69±6</td>
<td>61±137*</td>
<td>65±8</td>
<td>65±8</td>
<td>64±77</td>
<td>34±111</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>131±40</td>
<td>157±444***</td>
<td>139±81</td>
<td>146±49</td>
<td>159±39</td>
<td>192±307</td>
</tr>
<tr>
<td>AADist (PERvm)</td>
<td>0.70±0.45</td>
<td>0.63±0.62</td>
<td>0.44±0.30</td>
<td>0.59±0.39</td>
<td>0.50±0.35</td>
<td>1.38±2.28**</td>
</tr>
<tr>
<td>AADist (PERv)</td>
<td>16.0±8.0</td>
<td>8.6±4.9***</td>
<td>8.73±7.28**</td>
<td>9.14±6.30**</td>
<td>8.15±4.56**</td>
<td>8.61±5.61**</td>
</tr>
<tr>
<td>AADist (PER)</td>
<td>1.54±0.73</td>
<td>0.85±0.47***</td>
<td>0.85±0.40</td>
<td>0.81±0.40</td>
<td>0.79±0.40</td>
<td>1.36±0.63**</td>
</tr>
<tr>
<td>AADist (PERv)</td>
<td>0.28±0.05</td>
<td>1.30±0.76***</td>
<td>1.09±0.72**</td>
<td>1.36±0.63**</td>
<td>1.13±0.62**</td>
<td>1.98±1.14</td>
</tr>
<tr>
<td>AADist (PERm)</td>
<td>1.97±1.03</td>
<td>1.30±0.03**</td>
<td>1.08±0.63*</td>
<td>1.28±0.76**</td>
<td>1.51±0.77</td>
<td>1.38±2.28**</td>
</tr>
<tr>
<td>AADist (PERvm)</td>
<td>3.70±0.45</td>
<td>0.63±0.62</td>
<td>0.44±0.30</td>
<td>0.59±0.39</td>
<td>0.50±0.35</td>
<td>1.38±2.28**</td>
</tr>
</tbody>
</table>
P2837 | BEDSIDE
Optical coherence tomography imaging long term follow-up of renal arteries after radio-frequency catheter-based renal denervation
T.M. Roleder¹, M. Skowierski², W. Wanha³, T. Jadczyk³, L. Partyka³, G. Smolka¹, A. Ochala¹, M. Tendera¹, Z. Gasior¹, W. Wojakowski¹, Medical University of Silesia, Katowice, Poland; ²Krakow Cardiovascular Research Institute, Krakow, Poland

Aims: Optical coherence tomography (OCT) imaging at the time of renal denervation (RDN) showed that the procedure might cause spasm, intimal injury and thrombus formation. There is no data on long-term renal vascular injury after RDN. In the present study we assessed vessel-healing post RDN by OCT and angiography at long-term follow-up.

Methods and results: It was a single center study to assess renal arteries healing after radio-frequency (RF) RDN in 10 patients (20 arteries) by OCT and angiography at 19.2±5.6 months after procedure. There were no adverse events or complications during the long-term follow up. Nine patients (90%) achieved significant reductions of blood pressure without change of the antihypertensive medications. We demonstrated presence of 25 spots of focal intimal thickening found by OCT in 9 (90%) patients, in 13 (65%) arteries. The mean area of focal intimal thickening was 0.056±0.032 mm². No vessel dissection, thrombus, intimal tear or acute vasospasm were recorded during the OCT analysis. In addition, the quantitative angiography analysis (QCA) revealed that minimal lumen and proximal lumen diameter were smaller at follow-up, as compared to measurements obtained before RND.

Conclusion: Renal arteries present a favorable vessel healing post RDN at long-term follow-up. However, focal intimal thickening and reduction of the minimal lumen diameter may persist as results of RF denervation. Further studies are needed to determine whether intravascular imaging may help to monitor the vessel healing of RF RDN.

P2838 | BEDSIDE
Comparative study measuring the optic nerve sheath diameter with transorbital ultrasound in healthy women, pregnant women and pregnant with preeclampsia/eclampsia
E.G. Urias¹, J. Ortega², C.B. Arteaga³, ¹Centro de Investigacion y Docencia en Ciencias de la Salud, Anesthesiology, culiacan, Mexico; ²Instituto Mexicano del Seguro Social, Critical Care, culiacan, Mexico

Introduction: Preeclampsia/eclampsia is a potentially serious disease associated with maternal complications, including neurological. In patients with increased intracranial pressure, the diameter of the optic nerve sheath increases because of its close association with the flow of cerebrospinal fluid. Her measurements using ultrasound transorbital have shown correlation with increased intracranial pressure. 20% of patients with preeclampsia, the diameter of the optic nerve sheath increases because of its close association with the flow of cerebrospinal fluid. Her measurements using ultrasound transorbital have shown correlation with increased intracranial pressure. To compare the diameter of the optic nerve sheath transorbital measured by ultrasound between healthy women, pregnant women and pregnant women with preeclampsia/eclampsia.

Methods: Cross-sectional, multicenter study. 3 groups were included: Group 1: healthy women; Group 2: women with pregnancy; Group 3: women with preeclampsia/eclampsia. We obtained urine protein, serum creatinine and platelets, blood pressure, related symptoms. Diameter 3 mm behind the eyeball and an axis perpendicular to the optic nerve was measured. Three measurements of each eye were made, averaging them to give a mean to minimize the variability of the measurement.

Results: 60 patients, 20 in each group. The diameter of the optic nerve sheath was higher with statistical significance (p<0.05) for both eyes in patients with preeclampsia/eclampsia. In group 3, 20% in the right eye and 25% in the left eye had a diameter of optic nerve sheath above 5.0 mm.

Table 1. Comparison of medias between groups

<table>
<thead>
<tr>
<th></th>
<th>Right eye MEDI/A</th>
<th>Left eye MEDI/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagonal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy women</td>
<td>3.5±0.5</td>
<td>3.5±0.5</td>
</tr>
<tr>
<td>Healthy pregnant women</td>
<td>3.7±0.7</td>
<td>3.7±0.7</td>
</tr>
<tr>
<td>Preeclampsia/Eclampsia</td>
<td>4.3±0.9</td>
<td>4.3±0.9</td>
</tr>
</tbody>
</table>

*p<0.05 between preeclampsia/eclampsia vs healthy women and vs normal pregnancy women; **p<0.05 between preeclampsia/eclampsia vs healthy women and vs normal pregnancy.

Conclusion: Patients with the diagnosis of preeclampsia/eclampsia had diameters larger than the optic nerve sheath compared with women with normotensive pregancies and healthy women. In this sense, measurement transorbital DVNO by ultrasound appears as a new promising tool, affordable, accessible and non-invasive evaluation and timely care of patients with preeclampsia/eclampsia to rule elevated intracranial pressure.

P2839 | BEDSIDE
Catheter based renal denervation for resistant hypertension. 24 month results of the EnligHTN I Study using a multielectrode ablation system
C. Tsouflis, V. Papademetriou, K. Dimitriadis, A. Kasiakogias, M. Worthley, A. Sinhal, D. Chew, Y. Malisapian, D. Toussouls, S. Worthley, First Cardiology Clinic, University of Athens, Hippokration Hospital, Athens, Greece

Background and introduction: The EnligHTN I, the first-in-human study using a multielectrode ablation system for renal denervation (RDN) in patients with drug resistant hypertension (dRHT) demonstrated efficacy and safety at 6 and 12 months.

Purpose: The aim of this study was to report the complete set of 24 month data on office, ambulatory and home blood pressure (BP) changes as well as long term safety.

Design and methods: We studied 46 patients (age: 60±10 years, 4.7±1.0 antihypertensive drugs, body mass index:32±5 kg/m²) with dRHT on ≥3 anti-hypertensive medications with systolic BP >160 mmHg and diastolic BP >100 mmHg. At baseline, the average office BP, 24-hour ambulatory BP and home BP were 176/16/14 mmHg, 150±14/83±13 mmHg and 158±16/90±12 mmHg respectively. Bilateral RDN was performed using percutaneous femoral approach and standardized techniques.

Results: Reduction in office BP at 18 and 24 months from baseline were −24/−10 mmHg and −29/−13 mmHg, while the reduction in 24-hour ambulatory BP and in home BP at 24 months were −13/−7 mmHg and −11/−6 mmHg respectively (p<0.05 for all). Apart from higher body mass index (33.3±7.6 vs 29.5±2.2 kg/m², p=0.05), there were no differences in age, baseline office BP, heart rate, diabetes mellitus and baseline antihypertensive drug therapy in patients that were RDN responders at 24 months (defined as 10 mmHg decline in office BP compared to baseline (74%, n=34)). Stepwise logistic regression analysis revealed no prognosticators of RDN response (p=NS for all). At 24 months apart from a trend for renal function decrease, there were no new serious or life-threatening adverse events related with the procedure.

Conclusions: The EnligHTN I study provides evidence that the multielectrode ablation system constitutes a safe method of RDN in patients with dRHT and is accompanied by a sustained reduction of office, ambulatory and home BP at 24 months after the procedure. However, no predictors of RDN response were identified at long term follow-up.

P2840 | BEDSIDE
Challenges facing renal denervation: insight from real world experience at two UK centres
A.E. Burchell¹, K. Chan², E.C. Hart³, M. Saxena², A.K. Jain², D.J. Collie³, J.F.R. Paton³, A.K. Nightingale³, M.D. Lobo³, A. Baumbach¹ on behalf of BHI Cardiomics. ¹University of Bristol, School of Clinical Sciences, Bristol, United Kingdom; ²Queen Mary University of London, William Harvey Research Institute and Barts NIHR Cardiovascular Biomedical Research Unit, London, United Kingdom; ³University of Bristol, School of Physiology and Pharmacology, Bristol, United Kingdom

Background: Renal denervation (RDN) is a therapy targeting treatment resistant hypertension (TRH). Symplicity HTN-1&2 studies reported response rates of >80%, however sham-controlled, Symplicity HTN-3 failed to reach its primary endpoint (p=0.05). However, the study reported a significant reduction in office BP at 18 (p=0.04) and 24 months (p=0.001), with no difference between active and sham arms. In some patients baseline oSBP consistently predicts oBP decrease in 24 months and change in 24hr SBP (R=−0.69, p=0.009). Despite this, reduction in office BP at 24 months were −13/−7 mmHg and −11/−6 mmHg respectively (p<0.05 for all). Apart from higher body mass index (33.3±7.6 vs 29.5±2.2 kg/m², p<0.05), there were no differences in age, baseline office BP, heart rate, diabetes mellitus and baseline antihypertensive drug therapy in patients that were RDN responders at 24 months (defined as 10 mmHg decline in office BP compared to baseline (74%, n=34)). Stepwise logistic regression analysis revealed no prognosticators of RDN response (p=NS for all). At 24 months apart from a trend for renal function decrease, there were no new serious or life-threatening adverse events related with the procedure.

Conclusions: The EnligHTN I study provides evidence that the multielectrode ablation system constitutes a safe method of RDN in patients with dRHT and is accompanied by a sustained reduction of office, ambulatory and home BP at 24 months after the procedure. However, no predictors of RDN response were identified at long term follow-up.
### Results

**Abstract P2843 – Table 1**

<table>
<thead>
<tr>
<th>Tertile based on baseline office heart rate</th>
<th>Tertile 1</th>
<th>Tertile 2</th>
<th>Tertile 3</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline office systolic blood pressure, mmHg</td>
<td>159.9±23.3</td>
<td>163.9±22.9</td>
<td>166.9±25.4</td>
<td>0.006</td>
</tr>
<tr>
<td>Baseline 24-hour systolic blood pressure, mmHg</td>
<td>150.1±16.8</td>
<td>155.3±18.3</td>
<td>154.8±17.6</td>
<td>0.003</td>
</tr>
<tr>
<td>Six-month change in systolic blood pressure, mmHg</td>
<td>5.4±9.3</td>
<td>0.1±9.7</td>
<td>8.6±13.3</td>
<td>0.169</td>
</tr>
<tr>
<td>Six-month change in systolic blood pressure, mmHg</td>
<td>5.9±26.6</td>
<td>13.6±23.2</td>
<td>11.1±26.8</td>
<td>0.169</td>
</tr>
</tbody>
</table>

Results presented as percentage or mean ± standard deviation.

---

### P2841 | BEDSIDE

**Effect on heart rate following renal denervation: Insights from the Global SYMPLICITY Registry**

M. Boehm, M. Gancia, F. Mahlouf on behalf of Global SYMPLICITY Registry. 1Universitätsklinikum des Saarlandes, Homburg, Germany; 2University of Milan-Bicocca, Milan, Italy

**Background:** Renal denervation (RDN) has been shown to reduce systolic blood pressure (SBP) in patients with resistant hypertension. Previous initial reports have shown a reduction in heart rate following RDN in patients with elevated baseline heart rate that was not correlated with a reduction in SBP.

**Purpose:** We analyzed the change in heart rate and SBP among a large, diverse population of patients treated with RDN in the Global SYMPLICITY Registry.

**Methods:** The Global SYMPLICITY Registry is a prospective, open-label, single-arm, all-center worldwide registry evaluating the safety and effectiveness of treatment with the Symplicity(TM) RDN system. We analyzed the six-month change in heart rate and SBP by tertiles based on baseline office and 24-hour ambulatory heart rate.

**Results:** The 6-month change in office and 24-hour heart rate differed by baseline heart rate tertiles as shown in Table 1. There was a significant 6-month reduction in office heart rate among patients in the highest heart rate tertile (<0.001); however, the 6-month change in office SBP was similar in all three tertiles. This same phenomenon was observed when defining patient tertiles based on baseline heart rate and SBP.

**Conclusion:** In the Global SYMPLICITY Registry, RDN is associated with a significant reduction in office and 24-hour heart rate among patients with elevated baseline heart rate that is not associated with the reduction in SBP. This analysis supports previous reports of a direct cardiac effect of reduced sympathetic activity following RDN.

**Acknowledgement/Funding:** Medtronic, Inc. (ClinicalTrials.gov NCT01534299)

---

### P2842 | BEDSIDE

**Triple versus dual antiplatelet therapy in patients undergoing unprotected left main percutaneous coronary intervention**

S.W. Rha, B.G. Choi, S.Y. Choi, J.K. Byun, J.B. Kim, S. Xu, E.J. Kim, C.G. Park, H.S. Seo, D.J. Oh. 1Saarland University Hospital, Homburg, Germany; 2University of Milan-Bicocca, Milan, Italy

**Background:** Whether triple antiplatelet therapy (TAPT) is superior to dual antiplatelet therapy (DAPT) in patients (pts) undergoing unprotected left main percutaneous coronary intervention (uLM-PCI) in the era of drug-eluting stents (DESs) remains unclear.

**Methods:** A total 246 consecutive pts successfully underwent uLM-PCI with DESs were enrolled from Oct 2003 to Feb 2014. A total of 179 pts received TAPT for at least 1 month and 67 pts received DAPT. Complications and clinical outcomes were compared between the two groups up to 3 years.

**Results:** The baseline clinical, angiographic, and procedural characteristics were similar between the two groups except that the TAPT group was treated with more number of DESs from LM to left anterior descending artery, most frequently with sirolimus-eluting stents, whereas the DAPT group zotarolimus-eluting stents. The TAPT group had a less incidence of no-reflow than the DAPT group. At 3 years, the incidence of individual and composite clinical outcomes was similar between the two groups except the lower incidence of myocardial infarction (MI) in the TAPT group. Kaplan-Meier curve showed lower incidence of cumulative MI up to 3 years in the TAPT group (Figure). Multivariate regression showed that initial loading of TAPT (hazard ratio 0.27, 95% confidence interval 0.08 to 0.84, p-value=0.025) or TAPT for at least 3 months in survivors within 30 days (hazard ratio 0.30, 95% confidence interval 0.1 to 0.97, p-value=0.045) were an independent predictor for MI at 3 years.

**Conclusion:** TAPT administration in pts undergoing uLM-PCI with DESs seems to be safer and superior to DAPT in reducing the incidence of MI, suggesting the rationale for the routine TAPT in this high risk subset of pts.

---

### P2844 | BEDSIDE

**Sustained beneficial effects of multi-electrode renal sympathetic denervation on cardiac adaptations in resistant hypertension:**

C. Tsiofis, V. Papademetriou, K. Dimitriadis, A. Kasiakogias, D. Tsiahiris, C. Thomopoulos, I. Liakatis, D. Toussoulis, 1First Cardiology Clinic, University of Athens, Hippokration Hospital, Athens, Greece; 2Veterans Affairs Medical Center (VAMC), Washington, United States of America

**Background and introduction:** The favorable impact of renal sympathetic denervation (RDN) on cardiac parameters such as on left ventricular (LV) morphology, geometry and function has been shown up to 6 months after the procedure using diverse ablation systems.

**Purpose:** In this study we investigated whether multi-electrode catheter-based renal sympathetic RDN has favorable effects on LV structural and functional indices in patients with resistant hypertension after a follow-up of 24 months.

**Methods:** Twenty patients with resistant hypertension [age: 57±10 years, 13 males, office blood pressure (BP): 182/97±19/16 mmHg under 4.5±0.6 drugs] who underwent RDN were followed-up for 24 months. A full transmural echocardiographic study was performed in all patients and LV mass was calculated using the Devereux formula and was indexed for body surface area and height.

**Results:** Average office BP was reduced to 148±21/86±14 mmHg at 12 months and 140±23/83±14 mmHg at 24 months (p<0.001 for all). In the RDN group, LV mass index was significantly reduced from 136±20 g/m² (56.5±8.7 g/m²) to 121±16.6 g/m² (50.6±5.2 g/m²) at 12 months and 115.6±23.3 g/m² (48.8±13.9 g/m²) at 24 months (p<0.01 for all). RDN decreased mean intraventricular sep
Introduction: The accuracy of heart rate (HR) measurement by automatic oscillometric blood pressure (BP) monitors in patients with atrial fibrillation (AF) remains unclear. This study aimed to investigate the agreement between two automatic instruments and manual measurement of HR in patients with AF.

Methods: In 42 patients with persistent AF, HR was recorded using two automatic BP monitoring devices: Omron MS-I and Microlife BPA100 Plus. Meanwhile, manual counting of HR by stethoscope was treated as the reference. For each method, three readings were made at each 5-minute interval and the mean was calculated for comparison. In addition to paired t-test, the correlation between automatic and manual measurement was determined using Pearson’s correlation coefficient, and the agreement was validated using the Bland–Altman plot and the intraclass correlation coefficient (ICC).

Results: The mean of HR recorded by manual counting showed no significant difference in comparison with automatic measurement by Omron and Microlife devices. The correlation coefficients were 0.92 (Omron vs. manual) and 0.85 (Microlife vs. manual). The concordance is not modified if patient had manual counting HR below 80 bpm. If patients had HR above 80 bpm, the mean of HR (Microlife vs. manual) was calculated for comparison. The correlation between automatic and manual measurement was determined using Pearson’s correlation coefficient, and the agreement was validated using the Bland–Altman plot and the intraclass correlation coefficient (ICC).

Conclusions: There was high correlation between two devices and manually counting HR, which decreased slightly in patient with HR above 80 bpm via the Microlife device. Microlife device may over-estimate HR of AF patients.

P2845 | BEDSIDE Agreement between automatic and manual measurement of heart rate in patients with atrial fibrillation

T.T. Lin, C.L. Wang, C.L. Lai. National Taiwan University Hospital Hsin-Chu Branch, Internal Medicine, Hsinchu, Taiwan, ROC

The accuracy of heart rate (HR) measurement by automatic oscillometric blood pressure (BP) monitors in patients with atrial fibrillation (AF) remains unclear. This study aimed to investigate the agreement between two automatic instruments and manual measurement of HR in patients with AF.

Methods: In 42 patients with persistent AF, HR was recorded using two automatic BP monitoring devices: Omron MS-I and Microlife BPA100 Plus. Meanwhile, manual counting of HR by stethoscope was treated as the reference. For each method, three readings were made at each 5-minute interval and the mean was calculated for comparison. In addition to paired t-test, the correlation between automatic and manual measurement was determined using Pearson’s correlation coefficient, and the agreement was validated using the Bland–Altman plot and the intraclass correlation coefficient (ICC).

Results: The mean of HR recorded by manual counting showed no significant difference in comparison with automatic measurement by Omron and Microlife devices. The correlation coefficients were 0.92 (Omron vs. manual) and 0.85 (Microlife vs. manual). The concordance is not modified if patient had manual counting HR below 80 bpm. If patients had HR above 80 bpm, the mean of HR (Microlife vs. manual) was calculated for comparison. The correlation between automatic and manual measurement was determined using Pearson’s correlation coefficient, and the agreement was validated using the Bland–Altman plot and the intraclass correlation coefficient (ICC).

Conclusions: There was high correlation between two devices and manually counting HR, which decreased slightly in patient with HR above 80 bpm via the Microlife device. Microlife device may over-estimate HR of AF patients.

P2846 | BEDSIDE Quality of life after renar denervation: EuroQol 5 dimensions (EQ-5D) outcomes at 12 months in the Global SYMPLICITY Registry

J. Weil1, I. Kindermann2, G. Mancia3, F. Mahfoud2, M. Boehm2 on behalf of Global SYMPLICITY Registry. 1Sana Kliniken, Lübeck, Germany; 2Universitätsklinikum des Saarlandes, Homburg, Germany; 3University of Milan-Bicocca, Milan, Italy

Background: Renal denervation (RDN) has been shown to lower systolic blood pressure (SBP) in patients with uncontrolled hypertension. Less is known on its impact on quality of life. EuroQol 5 dimensions (EQ-5D) is a simple, self-administered survey that assesses health on five dimensions, including two attributes that may be related to hypertension: anxiety/depression and pain/discomfort.

Purpose: We evaluated changes in patients’ health status following RDN in the Global SYMPLICITY Registry as assessed by EQ-5D.

Methods: The Global SYMPLICITY Registry is a prospective, open-label, single-arm, all-comer worldwide registry that is evaluating the safety and effectiveness of treatment with the Symplicity RDN system. All patients are asked to complete the EQ-5D survey at baseline and at follow-up. Outcomes on 497 matched patients (baseline, 6- and 12-months) are currently available.

Results: Patients with baseline office SBP >160 mmHg reported improved anxiety/depression levels; the percent of patients reporting “no problems” with anxiety/depression improved from 66% at baseline to 75% at 12 months (p=0.003); these patients also had a 12-month change in office SBP of −24.2±24.4 mmHg (p=0.001) (Table). Patients with baseline SBP ≥160 mmHg and isolated hypertension (i.e., no other comorbidities) were also less likely to report “severe problems” in terms of pain/discomfort at 12 months (8% at baseline vs. 0% at 12 months, p=0.002).

Conclusion: Patients with office SBP >160 mmHg who underwent RDN in the Global SYMPLICITY Registry reported not only an improvement in SBP but also an improvement of anxiety/depression and pain/discomfort, as assessed by EQ-5D.

Acknowledgement/Funding: Medtronic, Inc. (ClinicalTrials.gov NC101534299)
We collected the 24-hour ambulatory BP, plasma aldosterone concentration, and plasma renin activity from all of the patients. The measured sleep-trough morning systolic blood pressure (SBP) increases were higher in the OSA group than in the non-OSA group (28.7±11.8 mmHg vs. 19.6±12.8 mmHg, P=0.008). The sleep-trough morning SBP increase was inversely correlated with the lowest O2 saturation (r=−0.272, P=0.039). OSA known to be associated with increased daytime and nocturnal sympathetic activity was associated with significantly higher sleep-trough morning SBP levels in this study.

Acknowledgement/Funding: The authors wish to acknowledge the financial support of the Catholic Medical Center Research Foundation.