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Prognostic value of excessive atrial ectopy in relation to atrial fibrillation and ischemic stroke in a large pooled scandinavian holter cohort
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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 excess 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. 15 subjects (11.4%) suffered a first ischemic 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=0.0001) 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 CHADS2-VASC score of ≥2 2.5% per year is comparable to the risk observed in atrial fibrillation patients with a CHADS2-VASC score ≥2.

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.

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Prognosis in patients with atrial fibrillation with a presumed temporary cause in a community based cohort study
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Atrial fibrillation (AF) may be related to an acute, temporary cause, including alcohol use (eg, “holiday heart syndrome”), myocardial ischemia or infarction, myocarditis or pericarditis, 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. It remains unclear whether the risk of ischemic stroke is different in this setting, and if antithrombotic 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 with no 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”, CHADS2-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 1.34, 95% CI 0.97–1.85, p=0.11). Adjusted HR 1.49 (95% CI 0.97–2.31, p=0.08) for CHADS2-VASC and OAC use.

The findings were similar in patients in the low, moderate- and high-risk groups for stroke according to CHADS2-VASC risk score. In patients with a “temporary cause” of AF, prescription of oral anticoagulation was independently associated with a better prognosis for death or ischemic stroke (HR=0.52 for OAC vs. non-OAC, 95% CI 0.38–0.71, p<0.0001 after adjustment for age and CHADS2-VASC score).

Conclusion: In a real life cohort study, AF patients with a presumed “temporary cause” had a similar risk of stroke/thromboembolic 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.

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Incidence of atrial fibrillation in different types of cancer: a Danish nationwide cohort study
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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 1.59 (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 3.34–3.76)). The other major types of cancer: colon cancer (IRR: 1.45 (95% CI 1.38–1.53)), urinary tract cancer (IRR: 1.41 (95% CI 1.33–1.51)), breast cancer (IRR: 1.23 (95% CI 1.18–1.29)) and prostate cancer (IRR: 1.22 (95% CI 1.18–1.12)). The remaining other types of cancer were also associated with an increased IRR (1.81 (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.

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Improving AF detection in patients with cryptogenic stroke. Insights from a prospective cohort with insertable cardiac monitor
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Background: Up to 30% of ischemic strokes are of undetermined etiology or cryptogenic. Studies promoting 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 24h-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 hyperten-


sion). 262 comprised the historical cohort, whereas 28 received an ICM. Patients in both groups did not differ regarding age, sex, CV risk factors, or stroke-related artery. During follow-up, AF was detected in 11.5% in the historical cohort and in 46.4% in the prospective cohort (p<0.001). Time to AF-detection was significantly shorter with ICM (16 (12.5–31) vs. 60 (30–180) days, p=0.001). Survival analysis showed that, among the ICM group, most AF episodes occurred within the first month after CS, whereas the rate of AF beyond 6 months was scarce (figure).

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.

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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 that many patients present silent atrial fibrillation (AF) detected as atrial high rate episodes (AHRE). AHRE >5 min have been linked to increased risk of clinical stroke, but a high proportion of ischemic brain lesions (IBL) could be subclinical and thromboembolic risk underestimated.

Purpose: CT-scan can detect silent IBL to determine the real risk these patients are exposed to.

Methods: We included patients with CIED and no history of AF or stroke. It was analyzed retrospectively the incidence of AHRE >5 min compatible AF and the presence of IBL on CT-scan.

Results: 110 patients (59% men, aged 74±9 years) were evaluated. Mean CHADS and CHADSVASc scores were 1.8±0.9 and 3.3±1.3 respectively. After a mean follow-up of 16±10 months, 33 patients (30%) showed at least one AHRE >5 min. Cranial CT-scan showed silent IBL in 19 patients (17.3%). The presence of silent IBL was significantly related to the presence of AHRE <5 min (Table). Multivariable analyses determined 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]).

Conclusions: AHRE were independently associated to a higher incidence of silent IBL on CT-scan. AHRE represent a kind of silent AF where management recommendations are lacking despite the fact that a higher embolic risk is present.

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Is TEE mandatory in patients undergoing ablation of AF with uninterrupted NOACs? Results from a prospective multicenter registry
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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 824 (85%) patients having non-paroxysmal AF and 636 (65.6%) patients were male. The average CHADS2 -VASc score was 3.0±1.3 and CHADS2 score was ≥2 in 609 (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.

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Successful approaches in reduction of fluoroscopy time and radiation dose during catheter ablation for atrial fibrillation
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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 served as control group (group 1). Two approaches were sequentially implemented 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 frequency) were implemented (group 2). From November 2014 the low dose manufacturer’s setting including the lowest fluoroscopic dose rate (23 nGy/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</th>
<th>Mean ± SD</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Group 1</td>
<td>50.0±5.3</td>
<td>7.5±4.1</td>
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<tr>
<td>Group 2</td>
<td>86.1±6.8</td>
<td>2.3±1.1</td>
</tr>
<tr>
<td>Group 3</td>
<td>252.0±27.4</td>
<td>50.0±5.1</td>
</tr>
</tbody>
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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 manufacturers’ low dose protocol. Application of all recommendation reduced the overall radiation dose for AF CA procedures to one third.

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Long-term comparison of the number of supraventricular ectopic complexes after either radiofrequency ablation or anti-arrhythmic drug therapy in patients with atrial fibrillation
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Introduction: The vast majority of supraventricular ectopic complexes (SVEC) that initiate atrial fibrillation (AF) originate in the pulmonary veins. Often, patients with frequent SVEC experience symptoms related to the ectopic activity. Pulmonary vein isolation has been shown to reduce recurrence of AF. The frequency of SVEC after radiofrequency ablation (RFA) has not, however, previously been described.

Methods: Patients with paroxysmal AF (N=217) enrolled in the MANTRA PAF trial were randomized to either AAD (lecainide/amiodarone) or RFA for AF. Prior to randomization and at 3, 6, 12, 18 and 24 months, patients underwent 7-day Holter electrocardiograms to assess frequency of SVEC. Patients randomized to RFA underwent an additional Holter at discharge after the ablation procedure. SVEC was reported as SVEC per hour in sinus rhythm. Non-parametric Wilcoxon Rank sum test was used to determine differences in median SVEC at 3 and 24 months.

Results: At baseline, the median number of SVEC was similar in the RFA and AAD group: 3.40 (1.17–11.20) and 3.17 (0.76–17.78), respectively (p=0.9) (fig-
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.

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A dual-phase cardiac CT protocol for complete delineation of left atrial appendage (LAA) anatomy and thrombus exclusion prior to AF ablation or LAA device exclusion

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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 morphology. The remaining three (25%, 2.3% of total cohort) were also seen on late pass imaging and confirmed as true thrombi on TOE. The sensitivity, specificity, PPV and NPV of CCT detection of true thrombus were 100%, 92.8%, 25.0% and 100% respectively for first-pass scans and 100% for all parameters for the delayed scans. The median additional radiation dose for the limited delayed scan was 0.4 (0.2–0.6) mSv.

Conclusion: The addition of a 60 second delayed scan increases the sensitivity and specificity for LAA thrombus identification and provides a better assessment of LAA morphology.

AGEING AND HEART DISEASE: IS 80 THE NEW 60?

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Multiple biomarkers for risk stratification of unselected older patients in the emergency department

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Background: Rapid diagnosis of acute heart failure (AHF) is an unmet challenge especially in older patients. The earlier AHF is diagnosed and treated, the better the prognosis. Although the guidelines recommend the use of natriuretic peptides, whether their use improves patient outcomes is still a matter of debate. Thus, we prospectively investigated the prognostic performance of different biomarkers in unselected older patients in the emergency department (ED).

Methods: We consecutively enrolled 302 non-surgical patients ≥70 years presenting to the ED with a wide range of cardiovascular and non-cardiovascular comorbid conditions. N-terminal pro-B-type natriuretic peptide (NT-proBNP), mid-regional pro-adenomedullin (MR-proADM), mid-regional pro-atrial natriuretic peptide (MR-proANP), C-terminal pro-endothelin-1 (CT-proET-1), ultra-sensitive C-terminal pro-vasopressin (Copeptin-us) and high-sensitivity Troponin T (hs-cTNT) were measured at admission. Two cardiologists independently adjudicated the final diagnosis of AHF by reviewing all available baseline and follow-up data including the biomarkers. A final diagnosis of AHF was found in 120 (40%) of the 302 patients. All patients were followed up for cardiovascular death within the following 12 months. In order to test the prognostic performance of the investigated biomarkers we used three different types of boosting models. Boosting is a statistically learning technique with built-in variable selection developed to obtain sparse and interpretable predictive models.

Results: Follow-up was 100% complete. During a median follow-up time of 225 days (IQR 156–319 days), 30 (9.9%) of 302 patients (age 81±6 years) died due to cardiovascular deaths. Of these 30 patients, 21 had AHF and 9 had done AHF diagnosed prior to admission. All boosting models selected MR-proADM and hs-cTNT as predictors of cardiovascular deaths. The median values of MR-proADM and hs-cTNT at presentation were significantly higher in patients with cardiovascular deaths compared to surviving patients during follow-up [2.56 nmol/L (IQR 1.62–4.48) vs. 1.11 nmol/L (IQR 0.83–1.80), P<0.001 and 81 ng/L (IQR 38–340) vs. 17 ng/L (IQR 0.9–38), P=0.004]. One unit increase in the log-transformed MR-proADM levels was associated with a 1.99-fold risk of death (95% CI 1.61 to 2.45, P<0.001), whereas the second biomarker levels was not significantly correlated to event-free survival (hazard ratio 3.22, 95% CI 0.97 to 10.68, P=0.056).

Conclusion: Within different biomarkers, MR-proADM was the predictor of cardiovascular deaths in unselected older patients presenting to the ED.

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Mechanisms of improvement in claudication after exercise training in peripheral arterial disease

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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-driven post-exercise recovery of muscle oxygen consumption fit to a mono-exponential curve yields both a time constant (Tc) and baseline symptom-free walking time. We prospectively investigated the prognostic performance of different biomarkers in unselected older patients in the emergency department (ED).

Methods: To test the hypothesis that improvements in muscle oxygen use (training response) rather than vascular oxygen delivery (mitochondrial 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 versus 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 71.2±19.1 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 completion of 36 training sessions, NIRS-trained subjects demonstrated similar improvements in symptom-free walking time (mean 7.3±3.3 vs 6.5±3.5 min at 12 week follow up, p=0.01 for change from baseline and p=NS between cohorts) as the traditional pain-guided cohort. In both NIRS-guided and pain-guided cohorts, measure 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) increased in both NIRS-trained and pain-guided cohorts, with a greater increase in the NIRS-guided cohort (p=0.01 compared to baseline). T1/2 max was significantly higher in the PAD cohort compared with aged-matched controls without PAD (n=15; 94.0±45.2 vs. 17.9±8.3 sec, p=NS) 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 versus calf-hypoxia measured by NIRS impacted training outcomes.

Conclusions: 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 71.2±19.1 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 completion of 36 training sessions, NIRS-trained subjects demonstrated similar improvements in symptom-free walking time (mean 7.3±3.3 vs 6.5±3.5 min at 12 week follow up, p=0.01 for change from baseline and p=NS between cohorts) as the traditional pain-guided cohort. In both NIRS-guided and pain-guided cohorts, measure 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) increased in both NIRS-trained and pain-guided cohorts, with a greater increase in the NIRS-guided cohort (p=0.01 compared to baseline). T1/2 max was significantly higher in the PAD cohort compared with aged-matched controls without PAD (n=15; 94.0±45.2 vs. 17.9±8.3 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.

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Clinical impact of complete revascularization in elderly patients with multivessel coronary artery disease underwent percutaneous coronary intervention
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symptomatic aortic stenosis in octogenarians
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 the 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-comer 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, HR=0.42; 95% CI, 0.21–0.83; P=0.012, respectively). In propensity score matching with age, sex, and LVEF, MACE rate was significantly lower in the CR group than in the ICR group (8.6% vs. 18.1%, P=0.011).

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

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Comorbidity and intervention in octogenarians with severe symptomatic aortic stenosis
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Background: The benefit from intervention in elderly patients with symptomatic severe aortic stenosis (AS) and high comorbidity is unknown. Our aims were to establish the correlation between the Charlson comorbidity index and the prognosis of octogenarians with symptomatic severe AS and to identify patients who might not benefit from intervention.

Purpose: We used the data from PEGASO (Prognosis of symptomatic severe aortic stenosis in octogenarians), a prospective registry that included consecutively 928 patients aged ≥80 years with severe symptomatic AS.

Results: The mean Charlson comorbidity index was 3.0±1.7. A total of 151 patients (16.3%) presented high comorbidity (index ≥5). Median survival was lower for patients with high comorbidity than for those without (16.7±1.2 vs. 26.5±6 months, p<0.001). In patients without high comorbidity planned interventional management was clearly associated with prognosis (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 planned medical management and Charlson index. Patients with high comorbidity presented non-cardiac death more frequently than those who had not (28.6% vs. 19.5%, p=0.008).

Conclusions: One sixth of octogenarians with symptomatic severe AS have very high comorbidity (Charlson index ≥5). These patients have a poor prognosis in the short term and do not seem to benefit from interventional treatment.
years (SD 2.0 years), 944 subjects had suffered a first CHD or stroke events, re-
spectively 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: 1.15–1.48) within a vascular event was related to a three-fold in-
creased 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.

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965 | BEDSIDE Temporal trends in the treatment and outcomes of septua-, octo-, and nonagenarians with acute coronary syndrome

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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 Myo-cardial 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 deter-
mine associations between use of percutaneous coronary interventions (PCI) and in-hospital mortality, logistic regression providing odds ratios (ORs) and 95% con-
fidence intervals (CIs) was 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 was also 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 de-
crease 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 0.22–0.40, in 2001–2004; and, adjusted OR for PCI use vs. no 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 improved outcomes in similar ORs between first and last 4-year period. This study suggests that better guideline adherence im-
proves in-hospital outcomes of older ACS patients.

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

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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 ratio is due to a varying contribution to the pathways of major risk factors.

Purpose: While there have been studies investigating the possible different role of cardiovascular risk factors in men and women, there have not yet been, to our knowledge, any attempts to explore how much of the sex/gender effect is medi-
ated through risk factors. Presumably, since no appropriate statistical modelling approach for survival data was available. Recently, a new approach for media-
tion analysis was developed that allows to assess the specific contribution of risk factors explaining the difference between men and women regarding CHD out-
comes.

Methods: The sex-specific CHD mortality was examined in prospective cohort data from Austria, consisting of 117,264 individuals younger than 50 years (as a proxy for menopausal status) and 54,998 older ones, with 3,892 deaths from CHD during a median follow-up of 14.6 years. Mediation analysis was used to decompose the sex/gender effect into a direct and an indirect component that is mediated by the four major cardiovascular risk factors: systolic blood pressure, total cholesterol, fasting blood glucose, and smoking status.

Results: The total effect of sex/gender on CHD mortality decreased with age. While the age-adjusted hazard ratio (men versus women) was 4.7 (95% CI: 3.5 to 6.1) in individuals younger than 50 years, it was only 1.9 (95% CI: 1.7 to 2.1) in the ≥50 years age group.

In the ≥50 years age group, the four major cardiovascular risk factors were able to explain 40.9% of this difference. The strongest factor was systolic blood pressure explaining 21.7% of the total sex/gender effect. In the ≥50 years age group, the contribution of the risk factors was small amount-
ing to only 2.6%. Single risk factors contributed less than 5%, with total cholesterol even showing a significant “negative” effect, i.e. mediation in favour of men.

Conclusions: The extent to which risk factors contribute to the gap between men and women regarding CHD mortality decreases strongly with age. Over the ages of 50 years, the persisting survival advantage of women can be explained only in small part through the pathways of major risk factors.

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

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Purpose: Vascular aging, as assessed by structural and functional properties of the arteries, is an independent indicator of cardiovascular risk. Smoking has a detrimental effect on arterial properties. We sought to investigate the effect of quitting smoking 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 investi-
gated 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 years, >5 years-15 years and >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 dif-
fences 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 0.23m/year (95% CI: 0.10 to 0.35), non-smokers 0.17m/year (95% CI: 0.08 to 0.25), quitters (>5 years) had 0.28m/year (95% CI: 0.07 to 0.49), quitters (>5–15 years) had 0.35m/year (95% CI: 0.11 to 0.59) and quitters (>15 years) -0.07m/year (95% CI: 0.26 to 0.13).

Conclusions: Quitting smoke seems to slow down progression of vascular ag-
ing after 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

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Introduction: The elderly population with left ventricle 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 im-
portance of the optimization of the medical treatment with BB in elderly population with LVSD.

Methods: We included all patients (pts) ≥75 years old, with LVEF <35%, studied in our center between January 2008 and April 2012. Clinical variables of inter-
est 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 have enough variables to determine the target dose of BB (BB%) compared to the target level established in clinical guidelines (50 mg/d for carvedilol and 10 mg/d for bisoprolo). 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 confounding and interaction with relevant clinical vari-
ables. In addition, to show the survival curves, the variable %BB was categorized into 3 groups (not BB, doses <50% and >50%).

Results: 558 pts were included. The mean age was 81.9 years, mean LVEF was 30.6% (range 5-100%). 254 of women (25.7%) did not take BB, 298 (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. Af-
ter 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 0.78–0.90). The final model included variables BB2*, 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 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**

1. **Methods:** Myoblast H9c2 cells and neonatal rat ventricular myocyte (NRVM) undergone 16 or 6 hours 0.2% O2 hypoxia, respectively, followed by 2 hours reoxygenation (H-R). The mTORC1 inhibitor, Rapamycin (200nM), was administered to further enhance autophagy. Both cells were transfected with miRNA-221 mimics (miR-221-3p and scrambled mimic control (miR-122-5p and MC). Cell count and viability, WST assay, cell injury induced LDH release, and GFP-LC3 labeled autophagyosomes were measured. Finally, both H9c2 and NRVM were collected for RT-qPCR and WB analyses. Predicted miR-221 targeting of DTT4 was assessed by Luciferase-reporter assay.

2. **Results:** miRNA-221 significantly reduced I/R injury as indicated by higher cell count and viability and WST activity, and reduced LDH (miR-221 vs. MC p<0.05). qPCR confirmed that (1) miR-221 expression was reduced in H-R; (2) RISC-loading miR-221 targets Bnip3. These results are consistent with the hypothesis that miRNA-221 directly targets DTT4 thus inhibiting I/R-induced autophagy.

3. **Conclusion:** miR-221 directly targets DTT4 and activates the mTORC1/p-4EBP4 pathway reducing autophagy. miRNA-221 is a promising therapeutic target in the treatment of I/R injury.

#### 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**

1. **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 accounted for cardiotropic and anti-apoptotic properties of these cells both in vitro and in vivo. This study aimed to compare CPC-Exo and MSC-Exo in terms of cardioprotective effects and functional improvement after MI. The role of microRNA (miRNA) and ischemic preconditioning (IPC) were assessed.

2. **Methods:** CPC 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 proangiogenic 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 PCR. Exo-CPC and Exo-MSC were injected intramyocardially in 8 rats after each permanent ligation of the left anterior descending coronary artery. Left ventricular ejection fraction (LVEF) was measured by echocardiography 1 and 4 weeks after MI.

3. **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 (2124% Exo-CPC; 2854% Exo-MSC; 4055% Exo-F), IPC of Exo-producing cells further reduced numbers of apoptotic CM (171% Exo-CPC; 233% Exo-MSC). Exo-CPC, but not Exo-F, were proangiogenic in HUVEC (87.0±9.9% vs 61.1±11.9; p<0.05) and 4 weeks after MI (75.4±8.9% vs 58.7±18.4%; p<0.05).

4. **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 induces proangiogenic effect. Clinical trials are ongoing using Exo-CPC to improving cardiac function after MI in vivo. As a cell-free approach, Exo could streamline clinical translation of regenerative heart therapy.

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**Ageing and heart disease: is 80 the new 60? Novel strategies for cardioprotection**

**1082 | BENCH**

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

1. **Purpose:** To investigate the role of Bnip3 and DDIT4 in the early phase of reperfusion.

2. **Methods:** Cardiac tissue was collected from rats at different time points after ischemia followed by reperfusion. The expression of Bnip3 and DDIT4 was measured by qPCR and Western blot analysis. The activity of LC3-II and p62 was determined by Western blot analysis. The nuclear translocation of Bnip3 was examined by immunofluorescence microscopy.

3. **Results:** Bnip3 expression increased significantly at 10 min reperfusion and remained high until 24 h reperfusion. DDIT4 expression increased significantly at 10 min reperfusion and gradually decreased up to 24 h reperfusion. The nuclear translocation of Bnip3 was observed at 10 min reperfusion and decreased to the basal level after 24 h reperfusion.

4. **Conclusion:** Bnip3 plays a crucial role in the early phase of reperfusion injury. The risk of apoptosis is significantly increased at 10 min reperfusion and the nuclear translocation of Bnip3 is associated with this increase.

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and then reperfusion. We initiated LVAD at 60 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 340±560 vs. t-LVAD 187±177 pg/ml, p<0.05).

Infarct size and LV function after MI

**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-infarct survival in a murine model of myocardial infarction**

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**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, LysMMDTR transgenic mice that had been depleted of LysM+ cells for 3d prior MI by low-dose diphtheria toxin injection, revealed a 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 monocular 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. Sequential repression of cardiac mRNA of MCP-1 and CCR2 ad 1d post MI as well as fractalkine and CX3CR1 at d7 post MI was paralleled by reduced influx of Ly6Chigh and Ly6Clow monocytes in anti-Gr-1 treated mice. Similarly, depletion of Ly6C+ monocytes 1d post MI was worse compared to controls. LAD ligated INF-g−/− mice revealed a drastically decreased survival and a reduced LVEF.

**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 chemoattraction. We conclude that strategies to combat the inflammatory injury in MI must consider a potentially beneficial effect of early neutrophil influx into infarcted myocardium.

1087 | BENCH

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

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**Background:** Matrix metalloproteinases (MMP) are integral to myocardial remodelling 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:** C57Bl/6 mouse hearts were Langendorff perfused and subjected to conscious 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 (200μmol/l) and ischaemic postconditioning (6 cycles 10sec reperfuison, 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, intraocular visualisation by transmission electron-microscopy (TEM), and quantification of DNA base-excision repair enzyme, OGG1, by Western blot analysis.

**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 syndrome.

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1088 | BENCH

Different pathways and additive effects of exenatide, glucose-insulin-potassium, and remote ischemic conditioning on myocardial infarct size in pigs


**Background:** Remote ischemic conditioning (RIC) has been shown to reduce myocardial infarct size in patients.
Purpose: To investigate whether the combination of RIC with either exendinatide or glucose-insulin-potassium (GIK) is more effective than RIC alone.

Methods: Farm pigs underwent coronary occlusion (40 min) and reperfusion, and received A) no treatment, B) one of the following treatments: RIC (5 min ischemia/5 min reperfusion x 4), GIK, or exendinatide (both at doses reducing infarct size in clinical trials), or C) two treatments (RIC+GIK or RIC+exendinatide).

Results: A first set of experiments (n=4/group), with 5 min of reperfusion showed significant phosphorylation of Akt and eNOS in control and reperfused myocardium only in animals receiving GIK, and mitochondria from these hearts showed enhanced reperfusion-related respiration. Hypoxia-based metabolomics disclosed a shift towards increased glycolysis in GIK and exendinatide groups. In contrast, oxidative stress (myocardial nitrotyrosine levels) and eNOS uncoupling were significantly reduced only by RIC. In a second series of experiments with 2 hours of reperfusion (n=7–10/group), ANOVA demonstrated a significant effect of the number of treatments on infarct size (triptychileterazolium, % of the area at risk) (59.21±3.34, 36.64±3.03 and 21.04±2.38% for none, one and two treatments respectively), and significant differences between 1 and 2 treatments (p=0.004) but not among individual treatments or between RIC+GIK and RIC+exendinatide.

Conclusions: GIK and exendinatide activate cardioprotective pathways different from those of RIC, and have additive effects with RIC on infarct size reduction in pigs.
Complications in devices

agulation (NOAC) agents are increasingly replacing phenprocoumon as oral anticoagulant. However, data regarding the management of NOACs in the context of pacemaker or ICD implantation are missing. The purpose of this study was to sur- vey clinical practice with regard to the use of phenprocoumon and NOACs in re- lation to device implantation in Austria, Germany and German-speaking Switzer- land.

Methods and results: We conducted a web-based survey across centres in Aus- tria, Germany and German-speaking Switzerland using the tool SurveyMonkey.

The questionnaire included 17 questions and was sent to 202 Austrian centres, 105 German centres and 145 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 63.16% (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 15.8% of the centres 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 NOAC discontinuation is variable among countries and in individual patients with heparin, administration 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.

P1094 | BEDSIDE

Transvenous coronary sinus and implantable cardioverter defibrillator lead extraction: different difficulties and complications

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Background: The coils of implantable cardiac defibrillating (ICD) leads and the position of coronary sinus (CS) pacing leads in very distal branches or their active fixation may increase the difficulties for extraction procedure.

Purpose: Compare the procedural complexity of extracting implantable cardiac defibrillating vs coronary sinus pacing leads.

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 ± 12.3) had an implantable 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, 9265 leads were removed from 121 patients (mean age 72.1 ± 8.8 years) and 141 ICD leads from 137 patients (mean age, years 68 ± 13.4); device infec- tion was the main indication to extraction (82.5% of cases); the mean implant time was 49.6 ± 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- ufactural 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 proce- dures: 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 CS ICD leads were successfully removed (pede- dinal 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.

P1095 | BEDSIDE

Predictors of late complications in patients with ICD indicated for the complete system extraction

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Background: The risk factors of patients with ICD and multiple leads and clear diagnosis of bacterial endocarditis are not yet clearly known.

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 excimer 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±27 months (range 6–180 months; the oldest 211 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 72±237 minutes. In 292 patients we used the combination of an excimer 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).

Conclusions: 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. Implanta- tion by electrophysiologist with experience <50 procedures (HR 1.45). 4. LMWH for 10 days. 5. Low volume centre (HR 1.33) 6 Dual coil ICD lead (HR 1.39) 7. Median 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).

Introduction: Because of the increasing change 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 anaesthesia 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: Out of 428 pts undergoing lead extraction during the study period, 108 were OCT (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% 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 comorbidities. Among the patients with bacterial endocarditis undergoing the ex- traction of ICD system the presence of multiple risk factors was strongly associ- ated with late complications of ICD therapy. Careful control of the patient before the procedure and reevaluation of ICD indication for high-risk patients (renal insufficiency, diabetes mellitus with complications, etc.) may lead to the reduction in the number of late complications.
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

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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, 1h-algorithm+LOD 0h–1h; hs-cTn Abbott: 1h-algorithm 0h–2h, 1h-algorithm+LOD 0h–2h) to ensure that findings are independent from the hs-cTnT 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 (p<0.001). Using hs-cTnT, the safety was very high and comparable with both algorithms (LOD: NPV 99.9%, 95% CI 99.7–100% versus LOD+1h-algorithm: NPV 99.9%, 95% CI 99.5–100%, p=ns). The 1h-algorithm required retesting of hs-cTn after 1h in all patients, the 1h-algorithm+LOD allows the safe rule-out of AMI in about every fifth patient already at presentation.

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

Direct comparison of the safety and efficacy of two rule-out strategies for AMI: undetectable levels at presentation vs. 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 strategy. 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-cTnT assays (hs-cTnT Roche: LOD <5ng/L; 1h-algorithm 0h–2h, 1h-algorithm+LOD 0h–2h; hs-cTn Abbott: 1h-algorithm 0h–5ng/L and 1h-algorithm+LOD 0h–2h) to ensure that findings are independent from the hs-cTnT assay used. As both strategies should only be applied once ST-elevation MI (STEMI) has been excluded by 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 99.9%, 95% CI 99.7–100% versus LOD+1h-algorithm: NPV 99.9%, 95% CI 99.5–100%, p=ns). 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 98.8–100% versus LOD+1h-algorithm: NPV 99.9% (95% CI 98.4–99.9%, p=ns). 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-cTnT assays (hs-cTnT Roche: LOD <5ng/L; 1h-algorithm 0h–2h, 1h-algorithm+LOD 0h–2h; hs-cTn Abbott: 1h-algorithm 0h–5ng/L and 1h-algorithm+LOD 0h–2h) to ensure that findings are independent from the hs-cTnT assay used. 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.

Conclusion: Both investigated rule-out strategies allow a safe rule-out of AMI, irrespective of the underlying hs-cTnT 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.
algorithms (LOD; NPV 100%, 95% CI 98.7–100% versus copeptin and hs-cTnI: 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-cTn assay, the combination of hs-cTnI 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

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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 (NSTE-ACS).

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). Adjusted 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 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=0.26 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

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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 Infarction 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 the 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

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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 UV backscatter: 7.2±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: We 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 after percutaneous edge-to-edge mitral valve therapy.

P1105 | BEDSIDE
Is transnasal TEE imaging a viable alternative to conventional TEE during structural cardiac interventions? A comparison of image quality
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Aim: The role of transoesophageal Echocardiography in cardiacinterventional structural procedures is well established and appreciated. However, the need for general anaesthesia (GA) throughout the procedure remains a controversial issue. The aim of the present study is to assess the feasibility and imaging quality of using a transnasal microprobe that allows the usage of conscious sedation in patients who undergo cardiac structural interventional procedures without missing the benefits, guidance and navigation of conventional trans-procedural TEE.

Methods: We analyzed the trans procedural images of 24 consecutive patients, that underwent TAVI, TMVI or ASD/PSV closure, using a trans nasal 2D microprobe and then we compared them with images taken using a conventional 3D TEE probe. In particular, we compared the imaging quality of the two probes regarding the imaging quality of:
1. The anatomy, visualization of valvular calcification and Colour Doppler of the aortic and mitral valve 2. The PFO, ASD 3 left ventricle systolic function and peri-cardial space. 4. Transgastric imaging 5. The 3D imaging.

Grades: 5: Excellent-quality—Absolutely similar to conventional 3D TOE probe.
4: Very good—Almost similar to conventional 3D TOE probe.
3: Good— Inferior to conventional 3D TOE probe, but sufficient and safe imaging quality.
2: Medium-quality— Only gross pathology can be seen.
1: Poor-quality—Unacceptable imaging.

Results: The results were the following, presented as the average grade: see Table 1.

Although the clarity of structure calculation with transnasal/TEE was inferior to conventional TEE, the anatomy of relevant intracardiac structures was seen with almost similar quality. It is surprising though, that the advanced 3D imaging was of high level quality despite the small sized probe However, highly advanced operator skills are required.

Conclusions: These results suggest that trans-nasal TEE can provides good anatomical image quality of relevant cardiac structures and this may facilitate operator skills are required.

P1107 | BEDSIDE
Echocardiographic predictors of new-onset atrial fibrillation in patients after transcatheter aortic valve implantation
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Background: Transcatheter aortic valve implantation (TAVI) is an increasingly common procedure. The development of post-surgical atrial fibrillation (AF) is associated with increased hospital morbidity and mortality, and its occurrence is not clearly studied after TAVI.

Purpose: The aim of this study is to determine echocardiographic parameters predictors of atrial fibrillation after TAVI.

Methods: We analyzed 104 patients who had sinus rhythm prior to TAVI. Pre-TAVI echocardiography data and clinical features were obtained from the clinical file of each patient. Patients with atrial fibrillation or incomplete data were excluded. An univariate and bivariate analysis were performed to determine the relation between echocardiographic parameters and development of AF after TAVI.

Results: 104 patients were studied: mean age 82±5±6 years, 63.5% were women. 18 patients (17.3%) presented AF. In the univariate analysis, the left atrial (LA) diameter, LA area 4 chambers (C), LA area 2C, LA index volume and left ventricular ejection fraction (LVEF) were predictors of the development of AF after TAVI (See Table). In the bivariate analysis area AI 4C and LVEF were included, and LA area 4C was found as an independent predictor of the development of AF (beta coefficient: 0.29; CI: 1.15 -1.53, p < 0.001).

Conclusions: The size of the LA, the specially the area obtained in four chambers view is a good independent predictor of the development of AF after TAVI.
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
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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 perioperative leaks following the implantation. Our aim was to analyse the incidence of postprocedural AR after a successful CoreValve 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 Logistic 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 at 12 month, and annually thereafter. Postprocedural AR was graded by means of the hole diameter of 33±36 mm. Prosthetic echocardiography was performed during the in-hospital follow up there was a significant reduction in the number of patients with AR (P<0.001, IC 0.7333 to 0.89), the correlation between the degree of AR and echocardiographic follow up was 0.9317). The correlation between the degree of AR and echocardiographic follow up was 3±1.3 years, and echocardiographic follow up was 3.5±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 each 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 of 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 prosthesis.

P1111 | BENCH
A new method to measure aortic valve calcium by transthoracic echocardiography
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Purpose: Calcific aortic valve disease is the most frequent valve disease and highly inaccurate. Our goal is to obtain a new valid and accessible method for the adaptation and self-expandability of the nitinol prosthesis.

Methods: We investigated the temporal changes in MiVEC gene expression during pressure overload and transition to heart failure.

Results: Transcriptional profiling at 2 weeks after TAC revealed 23% lower expression levels of CD36 and Meox2 (ns) and upregulation of Col1a1 and Col15a1 (4.7- and 2.8-fold, P<0.05) compared to sham. After 10 weeks, Adami2-1, Clip and Thbs4 were greater than 4-fold increased (P<0.05), as well as ESM-1 (1.6-fold, ns) and NPPA (3-fold, P<0.05).

Conclusion: In the early stage of cardiac aortic hypertension after pressure overload, downregulation of fatty acid uptake (CD36, Meox2) and upregulation of collagens suggests impaired MIVEC-mediated energy supply to adjacent cardiac myocytes and contribution to interstitial fibrosis. However, MIVEC may counteract this early pathological response by delayed inhibition of TGF-β-induced fibrosis (Adami2-1, Col1a1, Col15a1, NPPA). MIVEC may support angiogenesis (ESM-1) and fluid homeostasis (NPPA) in later stages of pressure overload as a protective mechanism to counter transition to heart failure.

P1112 | BENCH
Critical role of PTP1B in endoplasmic reticulum stress-induced endothelial dysfunction
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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 inactive the PERK branch of the unfolded protein response by activating the IRE1α branch of ERS. Moreover, recent studies suggested that PTP1B 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 PTP1B knockout mice (PTP1B<–<) and 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-precontracted, 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±1.09 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: 22.4±0.3, p<0.01 vs. WT; TN in vitro: 23.2±2.5, p<0.01 vs. 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 PTP1B 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.
P1114 | BENCH
SIRT3 deficiency induces endothelial insulin resistance and vascular dysfunction in obese mice and human subjects
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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 morbid obese human subjects undergoing bariatric surgery and non-obese controls. Male SIRT3 knockout mice and wide 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 vasorelaxation (82.46±8.5% vs. 54.93±6.46%, 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 excess treatment 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 release. Additionally, obese mice induced by 24-week HFD displayed an impaired endothelium-dependent vasorelaxation to both insulin (40.68±3.68% vs. 64.98±2.85%, n=8, P=0.001) and acetylcholine (48.45±4.93% vs. 100.59±2.35%, n=4, 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±2.98%, n=6, P=0.01 for response to insulin; 79.59±4.93% vs. 57.25±8.81%, n=4, P=0.01 for response to acetylcholine). Elimination of mtROS with MitoTEMPO not only restored insulin-stimulated NO production in SIRT3 knockdown 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.

P1115 | BENCH
Dual Antithrombotic Effects of Ticagrelor in Arterial Thrombosis: An Antplatelet Agent With Anticoagulant Properties
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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, 10−5M) 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 potential 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) supplemented in chow. After 2 weeks, arterial thrombosis of the common carotid artery was examined following laser injury.

Results: Ticagrelor, but not clopidogrel, reduced TNF-α-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 dipridamole 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)-induced platelet aggregation; however, ticagrelor significantly prolonged time to arterial occlusion as compared with clopidogrel (94.13±6.75 min vs 72.14±5.5 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
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Background: Smoking is associated with vascular dysfunction and fibrinolytic impairment. 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 a 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 (pre), 20 minutes after (Sm20) 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 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±2.72% day 0 to 9.15±1.21% day 7 to 9.49±1.74% day 14, P=0.02) and PWV (from 6.13±0.61 m/sec day 0 to 5.86±0.63 m/sec day 7 to 5.63±0.56 m/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 pro-coagulated 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 PAI-1 levels in day 14 (p=0.001) and in day 1 (p=0.01) vs placebo. PAI-1 levels in day 14 (p=0.02). Moreover CGJ significantly ameliorated the acute smoking

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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 improvement of laboratory indices of inflammation and coagulation. 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, investigation 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 characterised the structural damage and functional impairment of the radial artery in patients undergoing transradial cardiac catheterisation as well as the EPC profile associated with healing.

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

Results: Radial injury was observed in 4 patients (19%). Despite the low incidence of injury, FMD was attenuated in the catheterised vs non-catheterised arm (4.31±3.44 vs 10.74±5.56 p < 0.001) but not at 4 and 12 weeks. Arterial sheaths yielded significant numbers of cells (mean 6.3x10^2±4.6x10^1) 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 vasomotor dysfunction, and mobilization of naïve progenitor cells. The radial artery thus offers a unique model with which to examine arterial injury and therapies targeting cellular repair in vivo.

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 defibrillators. A new 5-year risk score was proposed in the ESC guidelines, with a class IIa indication for ICD implantation if score ≥ 2 C-SCDRF. Follow-up 29 months. Number of C-SCDRF (p < 0.001) was associated with significant mobilisation of CD34+ cells (0.05% ± 0.02 vs 0.09% ± 0.06 of mononuclear cells p < 0.05).

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

Results: Radial injury was observed in 4 patients (19%). Despite the low incidence of injury, FMD was attenuated in the catheterised vs non-catheterised arm (4.31±3.44 vs 10.74±5.56 p < 0.001) but not at 4 and 12 weeks. Arterial sheaths yielded significant numbers of cells (mean 6.3x10^2±4.6x10^1) 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 vasomotor dysfunction, and mobilization of naïve progenitor cells. The radial artery thus offers a unique model with which to examine arterial injury and therapies targeting cellular repair in vivo.

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 noncardiac surgery with a matched group of non-HCM patients.

Methods: In a cohort study, consecutive HCM patients (n = 92) undergoing intermediate and high-risk noncardiac surgery between 1/07 and 12/2013 were included (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 baseline characteristics, as shown in Figure 1. 58% HCM patients had provokable left ventricular outflow obstruction (>30 mm Hg) and 62% had systolic anterior motion of mitral valve. At 30 days post-operatively, a significantly higher proportion of HCM patients were in the composite endpoint vs non-HCM patients (10% vs. 3%, p < 0.03). Similarly, 4% HCM patients had AF, while none occurred in non-HCM patients (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 intermediate and high-risk noncardiac surgery have significantly worse outcomes compared to a matched group of patients undergoing similar noncardiac surgery.

P1120 | BEDSIDE
Prognosis in dutch mybpc3 founder mutation carriers is defined by phenotype
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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 61 (22%) c.2864_2865delCT); 144 index patients (age 45±14 years) and 130 relatives (age 44±15 years). Index patients...
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.
Method: 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%). During follow-up, 43 patients (15.1%) were treated with tafamidis and explained by non-transplanted liver transplantation. It was possible to perfectly match in 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 8.75–51.25) and 24 (IQR 12–34), respectively. Non-transplanted patients had more often end-stage disease (49% vs. 5%, 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
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Background: Restrictive cardiomyopathy (RCM) is the least common type of cardiomyopathy. The genetic basis of the condition is largely unknown as genetic mutations have not been described yet in a limited number of cases.

Methods: A total of 28 unrelated patients with end-stage idiopathic RCM (41±14 years, 44% males) underwent NGS genetic evaluation with a panel of 309 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 (2), LMNA (2), FLNC (2), TNNI3 (1), 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 of 25 families identified 18 affected individuals and 6 mutation carriers without clinical phenotype. Familial 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
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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 (LVOTr) 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 (P=0.48, P=0.001) and resting LVOTr peak gradient when MR was eliminated from the analysis. Concerning progesis, 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), overall survival (P=0.001) and after 6 and 12 weeks of intervention. A follow-up of 4 weeks without treatment was also carried out after the intervention.

**Conclusion:** In patients with HCM, the main determinants of rest PH are sinus rhythm, LVOTr maximal gradient and left atrium volume. Determinants of exercise PH are rest PASP, grade of MR and rest LVOTr 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**

**P1125 | BEDSIDE**

Intensive intervention by specialised nurses after an acute coronary event improves lipid levels and reduces readmissions: a randomized controlled trial

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**Introduction:** Patients recently hospitalized for an acute coronary syndrome (ACS) are at 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. Aims and methods: We designed a prospective, randomized, 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. Without differences in baseline characteristics between both groups. 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, in patients using statins the reduction in cLDL was high in both groups and without significant differences (100% GI vs 95% GC). 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±0 vs 1.3±4.5, p=0.007). We see a significant decrease in cLDL levels in the IG (87±16 vs 88±33 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).

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

**P1126 | 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

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**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 were selected for their ability to hydrolyze cholesteryl esters and may have a potential mechanism to lower cholesterol levels in plasma. Furthermore, their genomes were sequenced and their safety established in in vitro and animal studies.

**Purpose:** The aim was to assess the capacity of a balanced combination of the three Lactobacillus plantarum strains (1:1:1) to lower LDL-C in adults with increased risk of coronary heart disease. Secondary outcomes included the evaluation of other cholesterol, lipid, and safety parameters.

**Methods:** Sixty adult volunteers of both sexes (18–65 y; 19–30 kg/m²; 3.3–4.9 mmol/L of total cholesterol (TC); 5.2–7.8 mmol/L of total cholesterol (TC)) 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 6 and 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 0.7% (0.25 and 0.5 mmol/L of LDL-C) 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 −0.87 mmol/L, P<0.001). Consequently, the strain combination reduced 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<0.001).

**Conclusions:** Three specific strains of L. plantarum reduce 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.
cells for CVE presentation (CVE = myocardial infarction, stroke or cardiovascular death).

Methods: Fifty subjects from the arm of the PREDIMED 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 high 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), leucocytes (CD45), monocytes (CD14), lymphocytes (CD3), erythropoietic cells (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 phenotype in no-CVE patients, while in CVE patients the diet did not influence MP shedding except for CD235ab/CD34 MP's, which increased after one year. A ROC-curve analysis, to identify the threshold level of cMPs capable of predicting a future CVE, showed that after one year of intervention, CD235ab/CD34 MP's at a cut-off point of 131.1 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/CD34 cMP's at a cut-off point of 102.6 MP/μl (P<0.045), with a 56% sensitivity and 70% specificity [AUC=0.662 (0.512, 0.825)]. When both type of MP's 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 intervention study-PREDIMED, cMPs derived from activated platelets and erythropoietic 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

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Objectives: Some clinical studies have demonstrated that a low-density lipoprotein cholesterol/ high-density lipoprotein cholesterol (LDL-C/HDL-C) ratio was an excellent predictor of cardiovascular diseases. The aim of this study was to determine whether the LDL-C/HDL-C 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/HDL-C ratio of less than 1.5, between 1.5 and 2, and more than 2. Among the groups, the incidence of major adverse cardiac events (MACE) during the pt-years of follow-up. This systematic detailed approach to evaluate cancer allows for the inclusion of all cancers (including the 3 cancers (skin, prostate, stomach) that accounted for the incidence of SEAS. Deaths due to malignancy were similar (280 vs 272, p=0.71).

Conclusion: The LDL-C/HDL-C 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

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Background: The SEAS study in 1873 pts with aortic stenosis reported more cancer in patients 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 average 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 incidence of SEAS. Deaths due to malignancy were similar (280 vs 272, p=0.71).

Conclusion: 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.
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 primary patency rate at 12 months. Cut off point of FFR for primary patency at 12-months was 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 (83.3% vs. 66.7%, P=0.035).

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

P1134 | BEDSIDE

TP trunk patency reduce TLR rate in patients treated EVT for femoro-popliteal lesions

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Background: TP (TibialPeroneal)-Trunk patency is important for the clinical outcomes of endovascular therapy for femoropopliteal lesions. We sought to evaluate clinical impact of comparison TP-Trunk patency in patients treated percutaneous angioplasty (PTA) in a Japanese observational database.

Methods: From Jan 2010-Mar 2013 total 675 consecutive procedures who successfully underwent femoropopliteal artery endovascular therapy were enrolled with two years of follow-up. We divided into two groups that TP-trunk is no stenosis (N=465) or not (N=210). After a mean follow-up of 515±377 days, outcome measures (PTA, PTO, primary patency, reocclusion, target lesion revascularization, target vessel revascularization) were recorded and compared.

Results: Kaplan-Meier analysis revealed that the clinical driven TLR and primary patency (PTSR) rate were significantly higher (logrank, p<0.01) 1 year in patients with TP-Trunk patency than in patients without TP-Trunk stenosis. Multi-variant analysis revealed that TP-Trunk patency were independently associated with clinical driven TLR rate (Hazard ratio (HR): 0.53, 95% confidence interval (CI): 0.42–0.79; p=0.04).

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Predictors of 2-year mortality and risk stratification after surgical and endovascular revascularization for hemodialysis patients with critical limb ischemia: Due to infrainguinal artery disease

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Methods: From January 2004 to April 2014, 104 in-stent occlusion lesions after FP stenting were enrolled. Primary outcome was recurrent in-stent restenosis (ReISR), secondary outcome were recurrent target lesion revascularization (ReTLR) and occlusion (Reoclusion), respectively. ReISR or Reoclusion was defined as ISR or occlusion after TLR. Restenosis was defined as ≥2.5 of the peak systolic velocity ratio by duplex scan or ≥40% stenosis by angiography.

Results: Kaplan-Meier analysis revealed that the clinical driven TLR and primary patency (PTSR) rate were significantly higher (logrank, p<0.01) 1 year in patients with TP-Trunk patency than in patients without TP-Trunk stenosis. Multi-variant analysis revealed that TP-Trunk patency were independently factors associated with clinical driven TLR rate (Hazard ratio (HR): 0.53, 95% confidence interval (CI): 0.42–0.79; p=0.04).

Conclusion: Although BSX was feasible for in-stent occlusion after FP stenting, the use of DES is a good option because ReTLR and Reoclusion were similar.
P1137 | BEDSIDE
Relationship between primary patency and lesion length following bare nitinol stent placement for femoropopliteal artery disease
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Background: It remains unclear whether primary patency decreases proportionally to lesion length and which lesion length would be expected to have a 1-year primary patency above 66% which was determined as objective performance goal (OPG). 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 above 66% when the lesion length was ≤243 mm. After adjustment, the 1-year primary patency decreased linearly with the extension of lesion length. The 1-year primary patency was 83.2% (95% Confidential Interval [CI]: 79.8 to 86.1%) at 100 mm of LL, 76.4% (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 patency rate than 66% was 263 mm.

P1138 | BEDSIDE
Impact of patient’s activity on clinical outcome after femoropopliteal intervention
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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 to 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%, 86.2% and 82.7% 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. By 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.

P1139 | BEDSIDE
ST2-R2 score: degree of reverse remodelling and 4-year survival in patients with heart failure. A multicenter study
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Introduction: Recently, the ST-R2 score (ST2<48 ng/mL, non-ischemic aetiology, absence of LBBB, HF duration <12 months, baseline LVEF <24%, and β-blocker treatment) was developed to predict reverse remodelling (R2).

Purpose: To validate the degree of LVEF improvement and LV reduction at one year according to the ST2-R2 score and its prognostic implications up to 4 years.

Patients and methods: 569 patients with baseline LV ejection fraction (LVEF)<40% from 3 cohorts: Barcelona, TIME-CHF and PROTECT were included. For analysis patients were classified in 4 strata (0–8; 9–11; 12–14; 15–17) based upon their ST2-R2 score.

Results: A linear relationship was observed between ST2-R2 score and LVEF recovery (mean +5.6, +6.7, +11.3 and +17.3 respectively; p<0.001), and the reduction percentage of LVESVi (mean –6.1, –12.2, –25.6 and –32.1, respectively; p<0.001) and LVESDi (mean –1.1, –3.6, –9.3 and –18.6, respectively; p<0.001). A similar trend was observed with diastolic parameters. The improvement in LV function and size was accompanied by better outcome. Hazard ratios for risk of death taking the lower ST2-R2 group (0–8) as reference were 0.49 (p<0.001), 0.27 (p<0.001), and 0.17 (p<0.001) for scores 9–11, 12–14 and 15–17, respectively. Figure 1 shows survival curves according to ST2-R2 score subgroups.

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.

P1140 | BEDSIDE
Right ventricle myocardial perfusion pressure and outcome in pulmonary hypertension due to left heart failure

Aim: It has been demonstrated that in patients with pulmonary hypertension (PH), the right coronary artery flow and pattern is impaired due to changes in right ventricle (RV) pressures.

Purpose: The present study investigates the prognostic implications of changes in RV myocardial perfusion pressure due to PH in patients with chronic left heart failure (LHF).

Methods and results: Of 431 patients with chronic LHF who underwent right heart catheterization, 292 presented with PH. Myocardial perfusion pressure was defined as the gradient between the aortic pressure and the RV intra-cavitary pressure, in systole (SPP), and diastole (DPP). During the follow-up (median 33.9 months), 41.7% of patients with PH died, as compared with only 18.4% in the LHF
and non-PH group. The SPP was 87±3±2 mmHg in the PH group as compared to 107.1±24.8 in the non-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 mor-
tality 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 28.6%, 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 | BEDSIDE

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

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Background: Direct transcatheter aortic valve implantation (TAVI) has shown to be a comparably successful rate to TAVI with 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 ventricu-
lar ejection fraction (LVEF).

Purpose: 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 clini-
cal 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 to design 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 between the two groups (70% in the BAV group versus 74% in the direct 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 fea-
sible and has lower paravalvular leakage rates comparing to patients undergoing non-direct TAVI at 1-year.

P1142 | BENCH

Mechanistically independent ventricular beta 2-adrenoreceptor stimulation compensates for reduced contractile function in type-2 diabetes


Background: β-adrenoreceptor (AR) expression and functional β-AR responsive-
ness are key components of contractile function contributing to impaired cardio-
vascular health in type 2 diabetes. Changes in β-AR subtypes and the β1-AR associated stimulatory G (Gs) protein variables alter in contrastic response, whereas changes in β2-AR subtypes and downstream inhibitory G (Gi) proteins are suggested to evoke potential indirect functional and/or metabolic effects. How-
ever the individual β-AR subtypes contribute to cardiac function in type 2 dia-
abetes 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 (LVDPdev), a measure of myocardial function, was assessed in isolated Langendorff-perfused hearts from 20-week old rats. 116 rats were divided into a healthy (ZDF) rats and those with type 2 diabetes (ZDF rats with 16.5% and 17.6% obesity at age 8 months). The rats were then exposed to normal and limited food in either 1x10–8 M: 7±5 vs. 23±12 mmHg; p<0.001) and at 5 Hz (1x10–6 M: 73±5 vs. 18±4 mmHg; p<0.001). Specific β2-AR stimulation did not increase LVDPdev in control or diabetic rats, under both conditions. Interestingly, the LVDPdev response to non-specific β-AR stimulation was reduced in diabetic rats at their intrinsic rhythm (1x10–6 M: ND, 33±13 vs. 23, 5±6 mmHg; p<0.05) and at 5 Hz (1x10–6 M: 64±8 vs. 45±7 mmHg; ns). Protein expression levels of β1-AR and Gi were reduced, whereas levels of β2-AR and Gi and its downstream metabolic target P-AMPK were increased in the diabetic group.

Conclusion: Our data suggest that β2-AR indirectly support β1-AR-induced stim-
ulation of myocardial function, most likely through an increase in metabolic effi-
ciency by promoting metabolic pathways, such as β2-Gi-AMPK. Therefore specif-
cally increasing cardiac β2-AR activity in the large cohort of diabetic patients with heart disease may enhance myocardial metabolism and improve prognostic outcomes.

P1143 | BEDSIDE

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

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Background: Patients with type 2 diabetes mellitus (T2DM) have impaired my-
ocardial function. Collagen turnover and the renin angiotensin system (RAS) with type 2 diabetes dysfunction in T2DM patients.

Methods: A total of 123 patients (62 female, 60.8±8 years) with T2DM and no evidence of underlying coronary artery disease were recruited. All patients un-
derwent resting and exercise echocardiography. Resting and exercise echocardiography was analyzed by conventional parameters, E/E’ ratio (left ventricular filling pressure) and speckle tracking derived global longitudinal strain (GLS). Exercise echocardiography parameters included diastolic function reserve index (DFRI) and stress GLS. Plasma concentration of ECM turnover, including matrix metalloproteinase-1 (MMP-1), tissue inhibitor of MMP-1 (TIMP-1), procollagen peptides (amin-
oglycine propeptide of type I and type III procollagen [PINP and PIINP]) and RAS activity (PRA, angiotensin II and aldosterone) were also measured.

Results: Diastolic dysfunction was diagnosed in 75 (61%) patients: they had a higher plasma MMP-1 level of TIMP-1 (135.2±44.8 vs. 153.2±46.1 ng.ml−1, P=0.03) and PIINP (7.7±3.9 vs 9.4±4.9 ng.ml−1, P<0.05) than those with no diastolic function. Plasma TIMP-1 level was positively associated with left ventricular E/E’ and GLS both at rest (r=0.27, P<0.01; r=0.25, P=0.01) and during stress (r=0.33, P<0.01; r=0.25, P=0.01) and negatively with DFRI (r=−0.15, P=0.02). After multi-
variate adjustment, TIMP-1 level remained significantly associated with E/E’ at rest (r=−0.27, 95% confidence interval (CI) = 0.27–516, P=0.03) and at stress (r=−0.26, 95% CI = 0.26–5.01, P=0.01), as well as DFRI (β=−0.45, 95% CI = −0.85−0.05, P=0.03). The procollagen peptides and RAS activity showed no association with either echocardiography parameter.

Conclusions: In patients with T2DM, TIMP-1, an ECM regulator, is indepen-
dently associated with myocardial diastolic dysfunction both at rest and during stress. Measures that could reduce TIMP-1, such as statin therapy, may reduce myocardial dysfunction in these patients.

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 path-
ological (PohH) response of LV myocardium to increased cardiac load and is asso-
ciated with characteristic molecular changes. To date, a direct comparison of functional consequences of PhyH and PohH is missing.

Purpose: We aimed at investigating and comparing in vivo hemodynamic alter-
ations in rat models of PhyH and PohH by using LV pressure-volume (P-V) analy-
sis.

Methods: PhyH and PohH 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 car-
diac increase in the large cohort of diabetic patients with heart disease may enhance myocardial metabolism and improve prognostic outcomes.

Results: When detected by echocardiography, myocardial hypertrophy was more pronounced in PohH (LV mass: +14.3±1.5% M: 16±3 vs. 46±3% M: 18±4 mmHg; 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. Representative genes of the fetal gene program were observed only in the PhyH model. PhH was associated with unchanged LV pressure relations along with increased stroke volume and ejection fraction. In contrast, markedly higher LV end-systolic pressure, as well as unaltered stroke volume and ejection
contractility could be observed in both types of myocardial hypertrophy, characteristically differing in diastolic function and LV mechanics.

Conclusions: In this project we provided the first detailed, comparative hemodynamic characterization of Phy and Phah in relevant rodent models. Increased LV contractility could be observed in both types of myocardial hypertrophy, characteristically differing in diastolic function and LV mechanics.

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
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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 direct intramyocardial injection of saline (MI group, n=8); 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 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.

HYPERTENSION: DEVICES AND INTERVENTIONS

P1146 | BEDSIDE
Renal sympathetic denervation in patients with treatment resistant hypertension: a meta-analysis of randomized controlled trials
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Purpose: Renal sympathetic denervation (RDN) is proposed as a new treatment modality in patients with resistant hypertension (TRH). However, the evidence that RDN effectively lowers BP is contradictory. This meta-analysis investigated the current effectiveness of RDN for TRH.

Methods: We performed a systematic review and meta-analysis of the randomized controlled trials (RCT) that reported office and/or 24-h ambulatory systolic BP in RDN and control (maintenance or reinforcement of medical therapy) groups at 6 months of follow-up in patients with TRH by searching medical literature databases. Pooled effect sizes were derived, using a random-effects model.

Results: Five RCTs were identified that randomized 867 patients and used the single-electrode Symplicity catheter. In the pooled analysis, RDN was associated with a non-significant decrease in office systolic BP (weighted mean difference (WMD): -4.21 mmHg, 95% CI: -17.12 to 8.69, p=0.52), or in 24-h ambulatory systolic BP (WMD: -1.94 mmHg, 95% CI: -6.05 to 2.17 mmHg, p=0.36) compared to control at 6 months. The proportion of patients who normalized their 24-h ambulatory systolic BP in RDN group (reported in 3 RCTs) was 27.5% compared to 26.5% in control group at 6 months. There was significant heterogeneity among included studies with large between-patients variability in the BP response to RDN.

Conclusions: The overall BP lowering effect of RDN with the Symplicity catheter does not significantly differ from that of medical treatment in patients with TRH. Future research should identify the characteristics of patients who may respond to RDN, optimal catheter, effective ablation dose and biological measures that could confirm that RDN does occur. Accordingly, RDN should not be considered as a routine treatment modality of TRH.
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
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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 arterial 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 therapy.
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. Changes from baseline in office and 24-hr ambulatory blood pressure were 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 pooled patient-level ABPM meeting pre-defined quality criteria. 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 group compared with control patients with resistant hypertension and OSA appeared to have a greater reduction in office SBP and in average peak and maximum nocturnal peak SBP (p<0.05) 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
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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), as predictive result of a large randomized trial suggests there is still need for pre-clinical evaluation.
Methods: Catheter-based renal sympathetic denervation (RSD) was performed in 10 true resistant hypertensive patients due to the marked reduction in whole-body norepinephrine spillover and sustained decrease in sympathetic nerve traffic (MSNA), as predictive result of a large randomized trial suggests there is still need for pre-clinical evaluation.
Results: After renal denervation we observed a reduction in ADMA 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 change in plasma ADMA and SDMA respectively (Spearman r=0.87, 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
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Background: For blood pressure (BP) management, objective information that can be used in an ambulatory setting and easily modified, assessed by objective tools provides an attractive solution. Blood pressure (BP) monitoring with ingestible platforms offers a viable solution. These devices allow for continuous collection of blood pressure data while patients continue with their daily routine. Data from ingestible devices can be communicated wirelessly to an electronic patient record (EPR) and offer real-time feedback. Feedback–90% of patients did not mind swallowing the IS, and 75% had a positive result. With ambulatory BP monitoring, objective assessment, and digital communication, non-invasive evaluation of resistant hypertension may be possible.
Methods: 37 subjects (23 males; age 62±9 years) used the system for 6 weeks. Two digital medicine prototypes consisting 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 digital communication system (WDS) worn on the torso. The WDS stored ingestion dates and times, and daily step count, and relayed data automatically to a mobile computerized 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 predefined quality criteria. Within 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 taking 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 mean 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.
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
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Purpose: Catheter-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.
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 (MRgHIFU). MRI was used to evaluate the acoustic window, target sonication, monitor the near-field treatment region using MR thermometry imaging, and assess the status of tissues post-treatment. Animals were sacrificed 5–9 days post-treatment and pathological analysis was performed. Norepinephrine present in the kidney medulla was assayed post-mortem.
Results: 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 by the treated and untreated renal arteries was observed in 85% and 72% 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.
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.

**Methods:** We performed a nationwide population-based cohort study from 106 UK hospitals comprising 97,129 patients from 2005 to 2013. Data from the British Cardiac Intervention Society (BCIS) registry were matched by age, sex and year of PPCI to national population data. Estimates of cumulative relative survival (RS) rates and hazard rates were used to calculate expected survival, observed all-cause mortality rate ratios and excess mortality rate ratios (EMRR). Crude RS was estimated using the Ederer II method for the whole cohort and cumulative RS estimated by age, sex and biennial year of procedure. 

**Results:** Mean age (SD) was 63.4 (13.1) years, 25.7% were female. Crude RS compared to the general population estimated at 6 months, 1 and 5 years was 93.0%, 92.5% and 89.5%. The 5 year cumulative RS for patients $<55$ years was 95.4%. Compared with age $<55$ years, patients $>80$ had significant excess mortality both at $<4$ years (EMRR 6.63, 95% CI 6.07–7.24) and $>4$ years (2.56, CI 1.79–3.64) Male patients had significantly higher RS than females (EMRR 0.79, 95% 0.74–0.82). There was no temporal change in excess mortality, 2005/6–13 (EMRR 1.03, 95% 0.90–1.19).

**Conclusion:** Survival is excellent for young patients treated with PPCI and approaches that of the matched general population. However, there is evidence for excess mortality in females and the elderly.
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 | BEDSIDE
Impact of national PCI network on prognosis after acute myocardial infarction in Estonia
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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 after the implementation of national PCI network in Estonia.

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 40% to 15%). 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). 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 | BEDSIDE
Impact of complete revascularization in a real world population of patients presenting with STElevation myocardial infarction

Aims: Complete revascularization during primary percutaneous coronary intervention (PPCI) in patients with multivessel disease is associated with better outcomes. We intend to evaluate this subject in all-comers STE elevation myocardial infarction (STEMI) population.

Methods: Retrospective analysis of 1511 consecutive STEMI patients 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, 11% for rescue PCI and 7% for facilitated PCI. 53% had multivessel disease (median affected segments 2, IQR [1–3]) and 12.1% (n=183) were admitted 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, 95% CI 0.35–0.84, p=0.007). There was no difference comparing 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 long-term better outcome.

1201 | BEDSIDE
Frequency, reasons and predictors of unplanned cardiac rehospitalizations following primary PCI in STEMI patients: results of the Comfortable AMI trial
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Introduction: Rehospitalizations after STElevation myocardial infarction (STEMI) carry a significant economic burden and may adversely impact long-term prognosis. Although coronary events leading to rehospitalization have been previously studied, data on unplanned hospitalizations is sparse.

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. The most frequent reasons for UCRH were recurrent chest pain without evidence of ischemia (20.4%), ischemic events (16.9%), and heart failure (16.3%). On univariate analyses, the most significant baseline predictors of UCRH within one
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
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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).

Table 1

<table>
<thead>
<tr>
<th>Predictor of death or MI</th>
<th>OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MVD</td>
<td>1.62 (0.89–2.95)</td>
<td>0.109</td>
</tr>
<tr>
<td>Age (10 y)</td>
<td>1.67 (1.17–2.39)</td>
<td>0.005</td>
</tr>
<tr>
<td>TIMI risk index</td>
<td>1.04 (1.01–1.06)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Symptom onset-to-balloon (30 min)</td>
<td>1.04 (1.01–1.07)</td>
<td>0.010</td>
</tr>
<tr>
<td>Killip class II–IV</td>
<td>4.47 (2.18–9.14)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Open vessel before PCI</td>
<td>4.17 (1.78–9.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Final TIMI grade 2–3 flow</td>
<td>4.23 (2.33–7.71)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions: 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 Ibb/IIa inhibitors undergoing primary PCI for STEMI. Results of the prospective ALKK-Registry
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Background: There is still debate about the optimal antithrombotic therapy in patients undergoing primary PCI. Earlier randomized trials have shown a benefit of GP Ibb/IIa 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 Ibb/IIa 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 8964 (58.9%) received a GP Ibb/IIa inhibitor. Baseline characteristics, procedural features and in-hospital outcomes are given in the table.

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

Conclusion: In clinical practice GP Ibb/IIa inhibitors in Germany are used in more than 50% of the patients with primary PCI for STEMI treated with heparin. The use is 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 intravenous 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: an observational coronary intervention
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Background: Contrast induced nephropathy (CIN) is associated with increased mortality in ST Segment Elevation Myocardial Infarction (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 pPCI 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 kidney disease (CICKD) was defined as an estimated glomerular filtration rate (eGFR) <60 ml/min at admittance. Contrast Ratio (CR) was defined as the ratio between ml of CM effectively used and the maximum amount of CM calculated for the patient (following Cigarra formula: 5 x body weight (kg)/serum creatinine); we compared pts in high risk group (CR <1) with the others (CR >1). Independent predictors of CIN were evaluated with a multivariable logistic regression model; survival analyses were performed using Cox regression models.

Results: Patients with CR >1 (95; 11.8%) were older, had a higher incidence of type 2 diabetes and TIMI flow <3 after PCI, lower haemoglobin values at admittance and in-hospital left ventricular ejection fraction (LVEF) (p<0.001) had more frequently anterior MI, a higher Killip class, a higher baseline eGFR, (p<0.05). CR >1 was a predictor of CIN (OR 3.1 95% CI 1.4–7.1, 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-month (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 a 1 and 2-year mortality (HR 2.08 95% CI 1.04–4.17, p=0.039 and 1.83 95% CI 1.05–3.19, p=0.033, respectively) after adjusting for LVEF, age, OK 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
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Purpose: Primary angioplasty is the best reperfusion treatment in ST elevated myocardial infarction. The prevalence of very elderly patients (>75 years) un-
Serelaxin reduces oxidative stress in vitro and atherosclerosis in aortic smooth muscle cells. J. Zhong1, X. Rao1, S. Oghumu2, J. Deiuliis1, A.R. Satoskar2, M. Frieman1, S. Rajagopalan1.1 University of Maryland, Department of Medicine, Baltimore, USA, 2 Fudan University, Shanghai, China.

Methods and results: Using aortic smooth muscle cells, we evaluated the effects of serelaxin on oxidative stress and atherosclerosis. Serelaxin treatment reduced intracellular ROS production, enhanced the antiproliferative effects of angiotensin II, and improved endothelial function.

Conclusions: These results suggest a potential role for serelaxin in reducing oxidative stress and preventing atherosclerosis in vitro.

INFLAMMATION AND PLAQUE VULNERABILITY – ADVANCED INSIGHTS FROM MOUSE AND MAN

1215 | BENCH
Dendritic cells are involved in hypercholesterolemia after myocardial infarction
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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 pathway 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 represent 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/6J mice were randomly divided into three groups: 1/3 received STMI, 1/3 received vehicle, and 1/3 received DCs from sham mice. The distribution of CD11c+ DCs was examined before and after the addition.

Results: 1. Total cholesterol and LDL cholesterol in plasma were increased at 24 hrs post-AMI and slightly decreased on day 7 post-AMI but still higher than those in Sham mice. Plasma HDL cholesterol was decreased at 24 hrs and increased on day 7 post-MI compared to Sham mice. The distribution of CD11c+ DCs and the protein and the mRNA levels of AMPK-mTOR-SREBP signaling in liver were examined. 2. The exosomes from the DCs were added to the cultured mouse hepatocyte cell line (AML12). The protein and the mRNA of AMPK-mTOR-SREBP signaling in the cells were examined before and after the addition.

Conclusions: Total cholesterol and LDL cholesterol in plasma were increased at 24 hrs post-AMI and slightly decreased on day 7 post-AMI but still higher than those in Sham mice. Plasma HDL cholesterol was decreased at 24 hrs and increased on day 7 post-MI compared to Sham mice. The distribution of CD11c+ DCs and the protein and the mRNA levels of AMPK-mTOR-SREBP signaling in liver were examined. 2. The exosomes from the DCs were added to the cultured mouse hepatocyte cell line (AML12). The protein and the mRNA of AMPK-mTOR-SREBP signaling in the cells were examined before and after the addition.

Conclusion: Our results suggest a potential role for non-catalytic function of hemapoietic DPP4 in regulating atherosclerosis progression.

1217 | BENCH
Loss of hematopoietic DPP4 ameliorates atherosclerosis and vascular inflammation by non-catalytic mechanisms
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Background: Dipeptidyl peptidase-4 (DPP4) is a transmembrane protein that catalyzes the degradation of several peptide hormones. In vascular tissues, DPP4 is expressed in macrophages, smooth muscle cells, and endothelial cells. DPP4 regulates several inflammatory pathways.

Methods and results: We evaluated the effects of DPP4 on vascular inflammation and atherosclerosis using DPP4−/− mice. We observed reduced atherosclerotic plaque formation, decreased inflammatory cell infiltration, and improved endothelial function in DPP4−/− mice compared to wild-type controls.

Conclusions: These results suggest a potential role for DPP4 in regulating vascular inflammation and atherosclerosis progression. Further studies are needed to understand the mechanisms involved.

DPP4 and aorta. In this study, we aimed to understand the contribution of DPP4 non-catalytic function and the role of hematopoietic DPP4 in regulating atherosclerosis progression.

Methods: Our study involved the use of DPP4−/− mice and wild-type controls. We evaluated atherosclerotic plaque formation and inflammatory cell infiltration in the aorta and the kidney.

Conclusions: Our results suggest a potential role for DPP4 non-catalytic function in regulating atherosclerosis progression. Further studies are needed to understand the mechanisms involved.
SYSTOLIC HYPERTENSION

1237 | BEDSIDE
Rising systolic blood pressure leads to a continuous progression towards hypertensive heart disease: a prospec tive population study
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Imperial College London, Medical Research Council Clinical Sciences Centre, London, United Kingdom; Imperial College London, Department of Computing, London, United Kingdom; Duke-NUS Graduate Medical School 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-naïve 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 hypertrophic adaptation of the septum and anterior wall with associated normalization of WS in the lateral wall. In the lateral wall an increase in WS with rising SBP was not balanced by a compensatory 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 normalization 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 systolic hypertension in the elderly program
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1 Rutgers Robert Wood Johnson Medical School, Cardiovascular Institute, New Brunswick, United States of America; 2 Massachusetts 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, oHyper 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 hypotension 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 sdec study
Inserm U970 - Paris Cardiovascular Research Center (PARCC), 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>Number (%)</th>
<th>Working hours</th>
<th>Off hours</th>
<th>p.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>11280</td>
<td>60.77</td>
<td>62.34</td>
</tr>
<tr>
<td>Age (mean [median])</td>
<td>11378</td>
<td>71 (74)</td>
<td>70 (72)</td>
</tr>
<tr>
<td>Call-to-EMS arrival delay (mean [median])</td>
<td>12483</td>
<td>11 (9)</td>
<td>12 (9)</td>
</tr>
<tr>
<td>Home location</td>
<td>11295</td>
<td>73.57</td>
<td>84.51</td>
</tr>
<tr>
<td>Witness presence</td>
<td>9965</td>
<td>72.05</td>
<td>74.33</td>
</tr>
<tr>
<td>Bystander BLS-initiation</td>
<td>7570</td>
<td>48.80</td>
<td>46.27</td>
</tr>
<tr>
<td>AED use</td>
<td>4906</td>
<td>3.04</td>
<td>1.63</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>2291</td>
<td>50.27</td>
<td>51.97</td>
</tr>
<tr>
<td>ROSC</td>
<td>8623</td>
<td>31.59</td>
<td>28.32</td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>2379</td>
<td>55.56</td>
<td>54.73</td>
</tr>
<tr>
<td>Coronary angioplasty</td>
<td>1330</td>
<td>36.28</td>
<td>32.71</td>
</tr>
<tr>
<td>On-site death</td>
<td>11430</td>
<td>74.30</td>
<td>72.40</td>
</tr>
<tr>
<td>Death</td>
<td>11113</td>
<td>94.04</td>
<td>95.49</td>
</tr>
</tbody>
</table>

EMS, emergency medical service; BLS, basic life support; AED, automated external defibrillator; ROSC, return of spontaneous circulation.
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 bluntly initiated BLS and used AED. CPR was more often performed, whether or not 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 healthcare management, rate of public awareness and training programs in improving OHCA prognosis during off hours.

1321 | BEDSIDE
Duration of resuscitation efforts and survival after out-of-hospital cardiac arrest: an observational study

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Background: One of the biggest challenges facing emergency medical services (EMS) personnel or clinicians is the decision about when to stop resuscitation efforts for out-of-hospital cardiac arrest (OHCA) patients in the field. The 2010 guidelines for cardiopulmonary resuscitation (CPR) have not directly addressed the appropriate duration of resuscitation efforts before termination of CPR.

Purpose: We aimed to determine the relation between duration of prehospital CPR (CPR-to-ROSC time) and survival after cardiac arrest in non-ischemic cardiac disease.

Methods: We analysed the records of 17,238 OHCA patients (age, ≥ 18 years) who achieved return of spontaneous circulation (ROSC) before arrival at the hospital. Data were obtained from a prospectively recorded national Utstein-style database from 2011 to 2012. The time from initiation of CPR by EMS personnel to prehospital ROSC (CPR-to-ROSC time) was calculated to estimate the appropriate duration of prehospital CPR efforts by EMS personnel. The endpoints were 1-month survival and 1-month favourable neurological outcomes (cerebral performance category scale, category 1 or 2; CPC 1–2).

Results: Of 17,238 OHCA patients, 6347 (36.8%) survived at 1 month after OHCA and 771 (21.8%) achieved 1-month CPC 1–2. The CPR-to-ROSC time was significantly shorter in 1-month survivors than in non-survivors (median, 8 min [IQR 5–13] vs. 16 min [IQR 10–23], P < 0.0001). Logistic regression analyses revealed that the CPR-to-ROSC time was independently associated with 1-month CPC 1–2 in the unadjusted model (odds ratio 0.898; 95% confidence interval (CI) 0.893–0.903) and in the adjusted model for prehospital covariates (adjusted odds ratio 0.915; 95% CI 0.909–0.920). Analyses of the cumulative proportion of 1-month survivors by CPR-to-ROSC time showed that 99.1% of all survivors and 99.2% of non-ischemic cardiac disease patients 1–2 achieved ROSC within 35 minutes of CPR, 91.3% of all survivors achieved ROSC within 22 minutes, and 90.0% of survivors with CPC 1–2 achieved ROSC within 19 minutes. No patient with a CPR-to-ROSC time of ≥53 minutes survived 1 month after OHCA.

Conclusions: The possibility of survival with CPC 1–2 declines with each minute of CPR after OHCA. To obtain a ≥99% cumulative proportion of 1-month survivors with favourable neurological outcomes, at least 35 minutes of prehospital resuscitation efforts by EMS personnel are required.

1322 | BEDSIDE
Autopsy findings of victims with asystole or pulseless electrical activity vs. ventricular fibrillation at the time of cardiac arrest

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Background: Several studies have indicated that prevalence of asystole (ASY) or pulseless electrical activity (PEA) has been increasing and the prevalence of ventricular fibrillation (VF) has been declining in sudden cardiac arrests. There is limited information on the etiology of underlying structural heart disease in victims of sudden cardiac death (SCD) in PEASY/VS. This study analyzed the autopsy findings of 262 patients with non-ischemic SCD with PEASY/VS as VF at the presenting rhythm at the time of cardiac arrest.

Methods: Prevalence of PEASY/VS vs. VC occurring within one hour after onset of witnessed collapse was analyzed by the emergency personnel of victims of SCD. Underlying structural heart disease was diagnosed by medicolegal autopsy in the Finnish study of genotype and phenotype profile of SCD (FinGeniture) between 2008–2012.

Results: From a total number of 604 victims of cardiac arrest with a documented rhythm at the time of cardiac arrest 83 subjects underwent medicolegal autopsy. PEASY/VS was the presenting arrhythmia in 51 cases (61.4%) and VF in 32 cases (38.6%). There was no differences between the groups in age (mean 64.8 ± 62.7), body mass index (mean 30.9 ± 27.4), gender or in the time of delay between the onset of cardiac arrest and the ECG recording (mean 19 ± 15 minutes in PEASY/VS vs. 16 ± 14 minutes in VF). PEASY/VS was more prevalent than VF in cases with non-ischemic cardiac disease (35.3% vs. 3.1%, P < 0.001) at autopsy. Usage of psychotropic medication was also more common in PEASY/VS group (41.9% vs. 8.0%, P = 0.006). VF was more common among the victims of SCD without the history of primary cardiac disease (35.3% vs. 59.4%, P = 0.04).

Conclusions: PEASY/VS is a more common primary cardiac arrhythmia at the time of cardiac arrest in non-ischemic than ischemic cardiac disease. Decreasing trend of ischemic heart disease as a cause of SCD may partly explain the increasing trend of PEASY/VS.

1323 | BEDSIDE
German national experience with the wearable cardioverter-defibrillator (WCD)
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Background: In Germany, sudden cardiac death (SCD) is a leading cause of mortality. The wearable cardioverter-defibrillator (WCD) is prescribed to patients at increased risk of ventricular tachycardia/fibrillation (VT/VF). The WCD is capable of VT/VF detection as well as defibrillation, enabling resuscitation of patients independent of patient or bystander intervention.

Purpose: To determine prevention of SCD among WCD patients at risk for VT/VF.

Methods: From a total number of 604 victims of cardiac arrest with a documented rhythm at the time of cardiac arrest 83 subjects underwent medicolegal autopsy. PEASY/VS was the presenting arrhythmia in 51 cases (61.4%) and VF in 32 cases (38.6%). There was no differences between the groups in age (mean 64.8 ± 62.7), body mass index (mean 30.9 ± 27.4), gender or in the time of delay between the onset of cardiac arrest and the ECG recording (mean 19 ± 15 minutes in PEASY/VS vs. 16 ± 14 minutes in VF). PEASY/VS was more prevalent than VF in cases with non-ischemic cardiac disease (35.3% vs. 3.1%, P < 0.001) at autopsy. Usage of psychotropic medication was also more common in PEASY/VS group (41.9% vs. 8.0%, P = 0.006). VF was more common among the victims of SCD without the history of primary cardiac disease (35.3% vs. 59.4%, P = 0.04).

Conclusions: PEASY/VS is a more common primary cardiac arrhythmia at the time of cardiac arrest in non-ischemic than ischemic cardiac disease. Decreasing trend of ischemic heart disease as a cause of SCD may partly explain the increasing trend of PEASY/VS.

1324 | BEDSIDE
Orthostatic and postprandial hypotension in elderly patients with syncope
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Introduction: In the elderly, orthostatic hypotension (OH) and postprandial hypotension (PPH) are common causes for syncpe. 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. In a multidisciplinary program for the evaluation of unexplained falls and/or syncope in elderly patients we investigated all patients for OH and PPH. In a multidisciplinary program for the evaluation of unexplained falls and/or syncope in elderly patients we investigated all patients for OH and PPH.

Results: Of 262 patients evaluated, 117 patients had syncope and 12 patients were diagnosed with pre-syncope, mean age 80±7 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 the diagnosis of OH more active standing BPM should be performed in the week 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.

1325 | BEDSIDE

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

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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 epileptic seizures. Essential ion channels are co-expressed in the heart and in the brain. Accordingly, current theories suggest that some cases of synapses 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 LQT2 type (LQT2) have an increased prevalence of cerebral affection compared to other LQTS subclasses.

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

Methods: We studied 15 patients (age: 43 (21–72), 12 women) with a genotyped diagnosis of LQT2. We performed a standardized medical history with emphasis on the seminalization of previous synapses 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 synapses, 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 LQT2 diagnosis.

EEGs showed an increased frequency of theta activity fromo-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. Our study underlines the difficulties in differentiating between cardiac synapses and epileptic seizures clinically. However, our results may also indicate overlapping causative mechanisms in the two conditions.

1326 | BEDSIDE

The effect of fluoxetine on recurrent vasovagal syncope with anxiety sensitivity

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Background: The optimal medical therapy of patients with vasovagal syncope (VVS) remains controversial. Stress is generally associated with recurrent syncope episodes. Serotonin reuptake inhibitors (SSRIs), such as fluoxetine, exhibit central nervous system actions and their use has shown promising results for VVS therapy.

Purpose: To examine whether fluoxetine exerts beneficial effects relative to placebo in its ability to prevent VVS in the subset of patients with anxiety-related psychosocial distress.

Methods: We assessed 106 patients with typical history of recurrent VVS (at least 2 episodes during the preceding 6 months), without other comorbidities, all with a positive head-up tilt test (HUT). Their psychological, stress-related profile was assessed by the Beck Anxiety Sensitivity Index (ASI) questionnaire, a simple, 16-item questionnaire, assessing fear of presyncope during follow-up (for syncope: 5/40 patients with fluoxetine vs 9/20 with placebo, p<0.05). Initial anxiety levels were related to symptomatic recurrence in the placebo group, and not in the fluoxetine treatment group.

Conclusions: Fluoxetine is superior to placebo in recurrent VVS associated with psychosocial distress of the anxiety sensitivity type and may be a first-line pharmacological treatment in this difficult-to-treat group, which represents more than 50% of patients with frequent syncope episodes.

1327 | BEDSIDE

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. Tateno7, S. Sato1, N. Tauchi2, M. Nagashima3. 1National Hospital Organization Kagoshima Medical Center, Kagoshima, Japan; 2Centers for Public Health Informatics, 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; Aichi 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).
transfected 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, β2AR 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 α1-phenylphrine dosage curves to the right.

### Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>Alpha-1AAR Ab (%) above BB</th>
<th>Beta-1AAR Ab (RLU)</th>
<th>Beta-2AAR Ab (RLU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n=13)</td>
<td>63.2±7.7</td>
<td>3901±187</td>
<td>4212±251</td>
</tr>
<tr>
<td>VVS (n=7)</td>
<td>78±1.4</td>
<td>5209±95</td>
<td>6534±251</td>
</tr>
<tr>
<td>PoTS (n=18)</td>
<td>83±3.3</td>
<td>6172±176**</td>
<td>7505±238**</td>
</tr>
</tbody>
</table>

Antihypertensive serum activity among patients with PoTS, VVS, and normal age-matched controls.

**Conclusions:** These data support a pathophysiological relationship between α1 and β2 adrenergic AABs and PoTS; and suggest they are not restricted to classic PoTS alone but may also be present in other forms of dysautonomia such as VVS (p<0.001 vs. VVS; p<0.05 vs. STEMI). One-way ANOVA test for difference between groups: a1AR-AAb, p=0.0004; b1AR-AAb, p=0.0001; b2AR-AAb, p=0.0001.

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**1329 | BEDSIDE**

### Increased risk of occupational accidents following syncpe: a Danish nationwide study

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**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 syncpe 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 syncpe 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 resident patients we identified 20,911 patients with syncope (median age 46 years [IQR 31–58]; 51% women) who experienced 1080 (5.2%) occupational accidents during a median follow-up time of 2.3 years (IQR 1.1–3.6). Crude incidence rates of occupational accidents among the syncope and general population were 20.3 (95% CI 19.1–21.7) and 14.2 (95% CI 14.1–14.2) per 1000 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 1.05–1.26) among 18–27 year olds, 1.15 (95% CI 1.01–1.31) among 28–52 year olds, and 1.26 (95% CI 1.19–1.32) among 53–65 year olds. There was no difference in all-cause mortality within 30 days from the 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.

**Conclusions:** Increased risk of occupational accidents following syncpe, especially among the younger population, however, not accompanied by increased short-term mortality. Increased physician awareness of risk of occupational accidents following syncpe might be warranted.

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**1332 | 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. Funada 1, Y. Nakatsu-Goto2, 1Kanazawa 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 scale, category 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% (n=508) and 0.99% (n=73), 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<0.05), bystander-witnessed arrest (52/27 [71.2%] vs. 1830/7259 [25.2%], P<0.0001), initial shockable rhythm (28/73 [38.3%] vs. 241/7259 [3.3%], 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). Multivariate logistic regression analysis indicated that the following prehospital factors were associated with 1-month CPC 1–2: (1) initial non-shockable rhythm (ventricular fibrillation [VF]/pulseless ventricular tachycardia [VT]; adjusted odds ratio [aOR] 15.9; 95% confidence interval [CI] 8.0–32.0, pulseless electrical activity [PEA]; aOR 5.18; 95% CI 2.76–9.82) and (2) bystander-witnessed arrest (aOR 3.21; 95% CI 8.4–57.9). In witnessed-arrest children with aVF 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-asystole rhythm and bystander-witnessed arrest in OHCA children transported to hospital without a prehospital ROSC.

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**BEST POSTERS SESSION 2**

**BEST POSTERS IN Sudden Death**

**P1310 | BEDSIDE**

### Long term outcomes of out of hospital cardiac arrest

M. Shuvy1, L.J. Morrison 2, S. Cheskes4, P. Dorian2, D.C. Scales4, P.R. Verbeeck4, H.C. Wijeyunasara1, M. Koh2, D.T. Ko3, 1Sunnychek Brook Health Sciences Centre, Schulich Heart Centre, Toronto, Canada; 2St. Michael's Hospital, Toronto, Canada; 4Institute for Clinical Evaluative Sciences, Toronto, Canada; 4Sunnybrook Health Sciences Centre, Department of Medicine, Toronto, Canada

**Background:** Recent studies have demonstrated an improving trend in the survival rates of patients with out-of-hospital cardiac arrest (OHCA). However, little is known regarding their longer-term treatments and outcomes as to whether they are comparable to MI patients.

**Purpose:** To examine cardiac treatment, readmission rates, and mortality rates of OHCA survivors, and to compare them with STEMI patients.

**Methods:** Data from the Toronto Episty database were used to capture consecutive OHCA patients from 2005 to 2010. Patients with cardiac arrest and attempted treatment were included. STEMI survivors were captured using a provincial cohort that included all hospitalized patients. Outcomes of interest were available for all patients, and included the use of cardiac invasive procedures, all-cause readmission, and all-cause mortality.

**Results:** Among the 13,755 OHCA patients, 704 patients alive at discharge were included in this analysis and were compared with 14,811 STEMI patients. OHCA survivors were slightly younger than STEMI survivors (60 years vs. 62 years), but had substantially higher rates of prior myocardial infarction (9.4% vs. 4.2%), heart failure (10.4% vs. 2.4%), atrial fibrillation (6.7% vs. 2.1%) and ventricular arrhythmia (2.8% vs. 0.2%) (all P<0.001). At one year, readmission rate was significantly higher for survivors of OHCA at 34.8% vs. 29.8% than STEMI patients (P=0.005). Similarly, one-year mortality rate was significantly higher for survivors of OHCA (11.5% vs. 5.5%, P<0.001). The longer term survival is shown in Figure 1.
**P1334 | BENCH**

### Survival improved for men but not women, despite increased bystander CPR and first responder defibrillation for both: results form a statewide quality improvement initiative

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**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 disparities 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%), unwatched 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 (Figure) and overall survival with favorable neurologic outcome increased for men (from 6.4% to 11.7%, p=0.001) but not women (from 6.7% to 6.1%, p=0.7); similar gender-related differences in survival were observed among witnessed arrests, those who received bystander CPR and those with shockable heart rhythm. Survival increased for women but not men, also in multivariable models adjusted for age, witnessed status, bystander CPR and initial heart rhythm (men: Incidence Rate Ratio [IRR] 1.6 [CI95% 1.2–2.2]; women IRR 0.9 [CI95% 0.5–1.3]).

**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.

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**P1339 | BEDSIDE**

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

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**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 is suspected that this has been caused by prophylactically treating 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 (CAG). We also aimed to stratify patients without CAG due to progression to PCI.

**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.

**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.

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**P1343 | BEDSIDE**

### Very long-term follow-up of patients with out-of-hospital cardiac arrest due to idiopathic ventricular fibrillation: a single-centre experience

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**Background:** Out-of-hospital cardiac arrest (OHCA) in the absence of evident structural heart disease is rare, with a broad differential diagnosis that includes subclinical cardiomyopathy, channelopathies, and idiopathic ventricular fibrillation (IVF). To date, no systematic study has been carried out to assess the clinical features and the very long-term follow-up of survivors of OHCA due to IVF.

**Purpose:** The aim of this study was to investigate the clinical and ECG features of OHCA survivors presenting with IVF in the region of Ticino (Switzerland) over the last 14 years. The long-term follow-up and the evolution over the time of ECG and echocardiographic parameters were evaluated.

**Methods:** All survivors of OHCA presenting with VF and normal baseline ECG in the absence of structural and ischemic heart disease (non-diabetic, non-cardiomyopathy/MRI and cardiac catheterization) were considered eligible for this study.

**Results:** A total of 70 survivors of OHCA presenting with VF as first rhythm underwent an implantable cardioverter-defibrillator (ICD) implantation for secondary prevention from 2000 to 2014. Of those, 11 had a normal baseline ECG, MRI/echocardiography and coronary angiography. However, over a follow-up time of 85.2±47.3 months, ECG was found abnormal in 3 cases (1 long QT, 1 Brugada pattern, 1 early repolarization pattern) and no new echocardiographic abnormal findings were revealed in any patient.

**Conclusions:** IVF occurs in 11% of OHCA survivors presenting with VF as first rhythm. The initial diagnosis can change up to 27% of cases. Patients with IVF seem to have a good prognosis during a long-term follow-up. Larger studies are needed to confirm our results.

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**BEST POSTERS IN POST MYOCARDIAL INFARCTION OUTCOMES**
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 analyzes of whom 9,241 were acute/subacute procedures and 22,493 were elective procedures. In sensitivity analyzes 13,110 elective patients had stable angiina pectoris. Background population constituted 158,670 people from Western Denmark. Mean follow-up was 4.1 years CAG patients without obstructive CAD had a similar long-term risk of death (HR 1.02, 95% CI, 0.97–1.07) but a 15% relative reduced risk of MI (HR 0.85, 95% CI, 0.75–0.965) in all patients. Elective patients with stable angiina pectoris had a 36% relative reduced risk of both death (HR, 0.64, 95% CI, 0.59–0.70) and MI (HR, 0.637, 95% CI, 0.517–0.785).

Conclusions: Patients without CAD at first CAG have a similar risk of death and lower risk of MI compared to an age and gender matched background population. Furthermore, elective procedures with stable angina pectoris, but without obstructive CAD, have a 36% lower risk of death and MI than an age and gender matched sample from the background population.

P1338 | BEDSIDE
Relation between rate of reperfusion decisions in the ambulance and STEMI case load. An analysis of the eMust registry in 18,063 patients managed by 41 mobile intensive care units

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Background and aim: Number of PCI performed by center is a determinant of STEMI case load. An analysis of the eMust registry in 18,063 patients managed by 41 mobile intensive care units (MICU) and emergency medical system departments (SAMU: Service d’Aide Médicale Urgente) was a determinant of the rate of prehospital reperfusion-decisions.

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. The registry is ongoing and all data up to 2013 were used for the present analysis. MICU emergency physicians initiate treatment in the prehospital setting and take the initial decision of reperfusion therapy.

Results: During the 11-year study period, 18,063 STEMI patients were managed by 8 SAMU departments and 41 MICU dispatched on site. Median time from symptom onset to call to SAMU was 60 min [25–167 min]. The annual number of STEMI patients managed by each SAMU department ranged from 139 to 300, and that managed by each of the MICU from 7 to 152. Decisions to send the patients for reperfusion therapy ranged from 83% to 97% (primary PCI: 76% and fibrinolysis: 24%). There was no correlation between total case-load for each SAMU or MICU and rates of reperfusion-decisions (Figure).

Conclusion: In contrast with PCI volume in cath labs, quality of care evaluated by the rate of reperfusion-decisions in STEMI patients was not related to the annual case-loads of each of the SAMU departments or their MICUs.

P1341 | BEDSIDE
The declining frequency of inducible myocardial ischemia during cardiac stress testing in the last 39 years (1970-2009)

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Objective: To assess the rate of positivity during cardiac stress testing by 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 changing 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
in 20.6% of the patients. During follow-up end-points were noted in (9.9%) patients as inappropriate and 22.7% as uncertain. Ischemic response to DSCE was elicited in 57.1±10.1 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=58.8, p < 0.05), 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 an abnormal LVCR, the majority due to global abnormality where OCAD cannot be excluded. We suggest alternate testing e.g. pharmacologic stress imaging study or CT coronary angiography.

**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.

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**P1342 | BEDSIDE**

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

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**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 (58.4±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 57.1±10.1 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=58.8, p < 0.05), 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 an abnormal LVCR, the majority due to global abnormality where OCAD cannot be excluded. We suggest alternate testing e.g. pharmacologic stress imaging study or CT coronary angiography.

**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.

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**P1343 | BEDSIDE**

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

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**Introduction:** 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 gained 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±5 vs. 57±10 years, 71% vs. 59% men, p=NS). All the patients performed a supine bicycle symptom-limited exercise stress 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 significance 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<0.0001). The patients with the middle lesions of LAD had 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<0.00003), a lower ΔV (19±21 vs. 42±16 cm/s, p<0.000001), and a lower CFVR (1.6±0.7 vs. 2.4±0.6, p<0.000001) 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.

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**BEST POSTERS IN STEM CELLS AND CELL THERAPY**

**P1346 | BENCH**

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

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**Background:** Cardiomyocytes from patient-specific induced pluripotent stem cells (iPSCs) recapitulate key features of heritable diseases. Assays for drug-induced QT prolongation are a promising application. Conventional electrophysiology is restricted by limited throughput. We aimed at establishing optical action potential (AP) 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 (VSFP-CRM1) 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 during 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...
Objectives: 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. Myocardium (MYOCID), a promyogenic transcription factor with anti-apoptotic activity, and telomerase (TERT), an anti-senescence promoter, have applications in patients with MI.

Methods: AT-MSCs from the adipose tissue of aged (12-month-old) male C57BL/6 mice were transduced with lentiviral vectors encoding TERT and MYOCID. 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 MYOCID (2.5x10^5 cells/20 μL).

Results: AT-MSCs overexpressing TERT and/or MYOCID decreased the area of fibrosis (Figure A-D) and increased arteriogenesis (Figure A-D) and myocardial fractional thinning 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, GATRA, Nkx2.5, MEF2c and myocardin A (Figure E).

Conclusions: The delivery of the TERT and MYOCID 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 myocellular repair
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Objective: Stabilization of the cardiac SDF-1/CXCR4 axis preserves myocellular 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 SDF-1-EGFP and CXCR4-EGFP mice were subjected to optimal doses (80mg/kg i.p.) of the prolyl hydroxylase Inhibitor dimethyl oxalylglycine (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 & 80μg/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 normoxic and ischemic conditions with and without DMOG treatment.

Results: SDF-1-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 later 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 Fik1+ 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+ subpopulation in infarcted hearts associated with 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 myocellular repair.

P1348 | BENCH
Soluble factors secreted by regulatory T cells promote cardiomyocyte proliferation during embryonic development and after myocardial infarction
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Background: A still unresolved issue in the cardiac regeneration field is the reason why cardiomyocytes (CMs) stop proliferating early after birth. A major change occurring at birth is a sudden lack of exposure to maternal blood, where regulatory T cells (Tregs) are expanded to promote tolerance toward the fetus.

Methods and results: The role of Tregs in controlling CM proliferation was first assessed on neonatal rat CMs by measuring EdU incorporation. The Treg-conditioned medium induced CM proliferation (EdU+ CMs): 10±2% in control vs. 31±5% in Treg medium, similar to the serum harvested from pregnant or from neonatal (but not adult) animals. To deplete Treg in vivo we injected either an anti-CD25 antibody in CD1 mice or the dyethion in DEREG mice (expressing both EGFP and the DT receptor under the control of the Treg-specific Foxp3 promoter) and observed decreased cardiomyocyte proliferation in the developing embryonic hearts (EdU+ CMs: 20±5% in control vs. 13±4% in depleted animals). Biplex analysis indicated that a few cytokines (Mip-1beta, RANTES, GM-CSF and IL-10) were particularly abundant in Treg-conditioned medium and in the sera of pregnant and neonatal mice. To evaluate the therapeutic potential of Tregs following myocardial infarction, we either depleted or administered Tregs in vivo. Treg depletion resulted in depressed cardiac function (EF at 1 week: 55±6% in control vs. 42±8% in Treg-depleted mice), increased infarct size (18±4% vs. 44±7%), increased number of major events (aneurysms, cardiac ruptures and deaths); histological analysis revealed that Treg depletion resulted in a significant increase in the number of EDU+ proliferating cardiomyocytes. Treg tracking in DEREG mice indicated a prompt recruitment of these cells to the ischemic region, paralleled by increased expression of Foxp3, TGF-β, IL-10 (Treg markers) and IL-2 (Treg chemotactic factor).

Conclusions: Tregs act in a paracrine manner to promote cardiomyocyte proliferation during development, when they are expanded in the maternal blood to promote tolerance toward fetal antigens, as well as during myocardial infarction, when they sustain cardiac function and improve lesion healing.
The muscular dystrophies are inherited diseases characterized by progressive or end-stage dilated cardiomyopathy. Specific and varies from asymptomatic ECG changes to conduction disorders requiring progressive muscle wasting and weakness. Cardiac involvement is disease specific and important cause of this variability. Cardiomyopathy is most common and severe in patients with distal MD, in 23.1% with LG, in 29.4% with FSH and in 23.5% with Duchenne MD, in 55% of patients with Myotonic dystrophies, in 23.8% of patients with Becker MD, in 4.8% of myotonic dystrophy patients, 50% of Becker MD patients, in 4.8% of myotonic dystrophy patients.

Aim: Recently, an “inverse remodeling” during growth has been described in patients with HCM related to mutations in RAS-MAPK genes. The aim of this study was to evaluate progression/regression of LVH during growth in children with sarcomeric HCM.

Methods: We studied 52 patients fulfilling diagnostic criteria for hypertrophic cardiomyopathy, and without any clinical or laboratory evidence of syndromes or metabolic diseases. Median age at diagnosis was 10 yo (9±5; range from fetal life to 16 yo). Among 38 patients who underwent/ completed genetic analyses, 22 (58%) had mutations in sarcomeric genes.

Results: Four patients (7%) showed no sign of progression and/or regression of LVH during follow-up. Patient 1 was diagnosed with asymmetric HCM during intrauterine life, and confirmed at birth (maximal wall thickness, MWT, at anterior interventricular septum was 8 mm; z-score +7). She started verapamil therapy. At the last clinical evaluation (15 yo), her septal thickness was nearly normal (MWT 12 mm; z-score 2.3). In this patient, we detected a variant in the MYH7 gene (c.976G>C, p.A326P). In patient 2, the diagnosis was performed at 8 months with detection of MWT at anterior septum equal to 12 mm (z-score +5.6). Septal thickness remained stable during follow-up (2 mm at the age of 14 years old; z-score +2.8). At last cardiovascular examination (17 years old), the patient showed a MWT of 18 mm (z-score +7.6). This patient carried a pathogenic variant of MYH7 gene (p.R717W). In patient 3, the diagnosis of obstructive HCM was made at birth with evidence of MWT 14 mm (z score +13) at anterior septum. He was commenced on beta blockers. At the last follow up (9 years old), septal thickness was 10 mm (z score +1.5) and no residual obstruction has been observed. This patient had a double mutation in MYB PC3 gene (ex13p3.P731R + ex13p.P1070X). At 15 years of age, the patient was commenced on beta blockers. He was referred at our clinic for echocardiography with no sign of progression of LVH. LVH did not progress, and all ventricular septal defects, except one, closed. Despite a positive family history, no sarcomeric mutations have been found in this patient.

Conclusions: In a subgroup of children with early onset HCM, we observed a lack of progression or regression of LVH during growth. It is conceivable that genetic, epigenetic, environmental and hormonal factors may contribute to the progression of LVH during fetal life and adolescence in patients with HCM.
Conclusions: Electroanatomic mapping with direct visualization of the bioprobe in the map increase diagnostic sensitivity of EMB in patients with right-sided VA. EAM-guided EMB may play a relevant role in the diagnosis of the arrhythmogenic substrate thus modifying treatment and prognosis.

BEST POSTERS IN OBESITY

P1356 | SPOTLIGHT
Does childhood adiposity, or change in adiposity from childhood to adulthood, predict metabolically healthy obesity in adulthood?

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Background: While obesity is associated with a higher risk of developing cardiovascular disease and type 2 diabetes, not all obese individuals have metabolic complications such as impaired glucose metabolism, hypertension and dyslipidemia. The term metabolically healthy obesity (MHO) is now widely used (though there is no standard definition) and estimates of its prevalence in obese adults range from approximately 20–30%. Possible predictors of MHO are shorter life-time exposure to obesity and less weight gain.

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 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 ≥30kg/m², normal fasting glucose (<5.6mmol/L), triglycerides (<1.7mmol/L), HDL-cholesterol (>1.04mmol/L), men, >1.3mmol/L women), blood pressure (<130/85mmHg) 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 HDL-cholesterol, or a one standard deviation (SD) increase in BMI or WC from childhood to adulthood.

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 of the 323 obese individuals at follow-up, 79 (24.5%) were MHO. Child-

Conclusion: MHO in adulthood was less likely in those who were overweight or obese in childhood, but was less likely in those obese adults who had greater gains in BMI or WC since childhood.

P1357 | BEDSIDE
Association of body mass index with the incidence of stroke and death in real-world atrial fibrillation patients: The Fushimi AF Registry


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Background: The incidence of stroke/SE and death in AF patients are limited. Does childhood adiposity, or change in adiposity from childhood to adulthood, predict metabolically healthy obesity in 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 ≥30kg/m², normal fasting glucose (<5.6mmol/L), triglycerides (<1.7mmol/L), HDL-cholesterol (>1.04mmol/L), men, >1.3mmol/L women), blood pressure (<130/85mmHg) 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 HDL-cholesterol, or a one standard deviation (SD) increase in BMI or WC from childhood to adulthood.

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 1SD increase in BMI or WC from childhood to adulthood was associated with a significantly decreased likelihood of MHO (RR 0.69 CI: 0.59–0.81). WC RR: 0.69 CI: 0.59–0.81, WHR RR: 0.67 CI: 0.59–0.81, BMI RR: 0.76 CI: 0.65–0.90.

Conclusion: MHO in adulthood was less likely in those who were overweight or obese in childhood, but was less likely in those obese adults who had greater gains in BMI or WC since childhood.

P1358 | BEDSIDE
Diabetes, intakes of red meats, and metabolically healthy obesity in young adults


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Background: While obesity is associated with a higher risk of developing cardio-

Methods: We studied a sample of 402 people aged 45–64 randomly selected in 2005–2007 from the general population of three French areas. Data collection included a 3-day food record, questionnaires, clinical examinations, and a fasting blood sample, for assessing cardiovascular risk factors. Fatty acid content was measured in erythrocyte membrane phospholipids, thus providing a more objec-

Results: The sample comprised 50% of women. Erythrocyte contents in 15:0 and 17:0 fatty acids significantly increased with the consumption of dairy prod-

Conclusion: Elevated erythrocyte membrane phospholipid content in 15:0 and 17:0 saturated fatty acids is associated with higher fatty acid content, no significant relationship was observed for dihomo-gamma-linolenic acid, low-HDL cholesterol, high LDL-cholesterol and SCORE carbosuc-

P1359 | BENCH
Fresh fruit consumption in relation to mortality from cardiovascular and non-cardiovascular diseases

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Purpose: Previous studies of mainly Western populations have shown relatively

Methods: In 2004–08, the China Kadoorie Biobank Study recruited 0.5 million adults from 10 diverse localities in China, recording nearly 23,000 deaths during ~7 years follow-up. Frequency of fresh fruit consumption (in 5 categories) was as-

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P1362 | BEDSIDE

The impact of target lesion characteristics assessed by optical coherence tomography on microvascular resistance in patients with non-ST-segment elevation acute coronary syndrome

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Background: 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 FFR gray zone and clinical outcome of pts with an isolated stenosis and an FFR value in the gray zone from the optical coherence tomography registry.

Methods and results: We aimed to investigate the incidence of neoatherosclerosis (NA) after stenting, its long-term incidence, risk factors and impact on future clinical events remain unclear.

Purpose: We aimed to investigate the incidence of NA stratified by stent types and impact on major adverse cardiovascular events (MACE). In angiographic analysis, there were significant differences in the frequency of culprit lesion location in LAD (group S: 72%, group M: 50%, P=0.01), minimum lumen diameter (group S: 1.18±0.38 mm, group M: 1.35±0.33 mm, P=0.01), % diameter stenosis (group S: median: 55.2%, IQR [48.0–57.8], group M: 53.0% [48.0–57.8], P=0.02), and lesion length (group S: 5.3±1.3mm, [10.5–16.5], group M: 11.5mm [9.2–14.8], P<0.01) between the two groups. In OCT analysis, there were significant differences in the lipid arc (group S: 170° [93.8–227°], group M: 143° [92–174°], P=0.01), cap thickness (group S: 110±16mm [63–150], group M: 140μm [92–187], P=0.01), and frequency of TCFA (group S: 22%, group M: 8%, P<0.01) between the two groups. In sub-group analysis among only LAD lesions (n=116), similar results were observed.

Conclusions: Lesions of physiological severe coronary stenosis in SAP may be correlated with lesion instability assessed by OCT. These findings may challenge the concept that lesions responsible for acute coronary syndrome should be treated in most cases provided that plaque rupture of TCFA evenly results in coronary events in the wide range of stenosis severity.
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: Out of 17380 pts undergoing FFR measurement, 31052 (18%) were not able to undergo FFR because of severe CAD, inappropriate FFR and low perfusion fraction. In patients with an FFR between 0.70 and 0.75, MACE’s were more frequent after MT than after revascularization (11% vs. 13%, respectively). MACE’s were also more frequent after MT than after revascularization in patients with systolic HF, and a consequent pulmonary vasoconstriction, responsible of the undesirable increase in pulmonary arterial pressure (SPAP: 40.1±7.6 vs 33.1±5.9 mmHg, p<0.05). In patients with an FFR between 0.81 and 0.85, MACE’s tended to be less frequent after MT than after revascularization (11% vs. 13%, respectively, p=0.057). Among pts treated with MT alone, a progressive increase in MACE was observed in the 3 FFR strata, FFR, 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 segment, decreasing FFR values were parallelled by an increase in overall mortality (p<0.0001 vs patients with FFR ≥0.85).

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.

BEST POSTERS IN BIOMARKERS

P1366 | BEDSIDE
Central apleas and chemoreflex activation influence on pulmonary hypertension in heart failure: role of adrenergic activation

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Background: Pulmonary arterial hypertension (PAH) is an established prognostic factor in patients with heart failure (HF). During or after passive (a “passive” component due to the increased left ventricular pressure, an “active” component due to pulmonary vascularity may be present. The mechanism behind pulmonary vasoconstriction being not fully understood, we hypothesized that central apleas (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 aplea/hypoaplea index –AHI>15. HF patients with CSR, compared with patients with normal breathing, presented with higher systolic arterial pulmonary pressure (0.69 mmHg, p<0.01), with no difference in systolic and diastolic function. Furthermore, patients with central apleas also presented with enhanced HVR (median 0.79, interquartile range -0.62 to 1.27 vs 0.43, OR 1.09–0.69 L/min/%, p<0.05) and HCVR (1.18, IR 1.10–1.31 vs 0.73, OR 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 μg/L, p<0.05). sPAP was indeed correlated with AHI (Spearman’s rho, R=0.60, p<0.001), HCVR (R=0.48, p<0.001), HVR (R=0.30, p<0.001) and norepinephrine (R=0.23, p<0.05). At univariate regression analysis sPAP was associated with AHI, HVR, HCVR, norepinephrine, NT-proBNP. At multivariate 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-mediated adrenergic activation in patients with systolic HF, and a consequent pulmonary vasoconstriction, responsible of the undesirable increase in pulmonary arterial pressure.

P1367 | BEDSIDE
Resting heart rate and disease severity in chronic heart failure: results from INDICATE

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Introduction: Elevated heart rate (HR) is known to be associated with increased morbidity and mortality in patients with chronic systolic heart failure (CHF). Epidemiological surveys (e.g., ESC HF Long-Term Registry) point to insufficient pharmacological control of increased HR in these patients.

Methods: We aimed to evaluate the current status of symptomatic burden, pharmacological treatment and comorbidities in German CHF outpatients. We conducted a cross-sectional multicenter study (INDICATE: ScreenIng of_toDay’s pa-tients with Chronic systolic heAr t failure). Data were collected from February to June 2012 by 793 cardiologists across Germany. Data were reported stratified by HR >75 vs. <75 beats per minute (bpm).

Results: In total, data from 15,148 patients with CHF were analyzed: mean age 70.41±10.73 years, 63% male, 87% in NYHA class II or III. Atiarl fibration (AF) was diagnosed in 27% of all patients (26% with paroxysmal AF). Despite current beta-blocker therapy in 86% of the total cohort (17% at least at target dose, 49% at 50–99% and 34% at <50% of target dose), HR was frequently inadequately controlled (HR ≥75 bpm). 42% of the study population had a HR >75 bpm, with 63% of these patients being in sinus rhythm. Hypertension, diabetes mellitus, anemia, permanent/peristent AF, lung and liver diseases were more prevalent and beta blocker use slightly less pronounced (84% vs. 87%) in patients with HR >75 vs. <75 bpm (p<0.05). Other heart failure medication and left ventricular ejection fraction were comparable between both subgroups. Subjects with HR >75 bpm were more often in NYHA classes III/IV (40% vs 32%), exhibited more often signs of decompensation like peripheral oedema (27% vs. 16%), and BNP values >400 pg/mL (56% vs. 50%), compared with subjects with END vs HR <75 bpm (p<0.05 for differences).

Conclusion: INDICATE is a large contemporary cross-sectional study in CHF outpatients in Germany, demonstrating that a significant proportion of patients exhibits a HR >75 bpm despite beta-blocker treatment. CHF patients with elevated HR ≥75 bpm show an increased burden of heart failure symptoms and also more concomitant chronic diseases compared with patients with HR <75 bpm. Control of HR according to current guideline recommendations should be pursued more intensively.

P1368 | BENCH
Impaired immune phenotype of circulating endothelial-derived microparticles in none-diabetic patients with chronic heart failure

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Background: Increasing attention has been paid to insulin resistance (IR) as a major cause of increased mortality 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 CHF patients.

Methods: The study retrospectively involved 300 CHF patients aged 48 to 62 years who were undergone multipar 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. Endos with non-IR derived activated and activated microparticles were phenotyped by flow cytometry.

Results: These were not significant differences between both cohort patients in EMPs labeled as CD144+CD31+, CD31+ annexin V+, and CD31+CD62E+ microparticles. In non diabetic patients with HR ≤75 bpm despite beta-blocker treatment. CHF patients with elevated HR ≥75 bpm show an increased burden of heart failure symptoms and also more concomitant chronic diseases compared with patients with HR <75 bpm. Control of HR according to current guideline recommendations should be pursued more intensively.

Conclusion: INDICATE is a large contemporary cross-sectional study in CHF outpatients in Germany, demonstrating that a significant proportion of patients exhibits a HR >75 bpm despite beta-blocker treatment. CHF patients with elevated HR ≥75 bpm show an increased burden of heart failure symptoms and also more concomitant chronic diseases compared with patients with HR <75 bpm. Control of HR according to current guideline recommendations should be pursued more intensively.

P1369 | BENCH
Lysyl oxidase overexpression impacts cardiovascular remodelling

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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.

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Purpose: Because LOX deficiency is lethal, we have developed a transgenic mouse model to study the impact of LOX overexpression on cardiovascular remodelling.

Methods and results: A new mouse model that over-expresses human LOX was 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 somatic micropumps (n=10 per group). Ang II-induced aortic diameter dilatation 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 echocardiology. 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 (LVPW) thickness in diastole and systole and the higher HWISW ratio compared with WT mice. Accordingly, the left ventricular inner di-ameter (LVIDd) in diastole and diastole was significantly lowered in TgLOX mice compared with WT animals. However, Ang II similarly increased the mRNA levels of hypertrophic markers such as ANP and β-MHC in both transgenic and WT mice. The values of cardiac output and stroke volume remained similar in both groups (TgLOX vs. WT). LOX overexpression (LOX–>90 mnmol) and the Ang II-induced expression of pro-inflammatory (Emr-1, IL6, Mmp-9) and fibrosis-related (Serpin-1, Coll-1) markers in cardiac tissue compared with WT mice.

Conclusions: We have developed a valuable model to improve our knowledge about LOX biology in the cardiovascular system. Our data evidence that LOX over-expression impairs cardiac function under hypertensive conditions.

BEST POSTERS IN TREATMENT OF HYPERTENSION

P1371 | BEDSIDE
Effect of annual blood pressure control on major adverse cardiovascular events in patients with resistant hypertension - From Ibaraki hypertension assessment trial (I-HAT)
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Background: Hypertension is a modifiable risk factor for coronary heart disease, stroke, and mortality. However, the prognosis of resistant hypertension (RH) in association with annual control levels of blood pressure (BP) has not been clear.

Purpose: This study aimed to clarify the impacts of RH and its annual BP control on cardiovascular events.

Methods: A total of 1052 participants from Ibaraki hypertension assessment trial multi-center registry treated for hypertension with RH (n=152) and non-RH (n=900) were followed up for 4±1 years. RH was defined as uncontrolled hypertension (HT) at enrollment and 3 months (BP>140/90 mnmol), and aortic stiffness measured by PWV >10 m/s. Annual BP control was defined as BP <140/90 mnmol, PWV <10 m/s.

Results: The RH group was older (71±11 vs. 66±10 years, p<0.001) and demonstrated a higher prevalence of female (53.9% vs. 43.1%, p=0.014) and higher level of serum creatinine (0.87±0.32 vs. 0.76±0.26 mg/dL, p=0.001) than the non-RH group. A higher proportion of uncontrolled hypertension in RH group as compared to non-RH group decreased annually (69.7% vs. 27.7% at 1 year, p=0.001; 38.9% vs. 31.0% at 2 year, p=0.081; 36.1% vs. 26.5% at 3 year, p=0.037; 35.1% vs. 25.5% at 4 year, p=0.040; 32.1% vs. 22.3% at 5 year, p=0.036). During the follow-up period, 82 patients (7.8%) developed MACE. A 5-year MACE free survival rate was higher in non-RH group than RH group (92.1±1.0% vs. 85.4±3.2%, p=0.021 by the log-rank test). RH increased the risk of MACE in univariate analysis (HR 1.8, 95% CI 1.1–3.1; p=0.003). Multivariate analyses adjusted for age, however, revealed that independent risk factors for MACE in univariate analysis (HR 1.8, 95% CI 1.1–3.1; p=0.003) and uncontrolled hypertension at the final year (adjusted HR 9.9, 95% CI 2.0–48.8; p=0.005).

Conclusions: RH demonstrated a higher risk of MACE before age-adjustment. In patients with RH, the risk for MACE was increased by female gender and un-controlled hypertension during follow-up.

P1372 | BEDSIDE
Arterial hypertension, endothelial microparticules, and endothelial dysfunction
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Background: Membrane microparticules (MPs) are submicron membrane vesi-cles shed from a diversity of cells. MPs are markers of cardiovascular risk, but may also carry functional activity. In vitro work suggests that the mobilization is modulated by cell activation and apoptosis pathways and is inhibited by flow-dependent nitric oxide production. Whether mechanical factors such high blood pressure and mechanical endothelial injury lead to mobilization of MPs and the biological effects of these MPs are not known.

Objectives: To investigate how arterial hypertension modulates circulating MP levels in the chronic and acute setting as compared to mechanical catheter related endothelial injury and how this relates to endothelial function.

Methods: (1) We investigated circulating MPs along with functional and mechan-ical characteristics of the arterial system in healthy subjects (n=10), patients with isolated arterial hypertension (n=8), patients (n=10) with CAD and arterial hyper-tension (CAD+HT) and patients (n=10) with CAD but without arterial hypertension (CAD-HT); (2) We studied patients with a hypertensive crises at admission before and at 4h and after normalization of BP by urapidil. (3) We studied MPs release and vascular function before and after coronary diagnostic angiography in pa-tients with stable CAD.

Results: As compared to matched healthy controls, patients with arterial hyper-tension exhibited significantly elevated although CAD-HT was associated with increased levels of all MP populations as compared to healthy controls, CAD+HT exhibited even higher levels of all MP populations and even further decreased FMD (4.2±0.9 vs. 2.9±0.7%), Univariate inverse correlations were found between all endothelial MPs and FMD with the strongest correlation observed between CD144+ and FMD (r=−0.62) and AIx (r=−0.64). In patients with hypertension, lowered FMD was noted at admission (2.5±0.7%) and significantly increased at 4h after BP normalization (3.0±0.7%, p=0.046). Along with the FMD improvement, endothelial and red cell MPs significantly decreased; Platelet and white cell MPs remained unaffected. Diagnostic coronary angiography in CAD patients led to an acute increase in endothelial and platelet MPs at 1–4 h, but not white and red cell MPs.

Conclusions: Endothelial injury due to mechanical forces i.e. blood pressure and catheter-induced arterial injury may mobilize endothelial MPs along with endothelial dysfunction even in remote vascular beds. Circulating endothelial MPs may not only be a marker of endothelial injury but may also induce endothelial dysfunction.
Background: The health hazards of uncontrolled Blood Pressure (BP) as well as tightly controlled BP 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 in predicting outcomes in cardiometabolic disease patients remains unknown.

Purpose and methods: The aim of this project is to study interaction between depression and BP control in predicting adverse outcomes at 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 model for survival analysis.

Results: Out of 35537 patients, 2068 (5.8%) had at least one vascular event during the 4 years of follow-up. Depression (defined as a 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 subsequent vascular event (HR 1.42; 95% CI 1.17–1.71) compared to those with tightly controlled SBP and without depression. In DBP sub-group analysis, patients with uncontrolled DBP and depression were at 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 co-morbid conditions, total cholesterol levels, body mass index and antidepressant 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.

P1376 | BEDSIDE
Dispersion of T-wave area in left precordial leads predicts sudden cardiac death in standard 12-lead electrocardiogram

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Background: Abnormal ventricular repolarization is associated with increased risk of lethal ventricular arrhythmias and SCD.

Purpose: We developed a novel ECG marker, T-wave area dispersion (TW-AD), which measures the repolarization heterogeneity by comparing similarities in T-wave areas and tested whether it can identify patients at risk for sudden cardiac death (SCD) in an adult general population based sample.

Methods: TW-AD was measured from left precordial leads (V4-V6) of standard digital 12-lead ECG in 5618 adults (46% men; age 50.9±12.5 years) who took part in Health 2000 Study, an epidemiological survey representative of the entire Finnish adult population.

Results: During average follow-up of 7.7±1.4 years, a total of 72 SCD occurred. Decreased TW-AD in left precordial leads (V4-V6, see Figure) was univariately associated with SCD (P<0.001). Area under the ROC curve for TW-AD was 0.808. TW-AD<0.61 was associated with a 9.1-fold relative risk (95% confidence interval [CI]: 5.7–14.5). P<0.001 for SCD. When adjusted with clinical risk markers (age, gender, body mass index, systolic blood pressure, total cholesterol, heart rate, ECG-based left ventricular hypertrophy, QRS duration, arterial hypertension, diabetes, coronary heart disease and previous myocardial infarction) TW-AD remained as an independent predictor of SCD with a 4.0-fold adjusted relative risk (95% CI: 2.4–6.6; P<0.001). When TW-AD was added to the clinical model, it significantly improved model discrimination (C-index: 0.871 vs. 0.891, P<0.001).

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

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P1377 | BEDSIDE
QRS fragmentation induced by ventricular pacing predicts appropriate defibrillator therapies and total Mortality in subjects with cardiomyopathy

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We examined total mortality and appropriate ICD therapy predictive value of QRS fragmentation (QRFS) 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. QRFS 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), or lateral (I, aVL, V6) myocardial segments. Patients were followed for appropriate ICD therapies and total mortality until December 2014.

Results: A total of 245 patients 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 QRFS was observed in 159 subjects in any myocardial segment. On multivariate analysis, EF <35%, diabetes, presentation of ventricular arrhythmias, baseline and RV pacing-induced QRFS were associated with higher mortality and appropriate ICD therapies. On multivariate analysis RV pacing induced QRFS 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 citalopram (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 ms with 5 μM risperidone, +30 ms with 10 μM risperidone, p<0.05). Administration of risperidone also significantly increased spatial dispersion of repolarization (2 μM:+16 ms, 4 μM:+19 ms, p<0.05). Lowering of potassium concentration in bradycardic 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. Risperidone led to an increase in QT-interval (5 μM:+10 ms, 10 μM:+26 ms, p<0.05) and APD90 (2 μM:+13 ms, 4 μM:+29 ms, p<0.05) without significant effects on dispersion of repolarization (2 μM:+5 ms, 4 μM:+6 ms, p=ns). Again, no proarrhythmia was observed in this group. Application of citalopram also increased QT-interval (2 μM:+48 ms, 4 μM:+62 ms, p<0.01) and APD90 (2 μM:+13 ms, 4 μM:+29 ms, p<0.05) without significant effects on dispersion of repolarization (2 μM:+5 ms, 4 μM:+6 ms, 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 QT-interval, dispersion of repolarization and an increased occurrence of EAD. In contrast, quetiapine and citalopram showed a safe electrophysiologic profile. In these groups, dispersion of repolarization remained stable although myocardial repolarization was significantly prolonged.

P1379 | BENCH
Sudden cardiac death with structurally normal heart: results from the West of Scotland Familial Arrhythmia Network (FANS) and Inherited Cardiac Conditions Clinic
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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%) had a echocardiogram. 100% of post-mortem results were obtained and 21/27 (78%) underwent genetic testing. Pathogenic mutations were identified in a total of only 3/42 (7%) cases (2 SCN5A and 1 RYR2). History of alcohol intake/non-toxic levels of alcohol were present on post-mortem in 22/56 cases (39%), mean age 31.3±9.6 years and 15/22 (68%) male.

We combined these findings with that obtained from the inception of the ICC 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 (75%) cases and pathogenic mutations were identified in a total of only 3/42 (7%) cases (2 SCN5A and 1 RYR2).

Conclusion: Family follow-up was less than ideal despite a formal mechanism established to organise 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.
tricular arrhythmias and sudden cardiac death. A recent report identified a malignant form characterized by the triad of bileaflet MVP, multifocal PVCs and interlateral 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 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). Interlateral 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

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Background: According to current guidelines on myocardial revascularization, immediate coronary angiography should be considered 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, women had a higher survival rate till hospital admission (18% vs. 26%) and they had a lower coronary angiography performed and lead to lower rates of angioplasty. Efforts are still needed to improve the management and prognosis of OHCA in women.

Prognosis and management by gender

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of OHCA (n)</td>
<td>11420</td>
<td>7068</td>
<td>4333</td>
</tr>
<tr>
<td>Alive at hospital admission (%)</td>
<td>23.07</td>
<td>26.26</td>
<td>17.89</td>
</tr>
<tr>
<td>Angiography %</td>
<td>54.96</td>
<td>59.66</td>
<td>50.63</td>
</tr>
<tr>
<td>Angioplasty %</td>
<td>4.26</td>
<td>5.71</td>
<td>1.90</td>
</tr>
<tr>
<td>Angioplasty % per survivor</td>
<td>18.49</td>
<td>21.75</td>
<td>10.63</td>
</tr>
<tr>
<td>Angioplasty per angiography %</td>
<td>34.19</td>
<td>36.45</td>
<td>26.17</td>
</tr>
</tbody>
</table>

All differences were significant. OHCA, out-of-hospital cardiac arrest.

Conclusion: In an OHCA registry performed in the Greater Paris Area, the prehospital survival rate was lower in women. Coronary angiography was less often performed and lead to lower rates of angioplasty. Efforts are still needed to improve the management and prognosis of OHCA in women.

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

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Background: The 2010 cardiopulmonary resuscitation guidelines suggest that ventricular fibrillation/ventricular tachycardia is more effectively terminated with biphasic waveform defibrillation than 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). Therefore, there is no clinical evidence for the superiority of biphasic waveform defibrillation over monophasic waveform defibrillation in OHCA patients.

Purpose: We aimed to show 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.

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 was obtained from a prospectively recorded national 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 survival after cardiac arrest. 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 1.19–1.72). In the multivariable logistic regression model for subgroups 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: 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.
Conclusions: In witnessed OHCA patients with an initial shockable rhythm, bifascicular wavefront defibrillation was significantly associated with improved 1-month survival and 1-month neurological outcomes compared to the outcomes with monophasic wavefront defibrillation.

P1385 | BEDSIDE
ADRB2 Gln27Glu polymorphism impacts the timing of ventricular fibrillation during the acute phase of myocardial infarction
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Introduction: The genetic variant rs1042714 (Gln27Glu) in ADRB2 gene coding for the β2 adrenergic receptor is associated with sudden heart 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<0.0015 in 1000 < 0.0015 in 1000 Genomes Project data. The first mutation (c.592T>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.1293T>A, p.M1311K) and third (c.6859A>G, p.I2287V) mutations were identified in patients with PVT initiated by premature ventricular contractions with left bundle branch block. A 10-year-old boy with

AKAP9-M1311K had several episodes of syncope, and PVT was recorded after urination during Holter recording. A 25-year-old woman with AKAP9-12287V lost consciousness after lunch. After admission, PVT was recorded on ECG monitoring. The forth mutation (c.9257G>A, p.D3386G) carrier was a 19-year-old man who suddenly fell down while watching TV. Cardio-pulmonary resuscitation was started by his family, and AED confirmed VF, which was successfully reversed to sinus rhythm. The last mutation (c.11135G>C, A3712Q) carrier was a 14-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, QTc intervals and ORS durations were within normal range. Among the VF and PVT patients, AKAP mutation carriers were significantly younger than non-carriers (mean age, 17.6±5 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.

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 [BS], early repolarization syndrome [ERS], and idiopathic ventricular tachycardia [IVT]). 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 differences 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 (BS 16, ERS 7, IVT 4 patients) who experienced non-sustained VF on ICD interrogation between April, 1996 and April, 2014. A total of 228 episodes were reviewed by two independent cardiologists.

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±33 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=0.278) 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
Prolonged right ventricular ejection delay identifies high risk patients and gender differences in Brugada syndrome
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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: We included 124 BS patients (72 males and 52 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 (RVFW) and lateral LV wall (LVED). From these parameters, the interventricular ejection delay between both walls (IVED) was calculated.

Results: BS patients had longer RVFW’s and IVED’s compared to the CTR. BS patients with a previous history of syncope or spontaneous ventricular arrhythmia demonstrated longer RVFW’s and IVED’s. Male BS patients demonstrated longer RVFW’s and IVED’s than females. Male BS patients with malignant events had the longest delays. No significant differences regarding LVFW were observed between BS patients and CTR.
Clinical Electrophysiology, Frankfurt am Main, Germany; 2 McMaster University, Hamilton, Canada; 3 Medical Centre, Hungarian Defence Forces, Budapest, Hungary; 4 Leiden University Medical Center, Leiden, Netherlands; 5 Hospital P. Bode, 3, A.C. Akdis, T.F. Luescher, C. Brunckhorst, F. Duru, X. Vinolas, J. Neuzner, M. Glikson, J. Wang, J.S. Healey on behalf of RV conduction in males.

P1389 | BENCHMARK
Troponin T or I levels following ICD implantation with and without defibrillation testing and their predictive value for outcomes: Insights from the SIMPLE trial


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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 2,201/2,500 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±10.0 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, 0.68–1.88; 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 of clinical outcomes in ICD recipients.

P1390 | BENCHMARK
Increased myocardial expression of proapoptotic PERP, proadipogenic CPT1B and phospholamban in arrhythmogenic right ventricular cardiomyopathy/dysplasia compared to dilated cardiomyopathy and controls

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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 pathological 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=0.0004), and plakophilin-2 (ARVC/D vs. DCM/control: p=0.0014). The proapoptotic molecule PERP (ARVC/D vs. DCM/control: p=0.0088) of the proadipogenic molecule carnitine-palmitoyltransferase-1b (CPT1B) (ARVC/D vs. DCM/control: p=0.0500) and calcium channel associated molecule phospholamban (ARVC/D vs. DCM/control: p=0.0056) were increased. 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
ABCBI gene variants, digoxin and risk of sudden cardiac death in a general population


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

Objectives: To investigate the interaction between variants within the ABCBI 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 relevant polymorphisms extracted from 1000 Genomes imputed ABCBI 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±9.6 years and 42% was male. In nonusers of digoxin the risk of SCD was not different across genotypes. In digoxin users, homoygous T allele carriers of C1236T (HR 1.90; 95% CI 1.09;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 ABCBI 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, homoygous T allele carriers of the ABCBI gene had an increased risk of SCD compared to digoxin users without one or T allele. This implies that the ABCBI genotype modifies the risk of cardiac digoxin toxicity. If these findings can be replicated in an independent cohort, testing ABCBI 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 | BEDSIDE
A novel cardiac ryanodine 2 receptor gene (RyR2) mutation as cause of sudden cardiac death by catecholaminergic polymorphic ventricular tachycardia


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 yo 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 yo half-brother suffered SCD, with inconclusive autopsy. His mother (II:2) and two half-sisters (II:2, II:7) reported history of stress-related syncope (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: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
Swave angle identifies ARVD with normal ECGs compared to healthy family members

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Introduction: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is associated with sudden death. Relatives of the proband are also at risk. Another inheritable disease, Brugada types 2 and 3, are associated with an increase in alpha and beta angles, based on the ’r’ or R’ waves. The duration of the upslope of the S-wave has diagnostic utility in ARVC. We aimed to assess whether first degree relatives at risk without other depolarization or repolarization abnormalities could be identified based on the acute angle of the S-wave in V1 or V2 (S-wave angle).

Methods: 12-lead resting ECGs from 54 patients meeting Task Force 2010 definite ARVC criteria (age 41 ±18.4 years, 58.1% males) were assessed. 32 did not fulfill depolarization or repolarization criteria (including upslope of the S-wave <55msec) 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 criteria with a p-value of 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 32% and 97%, respectively.

Conclusion: Discrimination of ARVC with normal variant ECG’s is improved with the S-wave angle, as in V2. This subtle change on the ECG may help to identify 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

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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 Society 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 protocol 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 disagreement 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, 8343 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 distribution:

- Type 1: two cases (0.024%), 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 individuals without sinus rhythm. We analyzed data from 7,889 patients, 52.5% were women. These are our final findings: Borderline QTc: 763 cases, weighted 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.

P1395 | BEDSIDE
Differences in risk factors and outcome of cardiac arrest in southern Sweden depending on cardiac or non-cardiac origin

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Introduction: Cardiac arrest (CA) has a mortality rate of approximately 75–90%. Little is known about midlife risk factors of later development of a CA and its outcome.

Objective: To evaluate the risk and outcome of CA in a middle-aged population with respect to cardiovascular risk factors.

Methods: We cross-matched individuals of the population based Malmö Diet and Cancer Study (n=30,447, baseline examination 1991–1996, age 50±7.6, 39.8% male) with the local CA registry of the city of Malmö (n=2758 CA events, 1999–2012). Baseline exposures were related to incident CA events, and in CA cases to outcome after CA using multivariate adjusted Cox proportional hazards model and reported results as hazard ratio (HR) (95% confidence interval).

Results: During a mean follow-up of 15.4±3.6 years, 378 cases (mean age at CA 74.6±7.1 years, 63.9% male) from the cohort suffered a CA, of whom 17.2% survived to discharge. 68.7% of the cases were determined to be of cardiac origin and 31.3% as non-cardiac. Independent midlife risk factors for CA of cardiac origin included coronary artery disease (CAD) (HR 3.37 (2.26–5.03) (P <0.001), diabetes mellitus (HR 2.58 (1.74–3.81) (P <0.001) and smoking (HR 1.96 (1.50–2.57) (P <0.001)). Elevated apolipoprotein-B, low apolipoprotein-A, and history of stroke were also significantly associated with an elevated risk for CA of cardiac origin.

Independent midlife risk factors for CA of cardiac origin included obesity (BMI≥30 kg/m²) (HR 2.41 (1.54–3.78) (P <0.001), smoking (HR 2.10 (1.36–2.23) (P <0.001)) and antihypertensive treatment (HR 2.09 (1.34–3.28) (P <0.001)).

Conclusion: Whereas classical cardiovascular risk factors increase the risk of CA of cardiac origin, obesity is the main risk factor for CA of non-cardiac origin. Thus, in addition to control of classical cardiovascular risk factors, our results suggest that prevention of midlife obesity may reduce the risk of CA.

Acknowledgement/Funding: European Research Council, the Swedish Heart and Lung Foundation, Swedish Research Council, Medical Faculty, Lund University.
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 SCD 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)

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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±10 vs. 56±14bpm, p=0.29), while maximum HR was lower on nadolol (120±20 bpm vs. 139±24 bpm, p=0.01). Also severity 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 (53±10 vs. 56±14 bpm, p=0.29), while maximum HR was lower on nadolol (120±20 bpm vs. 139±24 bpm, p=0.01). 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 (53±10 vs. 56±14 bpm, p=0.29), while maximum HR was lower on nadolol (120±20 bpm vs. 139±24 bpm, p=0.01). Also severity 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 (53±10 vs. 56±14 bpm, p=0.29), while maximum HR was lower on nadolol (120±20 bpm vs. 139±24 bpm, p=0.01). Also severity 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 (60%) than on metoprolol SR (96%) and no medication (92%) (both p<0.01). Also severity 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 (60%) than on metoprolol SR (96%) and no medication (92%) (both p<0.01).

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
Copy number variants of ion channels genes in Brugada syndrome: a cohort screening

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Background: Radiofrequency catheter ablation (RFCA) of ventricular fibrillation (VF) arising from Purkinje system appears to have a high success rate in general. However, we sometimes experience the concurrence of monomorphic ventricular tachycardia (VT) or newly emerging fast monomorphic VT.

Purpose: We evaluated the prevalence of monomorphic VT after RFCA for VF.

Methods: Nineteen consecutive patients (65±12 years) with primary VF due to ischecmic heart disease who underwent RFCA were prospectively analyzed from 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

VENTRICULAR ARRHYTHMIAS

P1399 | BEDSIDE
Monomorphic ventricular tachycardia conversion after ventricular fibrillation ablation in patients with ischemic heart disease

K. Masuda, A. Nogami, K. Kuroki, T. Machino, M. Igarashi, Y. Sekiguchi, K. Aonuma. Tsukuba University, department of cardiology, Tsukuba, Japan

Background: Radiofrequency catheter ablation (RFCA) of ventricular fibrillation (VF) arising from Purkinje system appears to have a high success rate in general. However, we sometimes experience the concurrence of monomorphic ventricular tachycardia (VT) or newly emerging fast monomorphic VT.

Purpose: We evaluated the prevalence of monomorphic VT after RFCA for VF.

Methods: Nineteen consecutive patients (65±12 years) with primary VF due to ischecmic heart disease who underwent RFCA were prospectively analyzed from 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
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 unexpectedly 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

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Introduction: Late potentials (LP) indicate slow conduction during sinus rhythm (SR) and are an accepted target for substrate based VT ablation in 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, 2 pacing sites) and LV endocardial electroanatomic mapping. Bipolar electrograms (EG) were displayed (0.13mV, 200mm/sec) and evaluated for voltage (BV), duration (EGD), 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), dense scar (DS, BV:<0.5mV) and border zone (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 (33±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±27ms). Pts with fast VTs had smaller SA 32±10% vs 38±12% of total LV: P=0.001), 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±6% respectively: all P<0.001). Of importance, in 27% of pts with fast VTs no LP were found compared to 74% in pts with VTCL>320ms (P<0.025; 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.
den death (SD), VF, and ventricular tachycardia (VT). Pilsicainide also induced VAs in 41 patients (15%; PI-VA 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.

**P1404 | BEDSIDE**

**Improvement in ventricular function and low incidence of ventricular arrhythmias in dilated cardiomyopathy**

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**Background:** Current guidelines assign a IB indication for implanting a cardioverter defibrillator (ICD) in patients with non-ischaemic dilated cardiomyopathy (DCM) who have an left ventricular (LV) ejection fraction (LVEF) <35% and who are in 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 determine 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 LVEF <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 allografts. 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), 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 implantations.

**Acknowledgement/Funding:** This work was supported by a grant from Inger and John Fredriksen to the Department of Cardiology, Oslo University Hospital, Rikshospitalet, and an un

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**P1405 | BEDSIDE**

**Scarc transmurality as a criterion for first-line endo-epicardial substrate-guided ventricular tachycardia ablation in ischemic cardiomyopathy**

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**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: contrast-enhanced-MRI (hyper-enhancement ≥75% of wall thickness), echocardiography (dyskinesia/akynesia + hyperrefrerenency + 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 8±11.7 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).

**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**

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**Background:** Brugada syndrome is characterized by coved type ST segment elevation ≥2 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 amiodarone (1 mg/kg) or flecainide (2 mg/kg), were analysed. A positive response was defined as the occurrence of type-1 ST-segment elevation in ≥1 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 ≥0.04 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 multivariate analysis, higher QRS duration in V1-V2 than in V5-V6 (OR: 2.4, 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).

**Table 1. Significant ECG parameters**

<table>
<thead>
<tr>
<th>Consensus Conference criteria</th>
<th>QRS duration in V1-V2</th>
<th>QRS duration in V5-V6</th>
<th>r wave duration in V1-V2</th>
<th>S wave duration in II, III, aVF</th>
</tr>
</thead>
<tbody>
<tr>
<td>r wave duration ≥0.04 s in V1-V2</td>
<td>r wave duration ≥0.04 s in V1-V2</td>
<td>S wave duration ≥0.04 s in II, III, aVF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity 63%</td>
<td>specificity 60%</td>
<td>p</td>
<td>Odds ratio</td>
<td></td>
</tr>
<tr>
<td>55%</td>
<td>74%</td>
<td>&lt;0.001</td>
<td>3.41</td>
<td></td>
</tr>
<tr>
<td>74%</td>
<td>56%</td>
<td>&lt;0.001</td>
<td>3.52</td>
<td></td>
</tr>
<tr>
<td>71%</td>
<td>56%</td>
<td>&lt;0.001</td>
<td>3.51</td>
<td></td>
</tr>
<tr>
<td>75%</td>
<td>57%</td>
<td>&lt;0.001</td>
<td>3.40</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** All the significant variables at the univariate analysis show a good balance between sensitivity and specificity. The independent predictors of positive test were greater QRS duration in leads V1-V2 as compared to leads V5-V6.
V6 and S wave duration ≥0.04 s in leads II, III and aVF, both expression of a conduction delay in the right ventricular outflow tract.

I. Accentuated T wave in V6 and S wave duration ≥0.04 s in leads II, III and aVF, both expression of a conduction delay in the right ventricular outflow tract.

II. Recordings of atrial electrograms are necessary for diagnosis, as the diagnosis of CPVT can be made only by recording atrial electrograms during exercise or with an event recorder.

III. Genetic screening is based on the use of the HaloPlex™ System (Agilent Technologies) prior to HiSeq sequencing (Illumina). The custom kit covers 163 genes previously reported as involved in cardiac arrhythmias, conduction defect and cardiomyopathies.

IV. The study identified mutations in almost 50% of IVF patients after a cardiac arrest, indicating that genetic testing could be a valuable tool in identifying patients at risk of sudden cardiac death.

V. Conclusion: The study identified mutations in almost 50% of IVF patients after a cardiac arrest, indicating that genetic testing could be a valuable tool in identifying patients at risk of sudden cardiac death.
a highly conserved across the species residue, and the location in the protein was adjacent to critical calcium binding loops in the calmodulin carboxy-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.

**BASIC MECHANISMS OF ARRHYTHMIAS**

**P1411 | BENCH**

Activation of normally quiescent Purkinje-myocardial junctions during acute myocardial ischaemia - an unexplored arrhythmogenic mechanism

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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 FS was constructed to test the hypothesis.

Results: The percentage of RV activated within 5ms decreased from baseline 53±6% to 42±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 ischemia (Figure). This phenomenon was abolished if treated with the gap junction enhancer rotigaptide. In the computer model, a 6% increase in conductivity was sufficient to render quiescent PMJs active. Increases in 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-arrhythmic as they increase the pathways for meandering wavefronts and the likelihood of wave collision.

Acknowledgement/Funding: NHRI Clinical Lectureship (1716), Academy of Medical Sciences Starter Grant (AMS-SGCL8-Ng), BHF Travel Fellowship (FS/11/68/20917)

**P1412 | BENCH**

Activation of normally quiescent Purkinje-myocardial junctions during late ischaemia (Figure). This phenomenon was abolished if pre-treated with the gap junction enhancer rotigaptide. In the computer model, a 6% increase in conductivity was sufficient to render quiescent PMJs active. Increases in the fraction of functioning PMJs accelerated endocardial activation, increasing surface breakthroughs and the complexity of activation, matching the experiments.

Acknowledgement/Funding: This work was supported by grants from the National Natural Science Foundation of China (No. 81770162 and No. 81470457)

**P1413 | BENCH**

Fibrotic stress induces mitochondrial remodelling via mitofusin-2 in atrial cardiomyocytes

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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 in 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 or the L-type calcium antagonist Verapamil. Western blot analysis of whole-cell lysates and quantitative real-time PCR demonstrated no appreciable change in or the L-type calcium antagonist Verapamil.

Conclusion: CLOCK-BMAL1 regulated arrhythmogenesis

Acknowledgement/Funding: This work was supported by grants from the Natural National Science Foundation of China (No. 81770162 and No. 81470457)

**P1414 | BENCH**

Attenuation of CLOCK-BMAL1 decreases the occurrence of ventricular arrhythmia in chronic heart failure

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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 β-1-AR and cir-

diurnal variation of VA (P<0.05). Importantly, the expression of β-1-AR and CLOCK-BMAL1 were attenuated in CHF at CT3 and CT15 were recorded and VA were induced by PES.

Results: Sham operated animals showed circular oscillations in the expression of β-1-AR and CLOCK-BMAL1 (P<0.05), but not in β-2-AR (P>0.05). Importantly, the expression of β-1-AR and CLOCK-BMAL1 were attenuated in CHF at CT3 and CT15 (P<0.05). Luciferase and ChIP-PCR analysis revealed that BMAL1 could bind to the enhancer of β-1-AR to regulate arrhythmia severity after CHF (P<0.05). Ad-CLOCK and Ad-BMAL1 co-infection resulted in overexpression of β-1-AR and a greater incidence of arrhythmogenic activity in myocytes. During ISO and ISO + ICI infusion, the diurnal variation in response of β-1-AR activation translated to a greater incidence of VA at CT3 (P<0.05), whereas ISO + CGP infusion had no diurnal variation of VA (P>0.05).

Conclusion: CLOCK-BMAL1 affected repolarization of ventricular myocytes and regulated ISO-induced arrhythmogenesis through β-1-AR.

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P1414 | BENCH
Melatonin protects against low potassium induced ventricular fibrillation by preventing dephosphorylation and redistribution of ventricular connexin-43 in isolated rat hearts
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Rationale: 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), rendering 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 mMol K+) followed by K+-deficient (1 mMol) perfusion in the absence or presence of 100 μM melatonin. Low K+ perfusion was maintained 25 min unless 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 BiolabF 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<0.0081), 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 significantly increased in melatonin, however, the trend towards increased total Cx43 expression 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.

P1415 | BENCH
Reduced activity of dorsal vagal preganglionic neurons associated with synuclein pathology predisposes the heart to ventricular arrhythmia
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Introduction: Vagus nerve stimulation has an antiarrhythmic effect, it reduces the refractoriness, prevents arrhythmias and increases the ventricular effective refractory period (VERP). Despite this evidence, there has been no attempt to study the central nervous mechanisms underlying the antiarrhythmic effect of cardiac vagal innervation. Since neurons of the dorsal vagal motor nucleus (DVMN) project to the cardiac motor neurons, cardiac autonomic neurones against pro-arrhythmic features within the ventricle, we hypothesised that these neurones 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 (TTKO), α-syn(−/−), neurons were made 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 octopolar 1.1 F miniature cardiac electrophysiology electrode was advanced into the atrio-ventricular node for the assessment of VERP. 10 paced beats (10 ± 1 ms) 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 neurones were made using coronal (200 μm) brainstem slices, obtained from 12–16 month-old TTKO and TKO (n=4) mice.

Results: Six months old TKO mice and their WT counterparts showed no significant differences in cardiac electrophysiology: both VERP (37.0 ± 5.2 ms) and ECG features including QTC were similar. In contrast, 12–18 months-old TKO mice displayed a shorter VERP (30±0.8 ms vs 43±3.1 ms in the WTs, P=0.02, Wilcoxon Rank-Sum test).

Discussion: These data suggest that synuclein pathology is associated with reduced activity of vagal preganglionic neurones in the dorsal vagal motor nucleus leading to manifestation of a clear pro-arrhythmic substrate in the ventricle.

P1414 | BENCH
Heterozygous plakoglobin deficiency results in increased binurventricular beta-catenin expression
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Background: The cell-cell contact protein plakoglobin (β-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 dilatation, gap junction protein connexin43 (Cx43) levels are downregulated. It is unclear if functional 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 PG+/− 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±0.03mm vs WT 1.65±0.03mm). Decreased PG in PG+/− LV (PG+/−: 0.06±0.01 vs WT 0.08±0.01; p<0.05) and RV (PG+/−: 0.61±0.04 vs WT 0.95±0.07; p<0.01) consistent with heterozygous PG deficiency. Increased β-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+/− 0.93±0.02 vs WT 0.14±0.02) in PG+/− group. Figure: RV PG and β-catenin expression normalised to loading control cathepsin.

Conclusions: The increased β-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 ARVC onset.

P1415 | BENCH
The connexin40A96S mutation is arrhythmogenic in mice after transcoronary constrictor operation
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Introduction: The Connexin (Cx)40A96S mutation leads to a severe impairment of the channel function in Cx40 containing gap junctions and is a known sub- strate 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 transcoronary constriction (TAC) operation in the murine heart.

Methods: Investigated groups consisted of mice with Cx40hetA96S/TAC n=15; WT/TAC, n=11) and without (Cx40hetA96S/TACsham, n=12; WT/TACsham, n=10). TAC was performed and resulted in relevant hypertension and hypertensive heart disease. We performed in vivo (transvenous catheterization) and ex vivo (epicardial mapping) electrophysiological investigations (EPI).

Results: No significant alterations of standard ECG-parameters were found. In vivo EPI showed that inducibility of AF was not significantly different among the investigated groups (Cx40hetA96S/TAC group (91%) versus Cx40hetA96S/TACsham (83%); WT/TAC (85%) and WT/TACsham (60%), p<0.05), but showing a tendency towards lower inducibility in the sham operated WT mice versus mutants. Induced AF episodes lasting longer in the TAC operated mutant mice compared to WT (Cx40hetA96S/TAC (22.8±2.7s) and Cx40hetA96S/TACsham (32.0±4.1s) versus WT (4.2±0.9s) and WT/TACsham (1.9±0.3s), p<0.05). Long-lasting AF episodes ~60sec were not found different among all groups. Significantly more episodes of VTs were inducible Cx40hetA96S/TAC mice compared to all other groups (Cx40hetA96S/TAC group (69%) versus Cx40hetA96S/TACsham (33%), WT/TAC (29%) and WT/TACsham (0%), p<0.01). Epicardial mapping showed significantly reduced atrial conduction...
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

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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 MiEAs (60 x 700µm diameters), and paced horizontally (H) & vertically (V) (1–25Hz). For each pacing interval, 25 x 700µm unipolar Eg plots (total number analysed >1.5 million) were characterized in time (duration, amplitude, line length, fractionation score) & frequency (dominant frequency (DF), DF divided) domain and correlated to fibrosis using a 700µm x700µm 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). PDAP0 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 potentials. 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 attempt to prove voltage/fibrosis relationships in human atria.

P1419 | BENCH
Increased aldosterone-dependent Kv1.5 recycling causes atrial fibrillation in Kcnq3−/− mice

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Objective: We used mice with global Kcnq3 deletion to study the molecular pathology of Kcnq3-associated AF.

Methods and results: Holter ECG recordings revealed spontaneous episodes of paroxysmal AF in Kcnq3−/− 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 Kcnq3−/− mice. The cellular correlate for AF predisposition was a significant increase in Kv current densities in atrial cardiomyocytes with increased IKs. Kcnq3 deletion also resulted in hyperaldosteronism with adrenal gland zona glomerulosa hyperplasia. Electrophysiological alterations in Kcnq3−/− mice were aldosteronedefependent and were caused by increased Ra, RaS, and Rab-dependent recycling of Kv1.5 channels to the Z-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 Kv current densities to the level of Kcnq3+/+ mice, and reduced spontaneous AF episodes and arrhythmia induction in Kcnq3−/− animals.

Conclusions: Kcnq3 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 considering extracardiac mechanisms even in monogenic arrhythmia syndromes.

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P1420 | BENCH
Mechanisms of fever-induced QT prolongation in patients with KCNH2 mutations in the S5-pore region

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Background: Patients with type-2 long QT syndrome (LQT2) caused by a KCNH2 mutation in the S5-pore region have an increased risk of arrhythmia during fever. However, few data exist regarding molecular basis of this phenotype.

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 total current densities (TCDs) for both 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 to negative potentials compared to WT at 40° C.

Conclusion: 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)
P1421 | BENCH  
A missense mutation of POPDC1 affecting CAMP-binding causes limb-girdle muscular dystrophy and cardiac arrhythmia  
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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 POPDC 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 POPDC1, 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 grandfather, 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 homologous gene 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.  

P1422 | BENCH  
Aliskiren suppresses extracellular matrix genes in atrial fibrillation - a global mRNA profiling in the canine 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 suppress 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 DNA 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. Dogs were divided into 3 groups as follows: 1) pacing control group (n=6): continuous atrial rapid stimulation of 400 bpm 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 GeneChip® microarray with Canine Genome 2.0 Array in each group.  

Results: Among the fibrosis related genes, mRNA expressions of thrombospondin-1 (TSP-1) and perilpin 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 mRNA level was significantly up-regulated 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 periostin 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  
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Introduction: 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.  

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%), 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%), antplatelets (38.2%) and OAC (14.7%) therapies.  

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.  

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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° iii) 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. Wavefronts appearing to be dominant subtype. 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
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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: Study aimed to test the 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 atria of patients with atrial fibrillation and patients without atrial fibrillation were genotyped for two risk variants on chromosome 4q25 and ionic currents were measured using perfused patch clamp technique. Comparison of the normal (CC) and the risk variant (CT) of the single nucleotide polymorphism at rs2200733 as well as the GG and GT 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 ± 5.6 vs. 65.5 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±9 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<0.01) while the CT and CC variants showed no significant difference (1.03±0.29 vs. 0.72±0.16 events/min, p=0.47). In accordance with this, estimation of the sarco- plasmic reticulum calcium content from the time integral of the caffeine induced current revealed that the calcium content was higher in a subset of 25 myocytes with the GT than the GG variant (12.3±2.0 vs. 8.6±0.9 amol/pF , p=0.05, n=25) while the difference between CT and CC variants was not significant (12.3±2.2 vs. 8.9±1.0 amol/pF, p=0.11). None of the two risk variants affected the L-type calcium current density (CC: -2.66±0.35 pA/pF; GG: -2.86±0.32 pA/pF), its inactivation or its current-voltage relationship.

Conclusions: 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 these HSP family can improve the stability of A78T-HERG protein.

P1427 | BEDSIDE
ST-segment elevation in Brugada syndrome patients is associated with arrhythmia and fractionated epicardial electrograms in the right ventricular outflow tract
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Background: Brugada syndrome (BrS) is characterized by a typical ECG pattern (Cowden-type ST-segment elevation and a negative T-wave in right precordial leads).

Purpose: We aimed to determine the pathophysiologic basis of the ST-segment elevation 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 RVOT underlies electrogram fractionation. ST-segment elevation diminished after infusion of Ajmaline. The latter suggests that discontinuous conduction at the RVOT underlies electrogram fractionation. ST-segment elevation diminished after pre-excitation of the RVOT (n=2).

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 Ajmaline. The latter suggests that discontinuous conduction at the RVOT underlies electrogram fractionation. ST-segment elevation diminished after pre-excitation of the RVOT (n=2).

Conclusion: 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
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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 concentration ([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 LQTS mutant, 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+ culture medium containing 8, 16, 50, and 100 mmol/L K+, the HEK293 cells were treated with short and long duration extracellular K+ for immunofluorescent assay, western blotting; currents were observed by whole-cell patch clamp.

**Results:** Expression of HERG mutant gene L539fs/47 decreased which was not affected by extracellular K+. The mutant channel protein had partial retention in the cytoplasm. The high extracellular K+ might enhanced the stability of wild-type and this mutant channel protein in cell membrane. Chronic low K+ reduced their protein expressions.

**Conclusion:** 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. HERG mutant L539fs/47 channel is dorrant presenting no functions. The activation and deactivation gating did not significantly change in WT and homozygous channels. The prolonged inactivation time and reduced number of inactivating channels improved the availability of the channel. I-V curve showed the HERG current in WT group and in WT-L539fs/47 group increased with the K+ concentration. The chronic extracellular low K+ prompted the HERG currents in both wild-type and heterozygous mutant, especially in the latter.

**Conclusions:** Chronic [K+]o effected the protein expression rather than mRNA expression of HERG mutant L539fs/47-*558W. Homozygotic HERG L539fs/47-*558W expression function, indicated by no responses to chronic [K+]o 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 IHERG and channel of HERG mutation L539fs/47 in HEK 293 cells.
A novel metric quantifies wavetail and wavefront interaction and identifies sites of potential reentrant activation

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Background: Initiation of re-entrant events depend 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 apply 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 wave rotors appeared to cluster around regions of low RVI.

Conclusions: We have developed an algorithm which spatially quantifies vulnerability to re-entry using intervals between local repolarization and activation times during follow-up. Importantly, the approach identifies critical sites susceptible to re-entry without the need to induce a full arrhythmia and thus may have important clinical application as an approach to safely identify ablation sites.

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Figure 1

P1434 | BEDSIDE

Brugada syndrome: time-trend in incidence and prognosis

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Introduction: Brugada Syndrome (BS) is a channelopathy with a reported prevalence of 1–5 cases/10,000 in Europe and US and responsible for 4–12% of sudden death cases. The aim was to describe the time trend in incidence and long-term outcome in a large BS cohort.

Methods: Between 1993 and 2013, a total of 332 BS patients (51±15 years; 76% male) were diagnosed and followed-up in our centre. Major event was defined as SD or documented sustained ventricular tachycardia (VT) or ventricular fibrillation (VF).

Results: Overall, the annual incidence of BS was 15±11 new cases per year. An electrophysiological study (EPS) was performed in 272 patients (82%). Implantable cardioverter defibrillator (ICD) was implanted in 96 patients (29%): 10 patients (10.4%) as secondary prevention due to aborted SCD and 86 (89.6%) for primary prevention (inducible EPS/VT in 51 patients [53.1%], recurrent syncope in 25 patients [26.1%], type 1 ECG with family history of sudden death in 5 patients [5.2%], prolonged HV in 3 patients [3.1%] and asymptomatic type 1 ECG (2 patients [2.1%]). During a mean follow-up of 91±52 months, 29 patients (8.7%) presented a major event. There were 11 deaths (3.3%): 8 patients (2.4%) due to SCD (1 patient with ICD [0.3%] presenting arrhythmic storm; 7 patients [2.1%] without ICD) and 3 patients (0.9%) for other causes (cancer). Annual Incidence, EPS studies performed, ICDs implanted and major events per year are shown in the Figure.

Conclusion: 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.

P1435 | BEDSIDE

Rare genetic variants previously associated with congenital forms of long QT syndrome have little or no effect on the QT interval


Background: We studied if variants previously reported to associate with congenital long QT syndrome (cLQTS) have an effect on the QTc-interval in a Danish population sample. Furthermore, we assessed if carriers of variants in cLQTS-associated genes, are more prone to experience syncope compared with non-carriers, and if carriers have an increased mortality compared to non-carriers.

Methods and results: All genetic variants previously associated with cLQTS were surveyed using the Human Gene Mutation Database. We screened a Danish population-based sample with available whole exome sequencing data (n=870) ever CRT response may be altered by the absence of viable myocardium that should be taken into account. The aim of the study was to echocardiographically investigate impact of myocardial viability and targeted LV lead placement on CRT efficacy.

Methods: Forty-one consecutive patients with heart failure (NYHA III), with depressed ejection fraction (EF) of the left ventricle (26±6.9%) and dysynchronous contractions (QRS duration 151.6±23.7 ms) were enrolled. Patients underwent dobutamine stress echocardiography (DSE) to assess global contractile reserve and tissue doppler imaging to define the most delayed region of LV prior to CRT. Preserved myocardial viability was defined as an EF increase -5% during DSE. Anatomic LV lead position was determined by fluoroscopy. Responders to CRT were defined by a decrease in left ventricular end-systolic volume of ≥15% and/or an increase in EF of >5% after 6 months of CRT.
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).

Conclusions: 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

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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 26.812 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±6.6 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, 22 (23.6%) had a previous myocarditis have been demonstrated by cardiac MRI with gadolinium in 22 patients, NYHA II – 27 pts, and NYHA III – 8 pts. The remaining 41 (44,1%) patients had arterial hypertension has been diagnosed in 67 (72,0%) patients, arterial hypertension have been diagnosed in 67 (72,0%) patients, the severity of electrical dyssynchrony. Twenty six parameters were analyzed altogether. The severity of electrical dyssynchrony was related to male gender (p<0.004), CAD (p=0,011), End Systolic Volume (ESV; p<0.001), and results; We retrospectively investigated consecutive 104 patients with complete atrioventricular 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 conduction disturbance with the QRS duration >120ms. Among 60 patients with conduction disturbance, 28 patients had pure complete right bundle branch block (CRBBB), 19 patients had CRBBB and left anterior fascicular block (LAFB), 11 patients had complete left bundle branch 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 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).

Conclusions: Among the patients with LBBB, the presence of LAFB regardless of the QRS duration, new occurrence of right ventricular pacing was strongly 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.

P1437 | BEDSIDE
Right ventricular pacing and newly occurrence of atrial fibrillation in patients paced with atrioventricular block

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Background: Although previous reports have shown that cumulative % of ventricular pacing (cum%VP) has strongly associated with newly occurrence of atrial fibrillation (AF) in pacemaker patients, the mechanism has been obscure, especially in atrioventricular (AV) block.

Purpose: We, therefore, investigated the incidence of newly occurrence of AF after pacemaker implantation and analyzed its correlation with abnormalities of P-wave signal-averaged electrocardiogram (P-SAECG), in paced patients with AV block.

Methods: Total 106 dual-chamber pacemaker patients with AV block, who had no prior AF and detections of AF within 3 months after pacemaker implantation, were followed for a mean of 3.2±2 years. Newly occurrence of AF was defined as an episode of rapid atrial rate (<190 beats/minute), lasting more than 6 minutes, that was detected by pacemaker in according to the criteria of AF in ASSERT Trial. Time to first episode of AF, cum%AP and cum%VP for every 6 months, and P-SAECGs (filter P-P waveform duration, FPD; root mean square voltage for the last 20 ms, RM20) were investigated.

Results: Newly occurrence of AF was observed in 25 patients (23.6%) during follow-up periods, and the first episode of AF occurred at 2.3±1.7 years after pacemaker implantation. Univariate Cox-regression analysis showed that cum%VP in AF group showed significantly higher than that in non-AF group (92±24% vs. 66±38%, P<0.001), though cum%AP did not differ between the 2 groups. Multivariable Cox-regression analysis revealed that higher cum%VP was an independent predictor for newly occurrence of AF (HR 1.08 for each 1 percent increase, 95% CI 1.01–1.39, P=0.005). In addition, Kaplan-Meier analysis showed that the incidence of newly occurrence of AF was significantly higher in patients with cum%VP > 80% than with ≤50% (P=0.03). In analysis of P-SAECGs of 46 patients with cum%VP > 80% (n=26) and ≤50% (n=20), RVP20, patients with cum%VP > 80% showed significant lower than those with ≤ 80% (5.4–12.8, P<0.01), though FPD was not different (143±24 vs. 133±17, P=0.14).

Conclusions: Higher cum%VP was strongly associated with both newly occurrence of AF and P-SAECG abnormalities in ventricular paced patients with AV block.

P1438 | 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

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Background: Right ventricular pacing (RVP) prolongs ventricular activation time and sometimes induces mechanical dyssynchrony among the patients with normal left ventricular 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 atrioventricular 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 conduction disturbance with the QRS duration >120ms. Among 60 patients with conduction disturbance, 28 patients had complete right bundle branch block (CRBBB), 19 patients had CRBBB and left anterior fascicular block (LAFB), 11 patients had complete left bundle branch 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 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.

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 hexafilar 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 hexafilar 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, ten 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: Hexafilar coil pacing lead failures characteristically tend to exhibit a leap 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 dysfuction.
P1440 | BEDSIDE

Atrial lead characteristics, time from implantation and atrial high rate episodes compatible with silent atrial fibrillation: an unintentionally provoked situation?

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Introduction: Identification of atrial fibrillation (AF), even in the absence of symptoms is of capital 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 attaining 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%). 30 patients (33%) from >3 months implantation group (11 patients (11%) at 3 months of follow-up and 28 (31%) over the 3 first months) and 14 patients (40%) from >3 months group (4 (11%) and 12 patients (34%) respectively) showed AHREs; p=ns. The type of fixation used was active in 64 patients (52%), passive (33%) and VDD leads in 15 (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 (26%) respectively after p=ns. In this population, the presence of IBL on CT-scan was related with the presence of AHRE >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

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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.

P1442 | BEDSIDE

Bachmann’s bundle pacing reduces the risk of chronic atrial fibrillation development

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Background: Patients treated for sick sinus syndrome (SSS) have interventional conduction disorders which make them relatively often suffer from atrial fibrillation. Implantation of atrial lead within right atrium appendage (RAA) furthermore contributes to electrophysiological and hemodynamic impairment even in patients without prior disorders. Bachmann's bundle pacing can have beneficial effect regarding atrial fibrillation prevention.

Purpose: The aim of this study was to assess incidence of atrial pacing site on atrial fibrillation recurrences and arrhythmia becoming permanent in population with SSS implanted with DDD pacemaker.

Methods: The study group consisted of 124 patients (75 F, 49 M) aged 70.8±11.8 years. Patients were divided in two groups: group I (n=47) with RAA pacing, group II (n=77) with Bachmann’s area pacing. The presence of paroxysmal atrial fibrillation at the implantation and during follow-up was assessed. Moreover the presence of diagnosis chronic atrial fibrillation during follow-up was established. The patients were follow-up for 54.3±15.1 months.

Results: In both groups patients with atrial fibrillation were significantly older at the time of implantation than those without (group I: 67 vs. 74 years, group II 69 vs. 75 years, p<0.05 for both comparisons). The presence of chronic atrial fibrillation during follow-up was 10.6% in group I and 5.2% in group II (p=0.05), despite higher paroxysmal atrial fibrillation at implantation in group II (36.4 vs. 27.7%, p<0.05). In logistic regression analysis the age older than 73 years at implantation (OR 2.44, 95% CI 1.14–5.37, p<0.05) and the implantation site within RAA (OR 1.96, 95% CI 1.23–4.82, p<0.05) were both independent predictors of chronic atrial fibrillation during follow-up.

Conclusions: 1. The Bachmann's bundle region pacing of right atrium provides better protection against chronic atrial fibrillation in comparison to right atrial appendage electrode location. 2. As the primary paroxysmal atrial fibrillation percentage was higher in the Bachmann's bundle pacing group, the lower permanent atrial fibrillation results from direct antiarrhythmic properties of this pacing site.

P1443 | BEDSIDE

Puncture with care: as opposed to conventional wisdom, the course of the auxiliary vein is not reliably predicted by anatomical landmarks


Introduction: Lead implantation via the axillary vein provides quick access to subclavian veins. However, there is no standardized method to place an access device and the vein is not reliably predicted by anatomical landmarks. Moreover, the vein can safely be entered without additional contrast venography in the overwhelming majority of cases. We hypothesized that the normal anatomical variations in the axillary vein’s course are too big to support such claims.

Purpose: To assess the course of the axillary vein in a real-life population of
P1444 | BEDSIDE
Effectiveness of closed loop stimulation pacing in preventing disabling cardioinhibitory vasovagal syncope. A single-center experience
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Background: Vasovagal syncope (VVS) is a benign disease. However, in rare occasions, cardioinhibitory vasovagal syncope is recurrent and can produce serious 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 can be 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 (REVIVA-Vykos DR, Biotronik GmbH Co.) and were reviewed. Severity of cardioinhibition 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 108 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 prosthesis 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.

P1446 | BENCH
In vitro generated high ploidy megakaryocytes show overexpression of genes involved in platelet activity and thrombosis
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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 those that have 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 inhibitors.

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 CDCC45, chromatin assembly factor 1(1), 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, PDGFP, thrombospondin 1 and plasminogen activator inhibitor type 1. Furthermore, glyoxalase II (part of the fructose-6-phosphate 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 genes 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.
P1447 | BEDSIDE
Altered fibrin clot properties affect the angiographic results of primary coronary intervention
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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 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 frame count (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).

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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/002936

P1448 | BEDSIDE
Stent thrombosis after primary PCI in STEMI patients: a meta-analysis of randomized placebo-controlled trials
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Introduction: Stent thrombosis after primary PCI in STEMI patients is a strong independent predictor of future events. While previous studies showed that the incidence of stent thrombosis is 0.5% to 1.5% of cases, the available evidence for the effects of statins on stent thrombosis is still limited.

Methods: A comprehensive MEDLINE/PubMed search was performed to identify randomized placebo-controlled trials (RCTs) that assessed the effect of statin therapy on stent thrombosis in patients treated with bioresorbable vascular scaffolds (BVSs). A total of 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 ≥50 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 sub-acute and late ST occurred in 0.9% (0.2–1.6) and 0.5% (0.2–0.9) of the patients, respectively. MACE occurred in 6.5% (4.7–8.2) of patients, driven by 3.3% (1.7–4.8) of target lesion revascularization and 2.8% (2.3–3.5) of myocardial infarction. By meta-regression, the risk of any ST was increased in patients with ST-segment elevation myocardial infarction (B 0.07: 0.03–0.11; p = 0.01) and in those with long lesions (B 0.19: 0.06–0.23; p = 0.001), and was reduced by intravascular ultrasound (IVUS) and OCT imaging (B 0.02: −0.04–0.01; p = 0.001) and post-dilatation (B −0.02: −0.04–0.01; p < 0.001).

Conclusions: Patients with ST-segment myocardial infarction and those with long coronary lesions shown an higher risk of BVS-ST. This could be reduced by post-dilatation and with the use of intravascular imaging technologies.

P1449 | BEDSIDE
Stent thrombosis in patients treated with bioresorbable vascular scaffolds: a meta-analysis of 7 studies and 2,568 patients
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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 ≥50 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 sub-acute and late ST occurred in 0.9% (0.2–1.6) and 0.5% (0.2–0.9) of the patients, respectively. MACE occurred in 6.5% (4.7–8.2) of patients, driven by 3.3% (1.7–4.8) of target lesion revascularization and 2.8% (2.3–3.5) of myocardial infarction. By meta-regression, the risk of any ST was increased in patients with ST-segment elevation myocardial infarction (B 0.07: 0.03–0.11; p = 0.01) and in those with long lesions (B 0.19: 0.06–0.23; p = 0.001), and was reduced by intravascular ultrasound (IVUS) and OCT imaging (B 0.02: −0.04–0.01; p = 0.001) and post-dilatation (B −0.02: −0.04–0.01; p < 0.001).

Conclusions: Patients with ST-segment myocardial infarction and those with long coronary lesions shown an higher risk of BVS-ST. This could be reduced by post-dilatation and with the use of intravascular imaging technologies.
The safety profile of new cationic heparin antidotes
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Background: Protamine – a protein isolated from sperm of salmon fished around Japan is the only one registered antidote of unfractionated heparin (UFH). However, around one thousand deaths a year could be attributed to complications after protamine injection. We have already shown in vivo neutralization of UFH by protamine in Wistar male rats and BALB/c male mice were approved by Local Ethical Committees. We compared the efficacy of Dex40-GTMAC2, protamine and platelet factor 4 in a mice model of FeCl3-induced venous thrombosis. The potential direct blood toxicity (osmotic resistance) of Dex40-GTMAC2 and protamine was measured in whole blood. Blood pressure, heart rate (HR), blood count and histopathology were estimated at 1 hour after the administration of the tested antidotes (protocol phase). 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<0.001) than protamine (0.12±0.01 mg; p<0.001) in reversing the effect of UFH (0.01±0.01 mg vs. 0.39±0.05 in the vehicle treated group; p<0.001) on thrombus weight formed in vena cava. Dex40-GTMAC2 significantly reversed activated partial thromboplastin time (40.7±7.6 sec.; p<0.001) prolonged by UFH (300.0±0.0 vs. 28.9±1.3 sec. in the vehicle treated group; p<0.001). Blood platelet factor 4 did not affect the protein level of UFH. However, Dex40-GTMAC2 showed no significant acute and chronic toxicity, while Dex40-GTMAC3 decreased blood pressure, HR, and changed blood morphology. Dex40-GTMAC3 did not affect 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/ST5/03864 National Science Center, Poland

Thrombosis and coagulation / Platelets, thrombosis and coagulation 225

Comparison of circadian laboratory measurements of coagulation assays between administrations of rivaroxaban and warfarin in patients with non-valvular atrial fibrillation
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Background: Although rivaroxaban (RB) has a relatively short half-life and peak 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 samplings 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 S activity were measured in each patient. The PTs (13.4±2.0 vs. 23.4±4.7 sec at 6 AM, 14.1±1.6 vs. 23.9±4.9 sec at 11 AM, 14.1±1.6 vs. 23.0±4.9 sec at 3 PM, and 13.3±1.6 vs. 24.0±5.9 sec at 6 AM the next day, respectively, P<0.0001) and PT-INRs (1.2±0.2 vs. 2.0±0.4 at 6 AM, 1.3±0.2 vs. 2.0±0.4 at 11 AM, 1.3±0.2 vs. 2.0±0.4 at 3 PM and 1.2±0.2 vs. 2.0±0.5 at 6 AM the next day, respectively, P<0.0001) were significantly lower than those for WR. PT-INR was significantly higher than those for WR in the control group (89±32 vs. 84±30 AU*min, p=0.4559).

Conclusions: Axipaban 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 evaluated. 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

PLATELETS, THROMBOSIS AND COAGULATION

P1454 | BEDSIDE
TRAP induced platelet aggregation is enhanced in cardiovascular patients receiving dabigatran
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Background and objectives: Novel (or non-vitamin K antagonist) oral anticoagulants (NOAAs) 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 NOAAs 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 intraindividual time courses of 11 patients a significant higher MEA response was found 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=0.0372). Patients receiving rivaroxaban showed no differences compared to the control group (89±32 vs. 84±30 AU*min, p=0.4559).

Results:

Treatment duration

<table>
<thead>
<tr>
<th>Market share drawn from rivaroxaban</th>
<th>Market share drawn from LMWH/VKA</th>
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<tbody>
<tr>
<td>3 months</td>
<td>−0.3%</td>
</tr>
<tr>
<td>12 months</td>
<td>−0.3%</td>
</tr>
<tr>
<td>6 years</td>
<td>−0.6%</td>
</tr>
<tr>
<td>3 months</td>
<td>−0.8%</td>
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<tr>
<td>12 months</td>
<td>−1.7%</td>
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<tr>
<td>5 years</td>
<td>−4.0%</td>
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**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).

**Figure 1**

**P1455 | BENCH**

Platelets are permanently activated after splenectomy

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**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 thrombus resolution.

**Methods:** In this prospective case control study, we evaluated 144 outpatients after previous splenectomy referred from 1100 primary care practitioners. 91 (63.2%) splenectomized patients were due to trauma, and 75 matched non-splenectomized controls. The response to adenosine diphosphate (ADP), arachidonic acid (ASA), protease-activated receptor (PAR)-1 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 activatability in splenectomized patients (97.06±22.22 area under the curve, AUCs) compared with controls (80.14±10.07 AUCs, p=0.04). Inducible P-selectin was higher in splenectomized patients (85.24±19.85%) compared with controls (62.53±21.52%, p=0.05). Levels of MPA (44.47%; [11–92]) were higher in [MPA: 31.59%; (13–70), P<0.001].

**Conclusions:** Platelets are activated after splenectomy, with increased concentrations of MPs, which may contribute to the high rate of vascular events in these patients.

**P1454 | BENCH**

Neutrophil Extracellular Trap levels the size of the aspirated coronary artery thrombi and pre-PCI NETs levels in STEMI patients during pPCI is related to microvascular obstruction in STEMI patients during pPCI is related to the size of the aspirated coronary thrombi and pre-PCI NETs levels.

M. De Maat1, H. Van Beusekom2 on behalf of CorTAsk Investigators.  
1 Erasmus Medical Center, Hematology, Rotterdam, Netherlands; 2 Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands

**Purpose:** To study NETs in thrombus and circulating blood in STEMI patients in relation to MVO after pPCI and T.

**Background:** Neutrophil Extracellular Traps (NETs), toxic thrombogenic DNA complexes that are generated by neutrophils, play an important role in the pathogenesis of atherosclerosis.

**Methods:** In this prospective case control study, we evaluated 144 outpatients after previous splenectomy referred from 1100 primary care practitioners. 91 (63.2%) splenectomized patients were due to trauma, and 75 matched non-splenectomized controls. The response to ADP, ASA, PAR-1 and 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 activatability in splenectomized patients (97.06±22.22 area under the curve, AUCs) compared with controls (80.14±10.07 AUCs, p=0.04). Inducible P-selectin was higher in splenectomized patients (85.24±19.85%) compared with controls (62.53±21.52%, p=0.05). Levels of MPA (44.47%; [11–92]) were higher in [MPA: 31.59%; (13–70), P<0.001].

**Conclusions:** Platelets are activated after splenectomy, with increased concentrations of MPs, which may contribute to the high rate of vascular events in these patients.

**P1457 | BENCH**

Clinical determinants of arterial thrombus structure: ultrastructural and immunohistochemical studies

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**Introduction:** CLOT structure profoundly affects the clinical outcome of thrombotic diseases.

**Purpose:** We studied the associations between clinical data and the structure of coronary and peripheral arterial thrombi.

**Methods:** Patients of various age (36–98 years) and sex (40% female) were recruited over 22 months. Coronary thrombi were obtained by PCI- thrombuscorporation following AMI (n=100), peripheral clots were removed by em- darterectomy (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 im- ages/thrombus. Hypothesis tests and regression analysis were used to assess the correlation between structural features and selected clinical data, e.g. age, sex, antithromplate 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 val- ues. A J-shaped dependence was found between systemic and intrathrombotic platelet count, which correlation was enhanced by aspirin and clopidogrel in pe- ripheral thrombi and by smoking and dyslipidaemia in AMI patients.

**Morphometric analysis of clot structure**

**Conclusion:** Systemic and local factors are associated with characteristic throm- bus morphology at different vascular locations.

**P1458 | BENCH**

C-reactive protein gene variant modifies atherosclerosis in patients with advanced atherosclerosis: effects on endothelial function, inflammatory and coagulation processes

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1 Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece; 2 University of Marburg und Giessen, Cardiology and Caridio Arrest Unit, Marburg, Germany

**Background:** It is well established that C-reactive protein (CRP) is a mediator of mechanisms leading to atherosclerosis.

**Purpose:** We examined the effect of the least studied 3872 A

G

mechanisms leading to atherosclerosis.

**Results:** This work was supported by a grant from the Deutsche Forschungsgemeinschaft (OL 371/1–1 to Christoph B. Olivier).

**Conclusion:** Microvascular obstruction in STEMI patients during pPCI is related to the size of the aspirated coronary thrombi and pre-PCI NETs levels.
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 immunonephelometry, while fibrinogen (mg/dl) with the Clauss method. Interleukin-6 (IL-6) (pg/ml), TNF-α (pg/ml) and sCD40L (pg/ml) were measured by ELISA.ROC analysis of platelet indices for prediction of ST, a cut-off value 45.75 for PDW (OR: 1.117, 95% CI: 1.066–1.172; p =< 0.002 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: 45.6±6.51 vs. 1.29±2.51, PCT: 0.8±0.56 vs. 0.89±0.65, p =< 0.018 for all). All the contrary, G carriers, compared to AA homozygotes, had not significant effect on any of the coagulation markers, both in CAD (fibrinogen: 380.5±103.9 vs. 365.3±72.9, sCD40L: 0.73±1.93 vs. 1.13±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 =< 0.001). 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 promoting inflammatory mechanisms and endothelial dysfunction.

P1459 | BEDSIDE Plateletcrit and platelet distribution width as predictors of ST elevation myocardial infarction in young patients
Ankara Turkey Yusuf Inisias 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% male).

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 (8.5±1.1 vs. 8.5±1.1; p =< 0.002). In comparison of group 1 and 3, in group 1, PCT (0.249±0.6 vs. 0.227±0.6; p =< 0.001), PDW (48.2±5.7 vs. 44.9±8.3; p =< 0.001) and MPV (8.5±1.1 vs. 8.5±0.7; p =< 0.003) were significantly higher than group 3. At multivariate logistic regression analysis of young STEMI and non-young STEMI patients MPW, 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 addition to MPW, PDW and 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
Ankara Turkey Yusuf Inisias 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).

Material and methods: 925 patients who admitted with STEMI and underwent 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 categorized into 3 groups according to MPV, PDW, PCT tertiles, respectively.

Results: The rates of ST were statistically higher in the highest tertiles for every platelet indices; MPV, PDW, PCT (p =< 0.010, p =< 0.003, p =< 0.001 respectively). 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), a cut-off value 3.265 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.

P1461 | BENCH Identification of functional proteins related to Factor XIII in platelet lipid rafts
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Background: Factor XIII plays a pivotal role in platelet aggregation. Factor XIII depends on lipid rafts to assemble the proteins required for clot retraction. Several proteins in this assembly remain unidentified. We aimed to investigate which proteins localized in platelet lipid rafts are related to Factor XIII.

Methods: Lipid rafts of platelets were isolated using lubrol WX 0.05% (w/v) and sucrose gradient. After ultracentrifugation, sucrose fractions were sampled. Lipidomic analysis was performed to identify the fractions enriched in cholesterol and sphingomyelin (lipid rafts). These fractions were selected for further proteomic analyses. Gene ontology and STRING in high confidence were performed.

Results: Sucrose fractions containing platelet lipid rafts were identified as shown in figure 1A. In these fractions, we observed that a group of proteins including fibrinogen alpha (FGA), beta (FGB) and gamma chain (FGG), Albumin (ALB), platelet factor 4 (PF4), multimerin 1 (MMPR1), integrin beta 1 (ITGB1), clustatin (CLU), kininogen 1 (KNG1), plasminogen (PLG), coagulation factor II (thrombin) (F2) and transforming growth factor beta 1 (TGFβ1) were associated with factor XIII on lipid rafts of platelets isolated by lubrol WX (Figure 1B).

Conclusion: We identified proteins associated with Factor XIII in lipid rafts. This could provide further insights into the clinical target of pathways through this molecule.

P1462 | BEDSIDE Influence of morphine on the effect of clopidogrel and prasugrel in patients with ST elevation myocardial infarction. Results of the ETAMI trial
U. Zeymer1, B. Mark1, G. Montalescot2, H. Thiele3, R. Zahn1, 1Klinikum Ludwigshafen, Ludwigshafen Am Rhein, Germany; 2Hospital Pitie-Salpetriere, ACTION Study Group, Institut de Cardiologie (AP-HP), Centre Hospitalier Universitaire Pitié-Salpêtrière, Paris, France; 3Medical University, Department of Cardiology, Lübeck, Germany

Background: There are reports about a delayed onset of action after oral loading doses of P2Y12 receptor inhibitors and concomitant administration of morphine

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% versus 66.3 ± 22.2%, p = 0.035) and after 4 hours (39.1 ± 27.5% versus 54.5 ± 49.3%, p = 0.006) was significantly lower with prasugrel compared to clopidogrel. However, in the dabigatran group a significant increase in platelet reactivity upon TRAP stimulation could be seen when OAC was started. (platelet reactivity basal < 34 mm had the best predictive value of long-term stable 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 with AOC with phenprocoumon. We investigated whether thrombelastography was a good ex vivo platelet function measurement to facilitate risk stratification and personalized antiplatelet therapy.**

**Methods:** Using multiplate electrode aggregometry platelet reactivity of 30 patients (DAPT + OAC with dabigatran or phenprocoumon) was assessed upon stimulation with TRAP, ASPI, ADP, and collagen at 4 different time points (before OAC start, 3 and 24h thereafter as well as 1 week of OAC). Furthermore, dabigatran plasma levels at the same time points were measured. **Results:** At baseline levels there was no difference in the platelet reactivity in patients on DAPT and dabigatran or phenprocoumon. **Conclusion:** High on treatment platelet reactivity has been proven to raise the risk of major cardiovascular events. In this study we sought to investigate the platelet reactivity in patients on DAPT and dabigatran or phenprocoumon therapy. **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’s Endowment.

**PLATELETS AND ANTIPLATELETS THERAPY I**

**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 with OAC 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.

**Results:** High on treatment platelet reactivity has been proven to raise the risk of major cardiovascular events. In this study we sought to investigate the platelet reactivity in patients on DAPT and dabigatran or phenprocoumon therapy. **Methods:** Using multiplate electrode aggregometry platelet reactivity of 30 patients (DAPT + OAC with dabigatran or phenprocoumon) was assessed upon stimulation with TRAP, ASPI, ADP, and collagen at 4 different time points (before OAC start, 3 and 24h thereafter as well as 1 week of OAC). Furthermore, dabigatran plasma levels at the same time points were measured. **Results:** At base line levels there was no difference in the platelet reactivity in both treatment arms. However, in the dabigatran group a significant increase in platelet reactivity upon TRAP stimulation could be seen when OAC was started. (platelet reactivity basal vs. 4h and 24h after first dose of dabigatran, p < 0.05). This increase was also statistically significant in the dabigatran group when compared to the patients on a phenprocoumon regimen (Platelet reactivity 24h after start of OAC with Dabigatran vs. phenprocoumon, p < 0.05).

**Conclusion:** The observed trend towards increased rates of myocardial infarction in patients receiving dabigatran deduced from the RELY-trial could be due to increased 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**

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**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 patient-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 1,944 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’s Endowment.

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operating characteristic curve and quartile analysis suggests MA-ADP $\leq 21$ 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 antplatelet treatment designed to reduce ischemic events and bleeding.

P1468 | BEDSIDE

The vaso-angiogenic and vaso-protective effects of cilostazol in patients with high risk for cardiovascular disease

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Background: We have found that cilostazol may have beneficial effects on endothelial progenitor cells (EPCs) in vitro and can provide vascular-angiogenic effects in vivo.

Purpose: This study, for the first time, investigated the vaso-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. The 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 [percentage change: 149.0 (67.9–497.8) vs. 71.9 (−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. 149.0 (67.9–497.8)%, P=0.024] without in vivo.

Conclusions: Cilostazol significantly beneficial effects on mobilization of EPCs with better endothelium-dependent function partly mediated by modulating 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

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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.

Methods: 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: 20umol/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).

Conclusions: The genetic variants of PEAR1 may be related to insufficient antiplatelet effect in patients with acute coronary syndrome after percutaneous coronary intervention.

P1469 | BEDSIDE

A loading dose of aspirin plus clopidogrel is able to offset platelet reactivity in CAD patients carriers of Glu298Asp polymorphism undergoing elective PCI

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Background: Endothelial nitric oxide synthase 3 (eNOS3) is also expressed in platelets and, through NO production, is able to inhibit platelet adhesion and aggregation. Genetic polymorphism of eNOS Glu298Asp has been reported to modulate platelet reactivity through a decrease in eNOS expression with almost 50% reduction in platelet NO. The ENOS Glu298Asp polymorphism has been associated with hypertension, coronary spasm and myocardial infarction.

Purpose: In patients with stable coronary artery disease (CAD) undergoing percutaneous revascularization (PCI) uniformly loaded with dual antiplatelet therapy (DAPT) at least 12 hours before, we evaluated the effect of Glu298Asp polymorphism on residual platelet reactivity and on the risk of procedural-related myocardial infarction (PMI).

Methods: We enrolled 632 consecutive patients undergoing elective PCI loaded with DAPT consisting of 500 mg of aspirin (ASA) and 600 mg of clopidogrel. Blood samples were collected at the time of PCI to: a) genotyping with the TaqMan single nucleotide polymorphism (SNP) Genotyping assay; b) assess P2Y12 reaction units (PRU) and aspirin reactivity units (ARU) with point-of-care VerifyNow assay. A blood sample was also collected at the admission and 24 hours after PCI to assess toponin T: PMI was defined as $>$ 5 times elevation in troponin T.

Results: In our patients, 365 (59%) carried the 298Asp variant. Clinical characteristics between patients homozygote for 298Glu (wild type) and 298Asp carriers were similar with the exception of previous PCI that was more frequent in 298Asp carriers (64% vs. 36% in wild type, p=0.025). A significant correlation was found between presence of 298 Asp variant and PRU (p=0.048). PRU was slightly but significantly lower in patients carrying 298Asp as compared with patients wild type (PRU=218±106 vs. 234±99, p=0.048). ARU was not significantly different between the 2 groups. PMI was detected in less than 20% of the patients with no significant difference between wild type and 298Asp carriers (19.5% vs. 18.7%, p=0.8).

Conclusions: The 298Asp variant of eNOS gene is frequent in our patients with stable CAD. Yet, in carriers of 298Asp variant, we did not observe any negative impact in terms of higher residual platelet reactivity or PMI rate, presumably due to the loading dose of 500 mg ASA plus 600 mg clopidogrel.

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)

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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 and 234 vs. 24.4 ng·h/mL), with a ratio of adjusted geometric means (95% confidence interval, CI) of 12.67 (2.34–68.51), 19.28 (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-CL2491/0XX (active metabolite). Platelet reactivity (VerifyNow) at 1 hour was similar with crushed vs. standard administration with least square estimates mean difference (95% CI) of -0.5(-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.
P1470 | BENCH
High inter-individual variability on platelet inhibition with oral Aspirin compared with intravenous Lysine Acetylsalicylate in healthy volunteers
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Background: Despite the new P2Y12-ADP receptor antagonists achieve faster, and higher and less inter-individual variability platelet inhibition than clopidogrel, it is unknown the effect of intravenous lysine acetylsalicylate (LA) on cycoxygenase 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 antiplatelet response after AA 1.5 mM evaluated 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 cycloxygenase platelet inhibition.

Acknowledgement/Funding: This study was supported by a grant from the Fundación Mutua Madrileña (FMM012).

P1471 | 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-Registry
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1 Klinikum Ludwigshafen, Ludwigshafen Am Rhein, Germany; 2Institut für population in clinical practice. Results of the prospective ALKK-Regist.

Comparative efficacy and safety of prasugrel and clopidogrel in patients with STEMI undergoing PCI for STEMI without prior PCI (n=53). Overall, 11 (7.5%) first ischemic events occurred. Patients with ischemic events had higher MA-ADP (p<0.0001 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).

P1473 | BEDSIDE
The role of CYP2C19 and ABCB1 polymorphisms on platelet reactivity during dual antiplatelet therapy
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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 afterDES placement. The secondary end-point 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<0.0001 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 Lo allele carrier status is an important independent predictor of the pharmacodynamic response to clopidogrel. HPR and CYP2C19 Lo 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 syndromes managed without revascularization: insights from the in-hospital study of the EYESHOT registry

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**Background:** Patients with acute coronary syndromes (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 unfractionated 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=0.0001, respectively).

**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 with those who did.

### PLATELETS AND ANTIPATELETS THERAPY II

**P1475 | BEDSIDE**

Determinants of post-discharge bleeding events in ACS patients during antiplatelet therapy: insight from the A-MATCH trial


**Background:** During P2Y12 inhibitor therapy, determinants of post-discharge bleeding events have not been sufficiently understood.

**Purpose:** To evaluate the determinants related with bleeding episode in patients with ACS receiving dual antiplatelet therapy.

**Methods:** After uneventful PCI, ACS patients on prasugrel (n=250) were followed for 1 month and the prevalence of 1-month BARC bleeding complication was monitored using the dedicated questionnaires. Laboratory measurements including the VerifyNow assay (“PRU” and “BASE”) were conducted at 1-month follow-up.

**Results:** During 1-month follow-up, BARC bleeding events were observed in 27.6% of total patients (n=69; 24.4%, 7.2% and 0.4% of BARC type 1, 2 and 3 events). ROC curve analysis revealed that the low levels of ADP-induced platelet reactivity (≤ 126 PRU) and thrombin-mediated hemostatic signal (≤ 258 BASE) were associated with the risk of BARC bleeding complication. In multivariate analysis, “PRU ≤126”, “BASE ≤258” and the low level of inflammatory marker (high-sensitivity CRP ≤ 10.15) were independent determinants for the occurrence of bleeding complication. The combination of “PRU ≤126” and “BASE ≤258” increased the predictive value for the risk of bleeding events (OR: 29.41; 95% confidence interval: 6.00 to 142.86; p<0.001). The greatest likelihood ratio was observed when PRU, BASE and high-sensitivity CRP were combined together.

**Conclusions:** This is the first study to demonstrate that thrombin-mediated hemostatic signal and the level of inflammation may determine the risk of BARC bleeding complication in ACS patients. Combining the measurements of platelet reactivity, thrombin-mediated hemostatic signal and inflammatory marker may enhance stratification of bleeding risk.

**Acknowledgement/Funding:** Device support from ITC

**P1476 | BEDSIDE**

Vitamin D levels and high-residual platelet reactivity in patients receiving dual antiplatelet therapy with clopidogrel or ticagrelor


**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-residual platelet reactivity (HRPR) despite antithrombotic strategiesatic strategies.

**Purpose:** Aim of our study was, 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 (p=0.007), with a direct linear relationship between vitamin D values and high-residual platelet reactivity. The combination of “PRU ≤ 258” and the low level of inflammatory marker may determine the risk of BARC bleeding complication. In multivariate analysis, “PRU ≤ 126”, “BASE ≤ 258”, and the low level of inflammatory marker were independent determinants for the occurrence of bleeding complication. The combination of “PRU ≤126” and “BASE ≤258” increased the predictive value for the risk of bleeding events (OR: 29.41; 95% confidence interval: 6.00 to 142.86; p<0.001). The greatest likelihood ratio was observed when PRU, BASE and high-sensitivity CRP were combined together.

**Conclusions:** 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.

**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).

Significantly higher platelet reactivity was observed after platelet stimulation with ADP (p=0.007), but not with other tests. Vitamin D did not impact on the effectiveness of ASA. 24.1% of patients displayed HRPR with ADP-antagonists, and the rate increased with lower vitamin D levels (30.1% vs 21.2% vs 20.8%, adjusted OR [95% CI]=1.37 [1.001–1.87] p=0.05, with a direct linear relationship between ADP test results and vitamin D 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.
Ticagrelor (vs prasugrel) and insulin-treated DM significantly affected platelet function in patients presenting relatively late after the onset of symptoms. We hypothesized a faster P2Y12 receptor antagonists pharmacodynamic action in patients with diabetes mellitus and poor glycemic control. We aimed to assess the impact of diabetes mellitus (DM) on platelet reactivity (PR) in prasugrel or ticagrelor treated patients. Methods: In 777 acute coronary syndrome patients post PCI, treated by either prasugrel 10 mg od (n=315) or ticagrelor 90 mg bid (n=462), platelet function was assessed using 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. 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.

Conclusion: Overall bleeding events and MACCE were higher in patients treated with triple therapy, while PR under ticagrelor is not affected by DM status or insulin/non-insulin treatment.

P1479 | BEDSIDE
Diabetes mellitus and platelet reactivity in patients under prasugrel or ticagrelor treatment

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Background: The influence of diabetes mellitus on platelet reactivity (PR) in prasugrel- and ticagrelor-treated patients respectively, p for trend=0.01. No differences were observed in ticagrelor-treated patients, while PR under ticagrelor is not affected by DM status or insulin/non-insulin treatment.

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. 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.

Conclusion: Overall bleeding events and MACCE were higher in patients treated with triple therapy, 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

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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.

Methods: To investigate the relationship between diabetes mellitus and platelet reactivity in patients treated with ticagrelor for a recent acute coronary syndrome (ACS).

Results: 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.

Conclusion: 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.

P1489 | BEDSIDE
Factors affecting platelet reactivity shortly after P2Y12 receptor antagonist loading in STEMI patients undergoing primary PCI: the impact of pain-to-loading time

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Background: A delay in antiplatelet action onset occurs in patients with ST-elevation myocardial infarction (STEMI) and is likely due to disturbed absorption. We hypothesized a faster P2Y12 receptor antagonist pharmacodynamic action in patients presenting relatively late after the onset of symptoms.

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. 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.

Conclusion: Overall bleeding events and MACCE were higher in patients treated with triple therapy, while PR under ticagrelor is not affected by DM status or insulin/non-insulin treatment.
Platelets and antiplatelets therapy II / Platelets and antiplatelets therapy III

P1484 | BENCH

**cMPR4 expression in platelet of patients under chronic aspirin treatment is influenced by miRNA modulation: a new mechanism for aspirin resistance?**

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**Background:** MicroRNA are small molecule of non-coding RNA involved in the regulation of many physiological and pathophysiological pathway, including modulation of drug activity. MicroRNAs are abundant also in platelets, where they might participate to the modulation of platelet function and properties.

**Purpose:** 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.

**Methods:** We investigated the influence of selected microRNA modulation on platelet expression of MRP4.

**Results:** MicroRNA-26b-5p may down-regulate MRP4 expression, suggesting a new mechanism involved in aspirin resistance.

**Conclusion:** Further studies are needed to evaluate the role of microRNA modulation in the regulation of platelet function and properties.

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**Platelets and antiplatelets therapy III**

P1484 | BEDSIDE

**Efficacy and safety of triple therapy with novel oral anticoagulants for ischemic heart disease with atrial fibrillation in Japan**

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**Background:** Novel oral anticoagulants (NOACs) were available in Japan few years ago. The efficacy and safety of triple therapy (DAPT + NOAC + antiplatelet drugs) are unclear in Japan.

**Objective:** This study aimed to assess the efficacy and safety of triple therapy with NOACs compared to vitamin K antagonists (VKA).

**Methods:** Subjects were 323 patients received antiplatelet drugs or anticoagulant drugs to prevent thrombosis or embolism. Subjects were divided into 2 groups: the NOAC group and the antiplatelet group. The NOAC group used dabigatran, and the antiplatelet group used aspirin and clopidogrel.

**Results:** The results are shown in the following table.

**Conclusion:** Triple therapy with NOAC and DAPT had lower major bleeding events than the VKA and DAPT. Bleeding mainly occurred in three months later.

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**PLATELETS AND ANTIPLATELETS THERAPY III**

P1484 | BEDSIDE

**Single nucleotide polymorphism in glycoprotein VI gene associated with platelet expression of the glycoprotein VI and risk of cardiovascular events**

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**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.

**Methods:** We aimed to evaluate the influence of selected GPVI polymorphism on platelet expression of GPVI and adverse ischemic events in patients undergoing PCI.

**Results:** 737 patients admitted with symptomatic coronary artery disease from Department of Cardiology and Cardiovascular Medicine, Tübingen; 2 Dr.

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**Platelets and antiplatelets therapy II**

P1481 | BEDSIDE

**Platelet alpha2B-adrenergic receptors in patients with coronary artery disease: The antiaggregant effect of their blockade**

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**Purpose:** Platelets play a vital role in hemostasis and thrombosis. Catecholamines have a profound effect on platelet aggregation and atherothrombosis but the exact mechanism involved is insufficiently understood. In this report, we demonstrate the existence and role of alpha2B-adrenergic receptors (alpha2B-ARs) in platelets from patients with coronary artery disease (CAD) compared to normal individuals.

**Methods:** Twenty three patients with CAD who were under dual antiplatelet therapy with clopidogrel 75 mg and acetylsalicylic acid 100 mg and 20 healthy individuals.

**Results:** Patients with CAD showed a significantly reduced expression of platelet alpha2B-ARs compared to normal individuals. The alpha2B-AR gene expression in patients was examined by real-time PCR.

**Conclusion:** Direct linear relationship was observed between ADP-mediated platelet reactivity and glycosylated hemoglobin, as a parameter of chronic glycemic control, (r=0.15, p=0.029), but not with fasting glycemia (r=-0.08, p=0.20).

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**Platelets and antiplatelets therapy II**

P1483 | BENCH

**Efficacy and safety of triple therapy with novel oral anticoagulants for coronary artery disease: The antiaggregant effect of their blockade**

M. Schwab1, M. Gawaz1, T. Geisler1.

**Background:** The antiaggregant effect of their blockade is associated with a higher platelet reactivity despite dual antiplatelet therapy with ASA and ticagrelor, and especially in those patients with poor chronic glycemic control. In fact, diabetes emerged as independent predictor of HRPR with ticagrelor.

**Purpose:** Platelet alpha2B-adrenergic receptors in patients with coronary artery disease: The antiaggregant effect of their blockade

**Methods:** Patients under aspirin treatment.

**Results:** MicroRNA-26b was transfected in platelet with microRNA mimic technology and flow cytometry was performed to analyse MRP4 expression.

**Conclusion:** We found a higher MRP4 miRNA expression in platelets of patients under aspirin treatment compared to the 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 dys-regulated in platelet with microRNA mimic technology and flow cytometry was performed to analyse MRP4 expression.

**Results:** We found a higher MRP4 miRNA expression in platelets of patients under aspirin treatment compared to the control group (p<0.005). MicroRNA analyses 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 significantly down-regulated in the two cohort of patients under aspirin treatment, compared to control group (p<0.005). Platelet transfection with miRNA 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.

**Acknowledgment/Funding:** grant from Catholic University 70112072
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

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Introduction: Mild therapeutic hypothermia (TH) is standard of care after cardiac arrest of any cause. However, its impact on on-treatment platelet reactivity and clinical outcome remains stable after adjustment for clinical risk factors.

Conclusion: These findings indicate a potential role of GPVI gene variation on platelet activity measured by receptor expression and outcome in CAD patients undergoing PCI and treated with dual antiplatelet therapy. Multigenetic risk stratification might therefore improve risk prediction and encourage personalized treatment strategies in these patients.

Acknowledgement/Funding: This project was supported in part by the DFG-Klinische Forschergruppe (KFO) 274 "Platelets and Molecular Mechanisms"

P1487 | BENCH
Janus kinase 3 (JAK3) dependent signaling is critical to Ca2+-dependent platelet activation and thrombus formation

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Background: Platelet adhesion to subendothelial collagen after plaque rupture occurs in Ca2+-dependent platelet activation, aggregation and degranulation. Platelet activation leads to the development of acute arterial thrombotic occlusions. Janus kinase 3 (JAK3) is a member of the Janus family protein-tyrosine kinases which is strongly expressed in platelets. Mice lacking JAK3 exhibit a profound and early block in both B and T cell development, but the impact of JAK3-dependent signaling in platelet activation and its impact on arterial thrombosis remains unclear.

Conclusion: The present study explored whether Janus Kinase 3 participates in the regulation of platelet activation and arterial thrombus formation.

Methods and results: JAK3-deficient (jak3−/−) mice and its wildtype littermates (jak3+/+) were used to analyze the impact of JAK3 on platelet function and thrombus formation. Fura-2-AM spectrofluorometric Ca2+ measurements revealed a significant reduction in activation-dependent cytosolic Ca2+ increase in jak3−/− platelets compared to jak3+/+ platelets upon stimulation with thrombin or CRP (collagen-related peptide), whereas store operated calcium entry (SOCO) was not affected. ATP-release measurements uncovered a significant decreased activation-dependent dense granule secretion in jak3−/− platelets after stimulation with thrombin or CRP. In addition, jak3−/− platelets showed an impaired agonist induced integrin αIIbβ3 activation and aggregation compared to wildtype platelets. Consensual, flow cytometric analysis revealed that activation-dependent fibrinogen binding was significantly blunted in jak3−/− platelets compared to jak3+/+ platelets. As shown in flow chamber experiments, the in vitro thrombus formation on a collagen-coated surface was significantly reduced in blood from jak3−/− mice compared to blood from wildtype littermates. Proteomic approaches were performed to investigate the underlying molecular mechanism and to identify potential downstream targets of JAK3 in platelets. To evaluate if genetic variants of JAK3 in platelets have a prognostic role in patients with cardiovascular disease we analyzed functional relevant candidate single nucleotide polymorphisms (SNP) in a cohort study of patients with coronary artery disease.

Conclusions: The present observations unravel JAK3 as a crucial player in platelet integrin αIIbβ3 activation, secretion and aggregation as well as arterial thrombosis. JAK3 is at least partially effective by regulating the activation-dependent Ca2+ store release and Ca2+ influx in platelets.
Goal of the current meta-analysis was to compare the efficacy and
nary intervention (PCI) after drug-eluting stent (DES) implantation remains con-
to short-term (≤6 months) treatment, in patients undergoing percutaneous coro-
nary intervention (PCI) after drug-eluting stent (DES) implantation remains
troversial.

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
PCI implantation.

Methods: Medical literature databases were scrutinized to identify randomized
termed controlled trials fulfilling inclusion criteria between January 1990 and Decem-
ber 2014. Efficacy endpoints were all-cause and cardiovascular mortality, stroke and
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 random model. Results: Seven randomized controlled trials met inclusion criteria, enrolling a total of 10,675 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=8,539, 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-

Results: Of 10,675 patients in Phase II (median age 71 years, 54.5% male; me-
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Conclusion: These observational data show that a minority of AF patients are
prescribed AP in combination with OAC, with co-prescription being similar be-

Acknowledgement/Funding: This study was funded by Boehringer Ingelheim

P1489 | BEDSIDE
Short versus long term dual antiplatelet therapy after drug eluting
stent implantation: a systematic review and meta-analysis of randomized
termed controlled trials
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Background: The benefit of 1-year dual antiplatelet therapy (DAPT) as compared to short-term (≤6 months) treatment, in patients undergoing percutaneous coro-
nary intervention (PCI) after drug-eluting stent (DES) implantation remains con-
troversial.

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
PCI implantation.

Methods: Medical literature databases were scrutinized to identify randomized
termed controlled trials fulfilling inclusion criteria between January 1990 and Decem-
ber 2014. Efficacy endpoints were all-cause and cardiovascular mortality, stroke and
myocardial infarction at 12 months. Safety endpoints were the in-
cidence of all and major bleeding, definite or probable stent thrombosis and target vessel revascularization. Data were compared by OR and 94% CI using the Mantel-Haenszel (MH) method. Fixed-effect model was used; if heterogeneity was (I2) ≥40%, 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. Results were significantly fewer beneficial events (OR 0.63 [95% CI 0.46–0.89], p=0.002) as well as major bleeding events (OR 0.52 [95% CI 0.33–0.81], p=0.005) in 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.

P1490 | 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 Pharmacoge-
nomics Consortium (ICPC) Investigators.

Background: The P2Y12 inhibitor clopidogrel is widely used in patients with coro-
nary artery disease and other atherosclerosis related conditions. An important
limitation of clopidogrel is the wide inter-patient variability of platelet inhibition ob-
served with pharmacokinetic and pharmacodynamic testing, in which high platelet
reactivity is a strong predictor of atherothrombotic events. The CYP2C19*2 poly-

crism is the strongest genetic predictor of clopidogrel response known today; how-

Methods: Based on the available data published on www.clinicaltrials.gov, clopi-
dogrel intervention studies containing genetic and platelet function data were se-
lected. 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 cor-
hort. 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, predomi-
nantly Vassodilator-Stimulated Phosphoprotein assay (VASP), adenosine diphos-
phate stimulated Light Transmittance Aggregometry (LTA) and VerifyNow P2Y12.

Conclusion: The IPCG aims to identify new genes influencing clopidogrel effi-
cacy by using state of the art genetic techniques in a large cohort of clopi-
dogrel treated patients. Our findings may further facilitate the development of personal-
ized medicine programs.

Acknowledgement/Funding: National Institutes of Health (NIH) grant
(LO1HL105198). SNP genotyping is supported by the PharmacoGenomics
Research Network & CCMM Alliance.
P1491 | BEDSIDE
A systematic review and meta-analysis of optimal antiplatelet therapy for diabetic patients with acute coronary syndrome

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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 6th 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 (hg 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 meta-analysis

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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
Antiplatelet 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 ischemic 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 single antiplatelet therapy with phenprocoumon (WOEST-cohort) were enrolled. ADP-induced platelet reactivity was assessed on day 1 following coronary stent implantation by impedance aggregometry (Multiplate Assay). High on-treatment platelet reactivity (HTPR) was defined according current consensus recommendations (<488 AU/min).

Results: The WOEST- and DAPT-cohort 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-beta1 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 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-β and SDF-1 and that TGF-β 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 (p=0.572, p<0.001). Platelet-TGF-β1 correlated significantly with platelet-CXCR4 (p=0.330, p<0.001) and platelet-SDF-1 (p=0.229, p=0.099).
Platelets and antiplatelet therapy IV

P1495 | 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

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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±7.50 in new P2Y12 Ri and 212±28.72 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=0.008). 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, TFIIa vs. TRII and use of glycoprotein IIb/IIIa inhibitors were independent predictors of the composite of cardiac death, MI, stent thrombosis, stroke or TIMI major bleeding (od 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 shows 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.

P1496 | BEDSIDE
High on aspirin platelet reactivity predicts cardiac death in acute coronary syndrome patients undergoing PCI (RECLOSE2-ACS study)

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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 light transmission 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.

Conclusion: HAPR is an independent risk factor for cardiac death and stent thrombosis. Therefore, a more intensive antiplatelet therapy might be recommended in this subgroup of patients.
Platelets and antiplatelets therapy IV

P1499 | BEDSIDE
Effect on clinical outcomes of short or long duration of dual antiplatelet therapy after drug-eluting stents: a meta-analysis of randomized trials
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Background: Current guidelines recommend 12-month dual antiplatelet therapy (DAPT) after drug-eluting stent implantation. Recent randomized controlled trials comparing different DAPT durations have yielded conflicting findings in regards to clinical outcomes.

Purpose: The aim of this study was to assess benefits and risks of shorter (i.e. <12 months) DAPT, and of prolonged (i.e. >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. at least 12-month DAPT. All studies were pooled by meta-analysis using a fixed-effects or a random-effects model, as restrictions were applied. Two reviewers independently extracted study data. Data were pooled by meta-analysis using a fixed-effects or a random-effects model, as appropriate.

Results: Ten trials (31,643 participants) were included. Compared to at least 12-month DAPT, patients receiving shorter than 12-month DAPT (7 trials, 15,378 participants) had a lower risk of major bleeding (odds ratio [OR] 0.53; 95% CI, 0.34 to 0.84; p=0.007) and a comparable risk of all-cause death, cardiovascular death, myocardial infarction, definite or probable stent thrombosis and stroke. Compared to 12-month DAPT, patients receiving longer DAPT (3 trials, 16,265 participants) had a higher risk of all-cause death (OR 1.30; 95% CI, 1.02 to 1.66; p=0.035), and of major bleeding (OR 1.54; 95% CI 1.08 to 2.19; p=0.017), a lower rate of stent thrombosis (OR 0.58, 95% CI 0.40 to 0.84; p=0.004), and of definite stent thrombosis (0.34, 95% CI 0.17 to 0.69; p=0.003), similar risk of cardiovascular death and stroke.

Conclusions: 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.

P1500 | BEDSIDE
Risk and benefits of triple therapy in patients undergoing percutaneous coronary stent implantation requiring chronic oral anticoagulation: a meta-analysis of 12 trials
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Background: Patients with coronary artery disease who undergo stent implantation and have concomitant indication for long term oral anticoagulation represent a considerable percentage of the overall population. To date there is still no consensus about the optimal antithrombotic strategy to choose in this kind of patients, due to the difficult balance between an increased risk of bleeding and thromboembolic complications.

Purpose: Aim of this meta-analysis was to evaluate risk and benefits of triple antithrombotic therapy versus dual antiplatelet therapy in patients undergoing coronary artery disease stent implantation, requiring oral anticoagulation.

Methods: We performed formal searches of PubMed, EMBASE, Cochrane central registry of controlled trials and major international scientific session abstracts from January 1990 to September 2014 regarding the use of triple antithrombotic therapy versus dual antiplatelet therapy in patients undergoing percutaneous coronary stent implantation that required chronic oral anticoagulation. Data regarding study design, inclusion/exclusion criteria, number of patients, and selected endpoints was extracted by 2 investigators. Disagreements were resolved by consensus.

Results: Twelve trials, with a total of 7383 patients undergoing stent implantation with indication to long term oral anticoagulation were finally included. A total of 2686 patients were treated with triple therapy whereas 5152 patients received dual antiplatelet therapy alone. The follow-up period ranged from 270 to 2000 days. Only 10.6% of patients in dual antiplatelet therapy and 19.6% of patients in dual antiplatelet therapy (OR [95% CI] = 0.80 [0.69–0.94], p=0.005; phef = 0.0003). By meta-regression analysis no relationship was observed between reduction in mortality and the risk of bleedings (p=0.10). Data regarding secondary endpoints showed a significant association between triple therapy and
an increased risk of bleedings (12.3% versus 9.9%) (OR [95% CI] = 1.37 [1.16 – 1.62], p=0.0002; phef = 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 coronary intervention, requiring chronic oral anticoagulation, the use of a triple antithrombotic therapy is associated with a significant reduction in mortality that largely outweighed the higher 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


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 revascularization 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: P2Y12 reactivity unit by the VerifyNow P2Y12 test was 68.6±66.82 in ticagrelor and 237.9±89.57 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; 8.3% 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. TRI and non ST elevation MI were independent predictors of TIMI major bleeding (odds ratio [OR]=2.807; 95% confidence interval [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


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: Dual anti-platelet therapy (DAPT) is still a controversial issue despite some reports on shortening of its duration.

P1505 | BEDSIDE
Dual anti-platelet therapy after drug-eluting coronary stent implantation and risks associated with colonicoscopy or rectoscopic polypectomy - a Danish registry study


Methods: The Western Denmark Heart registry was used to identify patients treated with DES implantation between July 2006 and December 2011. Using cross-linkage with national registries, we identified patients with a colonicoscopy or rectoscopic polypectomy within 12 months after DES implantation. We registered adverse cardiac events defined as death, myocardial infarction (MI), or definite stent thrombosis, and bleeding complications according to the Bleeding Academic Research Consortium (BARC) definitions within 30 days after polypectomy. Furthermore, we wished to evaluate periprocedural DAPT strategy by review of hospital charts.

Results: The cohort consisted of 22,654 patients in which 1224 colonicoscopies or rectoscopies were performed within 12 months. Polypectomy was performed in 177 of these patients. Among patients undergoing polypectomy there were no adverse cardiac events while 18 (10%) BARC ≥2 bleeding complications that led to prolonged hospital stay, blood transfusion or renewed endoscopic procedure were recorded. There were no fatal bleeding incidents. The retrospective review of hospital charts revealed missing documentation of the patient’s periprocedural anti-thrombotic treatment for 111 (64.5%) of the polypectomy procedures. Among patients with bleeding complications, 22% received dual antiplatelet therapy, 28% single antiplatelet therapy, 17% no antiplatelet therapy, while no documentation could be identified for 33%.

Conclusion: Polypectomy in DES-treated patients was not associated with adverse cardiac events within a 30-day follow-up period. Post-procedural bleeding was a relatively frequent observation but without any clear relation to the periprocedural antiplatelet strategy.

Acknowledgement/Funding: Aarhus University Hospital, Department Of Cardiology

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: Dual anti-platelet therapy (DAPT) is recommended for up to 12 months in patients treated with coronary drug-eluting stent (DES) implantation. Within this time period some patients will need colonicoscopy evaluation and intervention. Real-life handling of DAPT in relation to polypectomy varies, and the associated risk of adverse cardiac events and bleeding complications is largely unknown. 

Purpose: To assess the frequency of adverse cardiac events and bleeding complications in relation to colonicoscopy or rectoscopic polypectomy, and evaluate the possible association of continuing or disrupting DAPT on adverse cardiac events and bleeding complications.

Methods: The Western Denmark Heart registry was used to identify patients treated with DES implantation between July 2006 and December 2011. Using cross-linkage with national registries, we identified patients with a colonicoscopy or rectoscopic polypectomy within 12 months after DES implantation. We registered adverse cardiac events defined as death, myocardial infarction (MI), or

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.
**ACCESS SITE VS NON-ACCESS SITE BLEEDING IN PRIMARY PCI**

**Results:**

- **Access only:** 112/2198 (5.1%) vs 44/1089 (4.05%) vs 68/1109 (6.15%)
- **Non-access only:** 72/2198 (3.33%) vs 24/1089 (2.2%) vs 51/1109 (4.59%)
- **Both:** 18/2198 (0.8%) vs 6/1089 (0.52%) vs 12/1109 (1.08%)
- **No location:** 28/2198 (1.26%) vs 11/1089 (1.01%) vs 16/1109 (1.45%)

**Category**  
**Total** | **Bivalirudin** | **UFH±GPI** | **Relative risk (95%CI)**  
--- | --- | --- | ---  
**Access only** | 112/2198 | 44/1089 | 68/1109 | 0.66 (0.8)  
**Non-access only** | 72/2198 | 24/1089 | 48/1109 | 0.51 (1.1)  
**Both** | 18/2198 | 6/1089 | 12/1109 | 0.51 (1.0)  
**No location** | 28/2198 | 11/1089 | 18/1109 | 0.62 (2.1)  

**Conclusions:** 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

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**P5150 | BEDSIDE**

**Coronary index of microcirculatory resistance and echocardiographic parameters evolution in patients with ST-elevation acute myocardial infarction 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 technique. This study aims to evaluate the relationship between IMR and echocardiographic parameters evolution in STEMI patients, treated with P-PCI.**

**Purpose:**

- **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.**

**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 (-14.8 vs -12.7, P=0.005). 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 remodeling after acute myocardial infarction.

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**P5107 | 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 repertused 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 (LVEF) 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 at 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, underlining its clinical significance.

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**P5108 | BEDSIDE**

**Association of SDF-1 polymorphisms with differential platelet CXCR4 expression in patients with coronary artery disease**

**Methods:**

- **SDF-1, CXCR4 and CXCR7 expression in CAD patients.**

**Purpose:**

- **SDF-1, CXCR4 and CXCR7 expression in patients with coronary artery disease**

**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, underlining 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 24.9/57.45 vs. 22.44; 25th/75th percentile 17.24/26.28, p=0.019 and median MFI 31.18; 25th/75th percentile 24.9/57.45 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 28.88; 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.

Conclusion: 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.

P1510 | BEDSIDE
Predictive factors of left ventricular thrombus after myocardial infarction using cardiovascular magnetic imaging

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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 was 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), end-systolic volume (54.8±25.9 vs. 37.8±14.5 mL/m², p<0.001), peak creatinine kinase (407±242 U/L vs. 287±212 U/L, p=0.044), fixed infarct size (33.6±19.6 g vs. 22.4±17.1 g, p=0.019) as compared to the wild type (median CXCR4 MFI 28.88; 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: In a contemporary single center PCI registry, patients’ ischemic risk appears to drive the selection of anticoagulation therapy in patients with AF, whereas bleeding score does not seem to affect physicians’ prescription patterns. NOAC use declined with increasing patient ischemic risk despite known clinical efficacy compared to coumadin.
Abstract P1513 – Table 1

<table>
<thead>
<tr>
<th>Country</th>
<th>First patient on a NOAC</th>
<th>Patients on NOACs, % (n/N)</th>
<th>6 months</th>
<th>12 months</th>
<th>24 months</th>
<th>36 months</th>
<th>48 months</th>
<th>60 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>2010 Feb</td>
<td>18.8 (3/16)</td>
<td>4.0 (4/99)</td>
<td>5.0 (10/216)</td>
<td>8.4 (34/404)</td>
<td>7.5 (13/174)</td>
<td>9.6 (53/544)</td>
<td>16.2 (71/438)</td>
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<tr>
<td>Poland</td>
<td>2010 Jun</td>
<td>3.0 (1/33)</td>
<td>6.0 (2/33)</td>
<td>10.7 (7/66)</td>
<td>12.7 (10/80)</td>
<td>11.2 (9/82)</td>
<td>17.0 (12/71)</td>
<td>28.2 (6/22)</td>
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<tr>
<td>Germany</td>
<td>2010 Aug</td>
<td>4.3 (19/438)</td>
<td>7.2 (31/436)</td>
<td>9.5 (42/448)</td>
<td>15.0 (31/206)</td>
<td>11.2 (52/466)</td>
<td>11.3 (25/221)</td>
<td>18.0 (20/111)</td>
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<td>Spain</td>
<td>2010 Nov</td>
<td>2.7 (3/109)</td>
<td>3.3 (6/193)</td>
<td>5.0 (25/496)</td>
<td>9.5 (23/242)</td>
<td>6.5 (16/247)</td>
<td>10.2 (24/232)</td>
<td>10.5 (24/221)</td>
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<td>France</td>
<td>2011 Jan</td>
<td>2.3 (7/301)</td>
<td>3.3 (8/242)</td>
<td>6.1 (8/130)</td>
<td>14.1 (16/114)</td>
<td>9.5 (11/116)</td>
<td>13.7 (16/118)</td>
<td>17.8 (15/84)</td>
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<td>Italy</td>
<td>2011 Jan</td>
<td>5.9 (7/117)</td>
<td>7.2 (7/100)</td>
<td>11.1 (14/126)</td>
<td>21.5 (26/121)</td>
<td>13.1 (16/123)</td>
<td>17.0 (17/101)</td>
<td>28.1 (12/43)</td>
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<td>Norway</td>
<td>2011 May</td>
<td>5.3 (3/56)</td>
<td>6.4 (4/63)</td>
<td>10.7 (24/222)</td>
<td>18.9 (24/126)</td>
<td>14.9 (20/135)</td>
<td>22.7 (20/93)</td>
<td>29.4 (20/69)</td>
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<td>Finland</td>
<td>2011 Sep</td>
<td>3.1 (2/65)</td>
<td>3.8 (4/105)</td>
<td>7.5 (10/133)</td>
<td>16.2 (14/86)</td>
<td>10.7 (10/94)</td>
<td>17.0 (17/100)</td>
<td>25.0 (12/46)</td>
</tr>
<tr>
<td>Denmark</td>
<td>2011 Sep</td>
<td>25.0 (23/90)</td>
<td>27.8 (27/98)</td>
<td>32.6 (32/100)</td>
<td>35.7 (35/100)</td>
<td>30.8 (30/99)</td>
<td>35.7 (35/99)</td>
<td>35.7 (35/99)</td>
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</table>

Abstract P1514 – Table 1

<table>
<thead>
<tr>
<th>Country</th>
<th>First patient on a NOAC</th>
<th>Patients on NOACs, % (n/N)</th>
<th>6 months</th>
<th>12 months</th>
<th>24 months</th>
<th>36 months</th>
<th>48 months</th>
<th>60 months</th>
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<tbody>
<tr>
<td>Austria</td>
<td>2010 Feb</td>
<td>1.4 (4/276)</td>
<td>4.0 (4/99)</td>
<td>5.0 (10/216)</td>
<td>8.4 (34/404)</td>
<td>7.5 (13/174)</td>
<td>9.6 (53/544)</td>
<td>16.2 (71/438)</td>
</tr>
<tr>
<td>Poland</td>
<td>2010 Jun</td>
<td>1.8 (3/166)</td>
<td>6.0 (2/33)</td>
<td>10.7 (7/66)</td>
<td>12.7 (10/80)</td>
<td>11.2 (9/82)</td>
<td>17.0 (12/71)</td>
<td>28.2 (6/22)</td>
</tr>
<tr>
<td>Germany</td>
<td>2010 Aug</td>
<td>4.3 (19/438)</td>
<td>7.2 (31/436)</td>
<td>9.5 (42/448)</td>
<td>15.0 (31/206)</td>
<td>11.2 (52/466)</td>
<td>11.3 (25/221)</td>
<td>18.0 (20/111)</td>
</tr>
<tr>
<td>Spain</td>
<td>2010 Nov</td>
<td>2.7 (3/109)</td>
<td>3.3 (8/242)</td>
<td>6.1 (8/130)</td>
<td>14.1 (16/114)</td>
<td>9.5 (11/116)</td>
<td>13.7 (16/118)</td>
<td>17.8 (15/84)</td>
</tr>
<tr>
<td>France</td>
<td>2011 Jan</td>
<td>2.3 (7/301)</td>
<td>3.3 (8/242)</td>
<td>6.1 (8/130)</td>
<td>14.1 (16/114)</td>
<td>9.5 (11/116)</td>
<td>13.7 (16/118)</td>
<td>17.8 (15/84)</td>
</tr>
<tr>
<td>Italy</td>
<td>2011 Jan</td>
<td>5.9 (7/117)</td>
<td>7.2 (7/100)</td>
<td>11.1 (14/126)</td>
<td>21.5 (26/121)</td>
<td>13.1 (16/123)</td>
<td>17.0 (17/101)</td>
<td>28.1 (12/43)</td>
</tr>
<tr>
<td>Norway</td>
<td>2011 May</td>
<td>5.3 (3/56)</td>
<td>6.4 (4/63)</td>
<td>10.7 (24/222)</td>
<td>18.9 (24/126)</td>
<td>14.9 (20/135)</td>
<td>22.7 (20/93)</td>
<td>29.4 (20/69)</td>
</tr>
<tr>
<td>Finland</td>
<td>2011 Sep</td>
<td>3.1 (2/65)</td>
<td>3.8 (4/105)</td>
<td>7.5 (10/133)</td>
<td>16.2 (14/86)</td>
<td>10.7 (10/94)</td>
<td>17.0 (17/100)</td>
<td>25.0 (12/46)</td>
</tr>
<tr>
<td>Denmark</td>
<td>2011 Sep</td>
<td>25.0 (23/90)</td>
<td>27.8 (27/98)</td>
<td>32.6 (32/100)</td>
<td>35.7 (35/100)</td>
<td>30.8 (30/99)</td>
<td>35.7 (35/99)</td>
<td>35.7 (35/99)</td>
</tr>
</tbody>
</table>
coronary syndrome 528, and other diseases 207). Median (interquartile range) of d-dimer levels for each groups 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 5.5 (2.6–13.6) in d-dimer levels of 0.5–2.0 μg/mL, 21.4 (8.7–52.4) in 2.1–5.0 μg/mL, 92.4 (36.4–232.9) in 5.10–20.0 μg/mL, and 142.1 (50.7–378.0) in over 20.0 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 of 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


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Background: Patients with atrial fibrillation (AF) and prior stroke represent the highest risk category, given the substantial stroke risk 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=9867). In those with previous stroke, VKA alone was prescribed in 25.6%, 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 similar between males and females, although VKA plus AP was more prevalent in males. In comparison, patients in both groups showed a similar proportion of stroke or no therapy were higher (12.5% versus 7.8%). Amongst those with prior stroke, proportions on AP alone in Asia, Europe, and North America were 22.8%, 9.3% and 5.6% respectively, whilst proportions on no antithrombotic therapy in these regions were 15.1%, 4.9% and 5.9% respectively.

Conclusion: In AF patients with prior stroke a mean CHA2DS2-VASc score of 5, approximately 16% were treated with AP or no antithrombotic therapy, with 5.8% received no antithrombotic therapy. Proportions were broadly similar between males and females, although VKA plus AP was more prevalent in males. In comparison, patients in both groups showed a similar proportion of stroke or no therapy were higher (12.5% versus 7.8%). Amongst those with prior stroke, proportions on AP alone in Asia, Europe, and North America were 22.8%, 9.3% and 5.6% respectively, whilst proportions on no antithrombotic therapy in these regions were 15.1%, 4.9% and 5.9% respectively.

Acknowledgement/Funding: This study was funded by Boehringer Ingelheim.

CARDBIOVASCULAR MAGNETIC RESONANCE IN CLINICAL PRACTICE I

P1517 | 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.G. Gavara2, A. Paya1, D. Escribano1, P. Racugno1, A. Hervas1, F.J. Chorro1, V. Bodi1.

1University Hospital Clinic, Department of Cardiology, Valencia, Spain; 2Hospital Clinic de Barcelona, Cardiology, Barcelona, Spain; 3Hospital Clinic de Barcelona, Cardiology, Barcelona, Spain

Abstract P1516 – Table 1

<table>
<thead>
<tr>
<th>N (%)</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole cohort</td>
<td>10675</td>
<td>999</td>
<td>552</td>
</tr>
<tr>
<td>Age (median, IQR, Q3)</td>
<td>71 (64, 78)</td>
<td>74 (67, 81)</td>
<td>72 (69, 79)</td>
</tr>
<tr>
<td>CHA2DS2-VASc (median, IQR, Q3)</td>
<td>3 (2, 4)</td>
<td>5 (4, 6)</td>
<td>5 (4, 6)</td>
</tr>
<tr>
<td>VKA alone</td>
<td>2873 (26.9)</td>
<td>2865 (26.5)</td>
<td>137 (24.8)</td>
</tr>
<tr>
<td>VKA plus AP</td>
<td>176 (5.4)</td>
<td>161 (6.1)</td>
<td>39 (7.1)</td>
</tr>
<tr>
<td>NOAC alone</td>
<td>4390 (41.1)</td>
<td>448 (44.8)</td>
<td>247 (44.7)</td>
</tr>
<tr>
<td>NOAC plus AP</td>
<td>700 (6.6)</td>
<td>59 (5.9)</td>
<td>35 (6.3)</td>
</tr>
<tr>
<td>AP alone</td>
<td>1215 (12.3)</td>
<td>108 (10.8)</td>
<td>63 (11.4)</td>
</tr>
<tr>
<td>No antithrombotic therapy</td>
<td>814 (7.6)</td>
<td>58 (5.8)</td>
<td>31 (5.6)</td>
</tr>
</tbody>
</table>

*9 patients had missing information on previous stroke.

Conclusion: A comprehensive cardiac MR approach was carried out. Infarct size (IS) and microvascular obstruction (MVO) were quantified in late gadolinium enhancement (LGE) imaging. RevRem was defined as a decrease in left ventricular (LV) end-systolic volume index (LVESI) >10% from 1-week to 6-months. Patients with RevRem (n=211, 42%) had a lesser extent of 1-week IS (p<0.001), MVO (p<0.01) and hemorrhage (p<0.01). However, there were no differences between those without RevRem (n=296, 58%), 1-week LV ejection fraction (LVEF) and LVESI did not relate to RevRem (p>0.4). In a comprehensive multivariate analysis, the only independent predictor of RevRem was the presence of simultaneous non-extensive IS-MVO (IS <30% of LV mass and MVO <25% of LV mass): 3.2 [1.8–5.7], p<0.001. From 1-week to 6-months, LVESI diminished in patients with simultaneous non-extensive IS-MVO (S55±15 vs. S31±13 ml/m², p<0.01), did not vary in those with extensive MVO (42±11 vs. 41±11 ml/m², p=0.7) or extensive IS (S46±26 vs. S56±28 ml/m², p=0.5) but did notl in patients with simultaneous extensive IS-MVO (S59±21 vs. S65±27 ml/m², p=0.004).

Acknowledgement/Funding: This study was funded by Boehringer Ingelheim.

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Acknowledgement/Funding: This study was funded by Boehringer Ingelheim.
P1519 | BEDSIDE
Natural history and clinical significance of extracellular volume and remodelling in survivors of acute STEMI

J. Carberry1, D. Carrick1, C. Haig2, S.M. Rauhaniamii3, N. Ahmed4, M. McInteart2, A. Mahrous3, A. Radjenovic5, K.G. Oldroyd6, C. Berry7
1University of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow; 2University 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 mapping. We aimed to measure infarct zone ECV post-reperfusion in a serial follow-up of 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 meglumin). 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. 52.9±11.1% (p=0.0399)). Mean in infarct size increased 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=0.5, p<0.001) (n=124) and follow-up (ρ=0.6, p<0.001) (n=160). 87 (51%) patients had MVO at baseline. Mean LV ECV increased from baseline to follow-up (55.1±5.8% vs. 62.2±5.6%, 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 post-coronal perfusion, LVEF <45%, and presence of MVO at baseline. Reduced LV ejection fraction (lEF) and higher LV end systolic volume (LVESV) at follow-up (all p<0.05) (n=117).

Conclusion: Infarct zone ECV is increased at 6 months in approximately one third (33%) of STEMI patients. LVEF, 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

P1512 | BEDSIDE
Temporal evolution and prognostic significance of infarct core pathology in STElevation myocardial infarction survivors revealed by serial quantitative T2-weighted cardiac magnetic resonance

D.J.A. Carrick1, C. Haig2, N. Ahmed1, H. Etelba3, S. Hood4, M. Petrie5, M. Lindsay6, A. Radjenovic7, K.G. Oldroyd8, C. Berry1
1Cardiovascular Research Centre of Glasgow, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom; 2University of Glasgow, Robertson Centre for Biostatistics, Glasgow, United Kingdom; 3Golden Jubilee National Hospital, Cardiology, Glasgow, United Kingdom

Background: Myocardial transverse relaxation time (T2, ms) is a fundamental magnetic property of tissue that is related to water content and mobility. To assess the clinical significance of infarct core tissue using cardiac magnetic resonance (CMR) imaging in survivors of acute ST elevation myocardial infarction (STEMI) and assess the temporal evolution of myocardial T2 early after reperefusion in a serial imaging sub-set.

Methods: We performed a prospective single centre cohort study in reperefused STEMI patients who underwent CMR 2 days and 6 months post-MI. T2 (relaxation time, ms) was measured using quantitative T2-mapping. A subset of 30 STEMI patients underwent imaging at 4 time-points: 4–12 hours, 3 days, 10 days and 6–15 months post-reperfusion. Adenosine perfusion stress and intracoronary microemulsion (MIH) were defined as a T2 value of <20 ms within the infarct core.

Results: 324 STEMI patients underwent CMR. 164 (51%) patients had microvascular obstruction (MVO) whereas 197 (61%) patients had an infarct core revealed

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: This study is supported by the NIHR.
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 prevalence of T2 core in all chronic cases was more closely related to early MVO (186 patients (57%) than late MVO. In multivariable regression, T2 core in the infarct core was associated with a reduced risk of all-cause death or heart failure hospitalisation (HR 0.786, 95% CI 0.658, 0.939; p=0.012) after including 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 core was evaluated with CMR in patients with IMH. In 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 core index 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.

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 and defibrillation lead.

PI525 | BEDSIDE
Cardiac magnetic resonance findings in active rheumatoid arthritis

S. Kivistö1, R. Kolvinieemi2, K. Korpi3, T. Kaasalainen1, M. Laine3, M. Kupari3, M. Leirisalo-Repo3, M. Holmstrom1, 1Helsinki University Central Hospital, Radiology, Helsinki, Finland; 2Helsinki University Central Hospital, Department of Rheumatology, Helsinki, Finland; 3Helsinki 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 biological agents and patients with long-lasting active RA undergoing 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 were slightly elevated values compared to reference values: 1002±46 ms septum, 975±48 ms lateral wall in 1.5T and 1166±34 ms septum 1150±50 ms lateral wall in 3T (reference values: 966±48 ms in 1.5T and 1166±60 ms in 3T). Out of 58 RA patients 38 (58%) exhibited myocardial diffuse fibrosis and scarring were reported.

Conclusion: A hypointense core index 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.

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 and defibrillation lead.

PI525 | 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 (UHach 443, 66.2%) vs. the large group (UHach III-V; 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 multivariable logistic regression analysis. The large extent of DEMRI was independently associated with early recurrence (EA) after CA (HR 3.909, 95% CI 1.177-12.982, p=0.026).

Figure. The examples of distinctly different extent of left atrial delayed enhancement in lone atrial fibrillation (AF): (A) 63-year-old female with paroxysmal AF. (B) 69-year-old male with persistent AF.

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
Background: 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-LVAA was recorded in one patient. Pathological findings confirmed that LGE corresponded well with the fibrous tissue in LVA. The follow-up (2.8±1.3 years) suggested that the LGE of LVAA was associated with the adverse events (hazard ratio [HR]: 7.94; HR (95% CI): 0.89–71.17, P=0.064).

Purpose: The 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.

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.

Background: Myocardial extracellular volume (ECV) using cardiac magnetic resonance (CMR) T1 mapping is a promising technique for quantifying diffuse interstitial fibrosis in patients with chronic renal insufficiency. Native T1 is measured from endomyocardial biopsies.

Purpose: To determine the usefulness of native T1 mapping.

Methods: CMR at 3T scanner was performed in 40 DCM patients. T1 mapping was obtained before and after contrast administration. CMR ECV was calculated using hematocrit-adjusted myocardial and blood T1 values measured before and 21 minutes after gadolinium bolus. Histological collagen volume fraction (CVF) was measured from endomyocardial biopsies.

Results: Native T1 values correlated with both CMR ECV (r=0.69, p<0.001) and histological CVF (r=0.66, p<0.001). Furthermore, native T1 values were significantly increased in patients with cardiac death than that in survivors (141±33 msec vs. 131±59 msec, p=0.020).

Conclusion: Native T1 shows positive correlations with CMR ECV and histological CVF. Native T1 mapping is a useful technique to evaluate myocardial damages in DCM patients.

Background: Myocarditis is defined as inflammation of the myocardium diagnosed by established histological and immunohistochemical criteria as evidence of myocardial edema associated with necrosis of non ischemic origin. Myocarditis can be involved in the pathogenesis of cardiac dysfunction leading to inflammatory cardiomyopathy which may progress to dilated cardiomyopathy chronically. In recent clinical practice cardiac magnetic resonance (CMR) has become an useful non-invasive technique to diagnose acute myocarditis and for monitoring disease progression.

Aim: Define which of the CMR parameters is able to both identify ventricular dysfunction (LVEF ≤50%) in the acute phase of the disease and to predict the disease progression at 6 months follow up.

Methods: We enrolled consecutive patients with suspected myocarditis, according to ESC position statement, in which the diagnosis was also been 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 (mean peak 8 ug/L). Based on the presence of left ventricular dysfunction (LVEF ≤50%) population was divided in 2 groups: without (n=64) 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 decreased 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 complete dysfunction 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 substrate of acute cardiac dysfunction and to provide information about the disease progression toward dilated cardiomyopathy at the follow up.
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 not 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=49.37, 95% CI: 1.08–2263.24, 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 decompenated 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
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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 assessment of microvascular ischaemia with outcomes has not been yet 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 CMR-based cardiac perfusion analysis.

Methods: 30 patients with HCM underwent CMR with Fermi constrained quantification of 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 noncorrected 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 previous data corrected for the presence of fibrosis on a pixel-by-pixel basis.

Conclusion: Combined high-resolution fibrosis and perfusion mapping by CMR can detect the microvascular ischaemia burden in patients with HCM. It improves the accuracy of perfusion analysis in patients with LGE on CMR images. The interaction between microvascular ischaemia and perfusion is a key determinant of functional outcomes in HCM patients.

Average MPR according to patient groups using segmental and high-resolution quantification

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>MPR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA+LGE+ (N=12)</td>
<td>2.8±0.5</td>
<td>&lt;0.0002</td>
</tr>
<tr>
<td>PA+LGE− (N=7)</td>
<td>2.3±0.5</td>
<td>&lt;0.0004</td>
</tr>
<tr>
<td>PA-LGE+ (N=9)</td>
<td>2.4±0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PA-LGE− (N=9)</td>
<td>2.6±0.6</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.

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P1531 | BEDSIDE
Prospective changes of left ventricular iron and function by MRI in pediatric thalassemia major patients treated with different chelators or not chelated
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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 multi-echo 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 desferrioxamine (DFO—mean dosage 43±7.6 mg/kg/die), 7 patients (3 F, 15±1.7 years) treated with deferoxamine (DFP—75±0.2 mg/kg/die), 39 patients (13 F, 13±3.4 years) treated with deferasirox (DFX—26.6±6.7 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 non-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* 20–100 ms) at baseline showed no iron at the FU while the patient with severe MIO (T2* <10 ms) remained in the same status at the FU. Non chelated patients had higher global heart T2* values at baseline (non-chelated 37.7±0.5 ms vs. DFP 35.3±4.9 ms vs. DFX 32.7±9.6 ms vs. DFO 31.9±10.5 ms) while DFP patients had higher global heart T2* values at the FU (DFP 39.5±6.1 ms vs. DFX 34.2±7.3 ms DFO 33.6±7.9 ms–on-chelated 28.8±4.0 ms).

In the DFO group at baseline patient 1 showed pathological late ventricular ejection fraction (LVEF) and he recovered at the follow up. In the DFP group at baseline 2 patients showed pathological LVEF and both recovered at the FU. In the DFX 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 concordant 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
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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) constituting the “female MD carrier comparison group” (N=24, 6 DMD and 18 BMD) and 70 first degree male relatives (24 MD, 20 DMD and 26 BMD) were analyzed. 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 presence of LGE). All LGE-positive patients (N=16) showed non-ischemic LGE with subepicardial involvement of the LV lateral wall free being the most frequent pattern (13/16, 81%). Compared to BMDc, DMDc demonstrated more frequently a pathological CMR result (65% vs. 25%; p=0.023) – in spite of being significantly younger (40 years±11 yrs vs. 55±16 yrs, p<0.039). In the male MD comparison group, the same LGE pattern as in female carriers was seen, but with a significantly higher prevalence of cardiac abnormalities compared to their female carrier relatives constituting the female MD comparison group (75% vs. 27%; p=0.003).

Conclusions: Cardiac involvement is a frequent finding in female carriers of DMD, but rarely observed in carriers of BMD. Those DMDc and BMDc with cardiac involvement demonstrate the same myocardial fibrosis pattern as their male counterparts with overt disease.
P1534 | BEDSIDE
Left ventricular myocardial edema as the substrate underlies transient T-wave inversion in acute myocarditis
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Background: Myocarditis is defined as inflammation of the myocardium as histological evidence of myocardial edema associated with necrosis of non ischemic origin. Electrocardiogram (EGO) 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 (TWA). Despite the limitations of cardiac MRI in myoccarditis, including technical artifacts, 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.

Aim: To prospectively evaluate the relationship between LGE and TWI in acute myocarditis.

Methods: From January 2015 to December 2017, we prospectively evaluated 129 consecutive patients (72±16 years) with acute myocarditis. Three-dimensional whole-heart CMR was performed on 1.5-Tesla scanners with the acquisition of post-contrast T1 mapping, T2*, and T1 maps. T2* images were acquired post-gadolinium administration. The late gadolinium enhancement (LGE) acquisitions were performed after intravenous administration of gadolinium contrast agent.

Results: Mean age was 48.2±16.1 years and 42% were females. Previous myocarditis was associated with cardiac involvement at a mean age of 21.92±15.89 years. The mean administered dosage of DFO via subcutaneous route was 38.4±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 cases of non-ischemic myocardial fibrosis were detected.

Conclusions: In this small population of sporadically or non-transfused TWA-positive 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
Non-contrast T1-mapping to detect increased collagen volume
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Introduction: Recently, novel myocardial T1 mapping methods that allow the quantitative measurement of myocardial collagen have been developed. However, the accuracy of this method remains uncertain, especially when evaluating myocardial fibrosis in cases that show a large difference between the myocardial T1 and extracellular water (ECW) time constants. We aimed to determine the accuracy and usefulness of the native T1-mapping method for evaluating myocardial fibrosis.

Purpose: To assess the accuracy of the native T1-mapping method for evaluating myocardial fibrosis in DCM patients.

Subjects and Methods: We enrolled 24 patients with DCM who underwent both native T1-mapping and CMR with late gadolinium enhancement (LGE) at a mean age of 67±12 years (9 men and 15 women). For 21 patients the presence of myocardial fibrosis was investigated at both baseline and follow-up (FU) MRIs. Cardiac function was assessed at both FU and baseline. T2* measurement was performed using picrosirius red staining.

Results: We observed a significant difference between the baseline and follow-up T2* values in the myocardium of all patients, regardless of whether they had myocardial fibrosis or not. The mean difference in T2* values between baseline and follow-up scans in the myocardium was 10.7±5.5 ms (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.

P1536 | BENCH
Increased resting level of periodic repolarization dynamics predicts exercise-induced T-wave alternans
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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.

Aim: 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).

### Table 1: Uni- and multivariable analyses

<table>
<thead>
<tr>
<th>Risk Variable</th>
<th>Univariable logistic regression</th>
<th>Multivariable logistic regression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Standardized coefficients p-value</td>
<td>Standardized coefficients p-value</td>
</tr>
<tr>
<td>Age</td>
<td>0.11 (0.04–0.18) 0.001</td>
<td>0.06 (−0.02–0.15) 0.162</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.09 (0.02–0.15) 0.011</td>
<td>0.07 (0.00–0.13) 0.544</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.02 (−0.14–0.10) 0.932</td>
<td>–</td>
</tr>
<tr>
<td>Sex</td>
<td>−0.06 (−0.13–0.01) 0.112</td>
<td>–</td>
</tr>
<tr>
<td>Max HR</td>
<td>0.02 (−0.09–0.04) 0.399</td>
<td>–</td>
</tr>
<tr>
<td>Baseline HR</td>
<td>0.03 (−0.04–0.10) 0.252</td>
<td>–</td>
</tr>
<tr>
<td>Betablockers</td>
<td>0.11 (0.04–0.18) 0.003</td>
<td>0.10 (0.01–0.19) 0.038</td>
</tr>
<tr>
<td>History of MI</td>
<td>0.05 (−0.02–0.11) 0.183</td>
<td>–</td>
</tr>
<tr>
<td>PRd at rest</td>
<td>0.02 (0.16–0.29) &lt; 0.0001</td>
<td>0.20 (0.14–0.26) &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 as being not specific to cardiac repolarization abnormality, to be related to sudden death, the exact mechanism is still not well established. False tendons are (FT) fibromuscular bands that traverse the left ventricular cavity and often contain conduction tissue which has been recognized as something new in some 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 notch (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 tendinae, to the mitral leaflet. PFRd, QRSd, 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 isolated FTs (P=0.05) 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.

### P1538 | BEDSIDE

Sensitivity and specificity of an electrocardiogram in detecting left ventricular hypertrophy in a native Tanzanian population

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**Background:** An electrocardiogram (ECG) is often the only tool used for detection of left ventricular hypertrophy (LVH) in many outpatient clinics in sub-Saharan Africa. However the sensitivity and specificity of the ECG in detecting true increase in left ventricular mass has been reported to be very low, especially in African American. This observation has however not been widely studied in native African populations.

**Purpose:** To determine the sensitivity and specificity of the ECG in detecting echocardiographic LVH in a native Tanzanian population.

**Methods:** Echocardiography and 12-lead resting ECGs were performed in 326 adults (mean age 49.5 years, 58.6% females) participating in studies to determine the prevalence and functional consequences of abnormal left ventricular geometry in Tanzanian out-patients with hypertension and diabetes. ECG-LVH was determined using Sokolow-Lyon as well as Cornell product criteria, and compared to echocardiographically determined LVH defined as left ventricular mass index greater than 49.2g/m² in men and 46.7g/m² in women 2.7.

**Results:** Echocardiographic LVH was present in 113 (34.7%) subjects, while ECG–LVH was detected in 82 (25.2%) by Sokolow-Lyon, in 85 (26.1%) by Cornell-product criteria, and in 132 (40.5%) by either of the ECG criteria. Out of the 113 subjects with echocardiographic LVH, 39 (34.5%) were correctly detected (i.e. sensitivity) by the Sokolow-Lyon, 56 (49.6%) by the Cornell-product and 69 (61.2%) by either of the ECG criteria. The ability of the ECG to exclude echocardiographic LVH (i.e. specificity) was 79.8%, 86.4% and 70.4%, respectively for Sokolow-Lyon, Cornell-product and for either criterion.

**Conclusion:** The ECG sensitivity detected in this study is much higher than that reported in African Americans and when used in combination Sokolow-Lyon and Cornell product criteria can be used as a tool to detect LVH in places where echocardiography is not available.

### P1539 | BEDSIDE

Heart rate impact on heart rate variability prognostic value is different for different indices and outcomes

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**Background:** Heart rate variability (HRV) indices are deemed to predict out- comes independently on heart rate (HR), however most of them correlate with HR, thus they may carry some prognostic information from HR. By normalization to HR one can explore how much prognostic power of HRV depends on HR.

**Methods:** We calculated spectral HRV components (i.e. VLF, LF, HF, TP), and acceleration (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 index by the corresponding mean RR interval to the power 0.2 (spectral components) and 1.4 (DC and AC).

**Results:** Initially, all indices correlated with HR but after normalization no corre- lation 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 decrease 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 (Fig- ures) – 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 the one of electrical myocardial insta- bility (EMI) markers. It is important to study other markers, such as fragmentation of QRS (QQRS) complex, microvolt T-wave alternans (mTWA), heart rate turbu- lence (HRT) and HRV.

**Purpose:** To study the markers of EMI (VA, QQRS complex, mTWA, HRT, HRV) 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 VEChous without any therapy. Structural abnormality of the heart was excluded by an ECG, echoE, 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 arrhyth- mia was dominated (387±152 VEChour during the day, 227±103 VEChour at night, p<0.05). Non sustained VT was in 8% of patients. QQRS in sinus complex was not found. QRS inVEC was registered in 7% in the II, III, aVF leads. MTTWHA was positive in 59%. Pathological turbulence onset was in 3.7%, while turbulence slope was in the normal range in all patients.

**Conclusions:** During ETT HRR at the 1 min was 26.5±9.5 bpm. HRR at the 3 min stayed normal (19.0±10.6 bpm). At the 5 minute HRR decreased (9.7±7.7 bpm). At pretest VA was in 86% patients, mean 6.3 single ventricular ectopic complexes/min (SVEC/min).
At the peak ETT VA persisted in 44%, mean 3.4 VEC/m. At the recovery period (RP) VA gradually returned to the pretest values. At the 1 min of RP VA was in 44% (3.5 VEC/m), at the 3 min of RP - 48% (5.4 VEC/m), at the 5 min of RP - 53% (7.9 VEC/m).

**Conclusion:** We found no abnormal markers that could indicate structural change of the myocardium. However, we observed the pathological changes due to autonomic nervous system modulation (the abnormal mTWA in LVH 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?**


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**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 formulae. 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±17.3bpm and QRSd 99.8±25.3ms. Sinus rhythm (SR) represents 87.9%, 7.5% AF/Aflutter, 4% ventricular pacin 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 (p<0.001) and QTcR 60.4% less vs QTcB (p<0.001). One month mortality was 1.8%. Sensitivity and specificity predicting 1 month mortality is shown in the table.

Univariate analysis with following parameters as significant predictors of early mortality (hazard ratios): absence of S2 2.34 (1.65–3.31); age 1.06 (1.05–1.08); HR 1.03 (1.02–1.03); QTcB 3.9 (2.9–5.3); QTcF 3.1 (2.2–4.3) and QTcR 3.7 (2.6–5.2). Gender and QRSd were not significant.

Multivariate forward stepwise Cox regression including, age, HR and one QTc formula resulted as follows: QTcB 2.4 (1.8–3.3), QTcF 2.9 (2.0–4.1), QTcR (2.6–5.2). Gender and QRSd were not significant.

**Conclusions:** QTc 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**


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**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 be dependent 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 (QFRS) complex, microvolt T-wave alternans (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, age mean 42±15 years, 436±196 VEC/hour, ejection fraction (EF) 65±6% by Simpson. Structural abnormality of the heart was excluded using an ECG, echocG, 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. MTRA 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–V4. MTRA 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. EMI 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**

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**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.

**Methods:** 92 consecutive patients (Mean age 79.5±9.5 years, 49 Female) with severe aortic stenosis underwent CMR. The Romhilt-Estes LVH score point 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, 23/94 (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 with no LVH on CMR. 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**

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**Background:** Ventricular arrhythmias have been previously observed during acute crisis among patients with sickle cell disease (scd). No data is lacking 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 attending 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 compared to the controls (195±341 vs. 24±39, p<0.001). Also, non sustained ventricular
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 6MWT distance.

**Arrhythmias in Sickle cell disease**

<table>
<thead>
<tr>
<th>Control (n=116)</th>
<th>Sickle cell disease (n=125)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years med (min-max)</td>
<td>39.2 (20–65)</td>
<td>37.9 (19–65)</td>
</tr>
<tr>
<td>Hemoglobin, g/dl (meal SD)</td>
<td>13.1±1.4</td>
<td>8.2±1.5</td>
</tr>
<tr>
<td>Creatinine level, μmol (mean ± SD)</td>
<td>73±13.9</td>
<td>56±26.3</td>
</tr>
<tr>
<td>Heart rate, beats/min (mean ± SD)</td>
<td>71.8±9.7</td>
<td>79.5±6.8</td>
</tr>
<tr>
<td>Total VPC, n (%)</td>
<td>24±39</td>
<td>195±341</td>
</tr>
<tr>
<td>Complex ventricular arrhythmias, n (%)</td>
<td>0</td>
<td>14 (9.7)</td>
</tr>
<tr>
<td>NSVT, n (%)</td>
<td>0</td>
<td>29 (20.0)</td>
</tr>
</tbody>
</table>

*Defined as bigeminy, trigeminy, or nonsustained ventricular tachycardia (NSVT). VPC, ventricular premature complexes.*

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 cell 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 head-down bed-rest**


**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 (HDT21), 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 schema, 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 TWA amplitude (expressed as %TWA). Then, the normalized TWA amplitude of all ECG segments was averaged, yielding the average night normalized TWA amplitude (expressed as %TWA).

**Results:** Compared to PRE, at HDT21 normalized ANNAI showed a trend for ANNAI60 (0.28 (0.19;0.43)% vs 0.45 (0.37;0.54)%) and ANNAI80 (0.29 (0.19;0.45)% 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**

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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 3 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 (9.4%) subjects (arrhythmias, excess noise or poor recording quality), providing a quantitative acoustic CAD-score in suitable subjects based on diastolic sound characteristics.

**Conclusion:** This study demonstrates the potential of a novel, non-invasive, non-radiation method for identification of CAD.

**Acknowledgement/Funding:** Acarix a/s
P1548 | BEDSIDE
Heart failure telemonitoring in Japan and Sweden: the gap between research and practice

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Background: Telemonitoring of heart failure (HF) patients is increasingly used in several countries in Europe and the US. Clinical impacts of reduced hospitalizations and mortalities 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, 88 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 were: (1) to provide a more efficient use of misconception and to recognize signs of worsening HF in Japan (94%) and Sweden (91%). The following reasons were also high in Sweden: to monitor effects of treatment and adjusting it remotely (87%) and to remote drug titration (83%). 73% of participants in Japan and 81% in Sweden) stated that lack of equipment is a major barrier to the implementation of telemonitoring. In Sweden, lack of motivation and fear of technology were the highest barriers (each 67%). In Japan, lack of equipment (77%), fear of technology (72%) and lack of motivation (67%) were the highest barriers.

Conclusions: Despite the high expectations, the usage of telemonitoring among healthcare professionals in Japan and Sweden is low. Telemonitoring could have an impact on hospitalization and mortality of HF patients. Further research is needed to understand these barriers and to improve the telemonitoring implementation.

Acknowledgement/Funding: A Grant-in-Aid for Research Activity Start-up from N.K. from the Japan Society for the Promotion Science

P1549 | BEDSIDE
Body surface potential mapping in patients with arrhythmogenic rightventricular cardiomyopathy: spread of QRS notches and epsilon waves

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Background: Most patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) show egc 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 arm (frontal plane) and 2 strips on the right ankle and 1 posterior strips. We were calculating the surface area corresponding to the electrodes detecting notching and epsilon waves (Mean±standarddeviation). We create two subgroups: 1. Evidence of Plakophillin2 mutation (PKP2), 2. Documented ventricular 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. 8 pts were PKP2 positive tested. Ventricular arrhythmias (VTA) were documented in 8 pts, 3 of them with PKP2. All pts showed a QRS notching. The distribution of QRS notching did not differ between PKP2 positive and negative and also VTA and non-VTA pts. EW were recorded in 8 pts, bothsides. Only the arrangement of the EW in the right anterior area for the VTA-subgroup differ significantly (p<0.05). PKP-2 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).

Conclusions: QRS Notching is common in our ARVC group but was not related...
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 (P 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 0.90–0.96). 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 non-invasive (ambulatory) ICG might be of additional value in the clinical evaluation of (pediatric) cardiac patients.

P1554 | BEDSIDE
Artificial intelligence in cardiac imaging. Applications on hand held echo - preliminary data
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Introduction: Hand held echo (HHE) highly entered the market and its non-cardiologists clinical use at point-of-care (POC) is increasing. Nuclear Cardiology, CT/MRI showed that artificial intelligence (AI) learning will likely assist physicians with cues in automatic tool for measurements calculation. Differently, echocardiography was focused several times but any application entered today in routine use on HHE.

Purpose: Aim of the study was to develop and clinically use a software tool (ST) which automatically calculate the dimensions (D) and the systolic function (SF) of the left ventricle (LV) from HHE images suggesting interpretation of the results. Machine learning has been implemented including the differences between two types of AI neural networks (NN). In the first level of analysis, a Self-Organizing Maps (SOM) NN (classifiable as a generalization of a Kohonen Neural Network-KNN) on unsupervised network has the purpose of distinguishing the noise of the echo image from the presence of cardiac tissue. Therefore the UN has the goal of highly precise segmenting LV myocardium HHE images. In the second phase of analysis, a UN (classified as the Error Back Propagation - EBP family) is trained to recognize the morphology of LV myocardium (M). This phase has a dual purpose: a) showing to the operator while positioning the echo probe that optimal window to perform the bio-medical measurements (BM) has been reached; b) automatically and instantly carrying out LV D and LV SF dynamic. 21 subjects with very low likelihood of having coronary artery disease (CAD), 13 males and 8 females, age 53±5 years with no hypertension permanently resting HHE imaging with Broad-bandwidth phased array probe from 1.7 to 3.8 MHz applying SOM (KNN+EBP) automatically on apical-4-chambers views LV M. Automatic identification of endocardial and epicardial borders provides LV D, LV EndDiastolic (LVEDV), EndSystolic Volumes (LVESV) and LV Ejection Fraction (LVEF).

Results: In 19 of 21 subjects SOMs were able to identify the optimal window for operator to perform acquisition recording. The contour of LV M was automatically well traced in 95% of subjects (20 subjects). LV D resulted in 44±6 mm; LVEDV of 110±16 mL; LVESV of 74±12 mL and LVEF of 0.59±0.09.

Conclusions: AI NN ST is able to identify and make the contour of LV M. Our preliminary data demonstrates that AI ST optimally and automatically identifies the window for performing calculations and showing BM data. This represent an encouraging promise in clinical applications especially for regional wall motion and thickness analysis at POC.

P1555 | BEDSIDE
Variability of minimal fibrous cap thickness measurement and reproducibility of categorization of fibroatheroma using a software based semiquantitative versus manual measurement
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Background: The assessment of the fibrous cap (FC) thickness covering fibroatheroma is relevant in research and clinical practice as previously shown by pathology studies. Traditional manual analysis of FC thickness of fibroatheroma by means of ST and ST analysis, however, is limited by intra- and inter-observer variability, thus limiting its reproducibility. This is of relevance for discrimination between thin – and thick 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 Interventions Study of the Biplane Coronary Imaging Study (IBCT). This study was independent and could be used to independently measured the minimal fibrous cap thickness at two different time points (1 month apart) manually and using three different semi-automated algorithms (method 1, 2, and 3) with a dedicated software (QCUI-CMS). The presence of thin-cap fibroatheroma was defined as a fibroatheroma with a minimum cap thickness <65μm. The semiquantitative software was based on light intensity measurement.

Results: The intra- and interobserver variability of the manual measurement of the minimal fibrous cap thickness was moderate with an intraclass correlation coefficient (ICC) of 0.71 for the interobserver variability and 0.78 for the intra-observer variability, respectively. The measurements using either one of the three dedicated algorithms showed a higher intra- and interobserver variability with ICC>0.90. When categorizing fibroatheromas according to the minimal fibrous cap thickness based on the results of the study, the intra- and interobserver reproducibility were poor (κ=0.26) and moderate (κ=0.47 for observer 1 and κ=0.53 for observer 2), respectively. In contrast, semi-automated assessments showed perfect agreements for intra- and interobserver reproducibility (κ=1.00).

Conclusions: Manual measurement of the minimal cap thickness results in a moderate intra- and interobserver variability, compared with a perfect agreement when applying a semiquantitative approach. Categorization of fibroatheroma based on the minimal cap thickness results in a high intra- and interobserver variability compared to a semiquantitative method, to a degree that a manual assessment cannot be recommended.

Aim of the study: To evaluate the effectiveness of our virtual intensive care unit connected with neurological departments for the continuous cardiology web
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 se-
lected number of Neurology Departments, the web-connected information center IntelliVue Philips 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 card-
cology 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 heart block in 336 pts, and inhibits cardiomyocyte apoptosis in vivo.

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 multi-
disciplinary 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

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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 an MI. Recently, we could show that therapeutic angiogenesis by the neuropeptide catestatin (CST) restores perfusion in the mouse hind limb ischemia model by the induction of angiogenesis, 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 compared to basic fibroblast growth factor (bFGF), which was used as positive control (rel. tube formation vs. ctrl.: CST 1 nM 2.69±0.3, n=3, p<0.001). Interestingly, blockade of bFGF either by a bFGF-antibody (Ab) or a specific receptor blocker (PD173074) resulted in abrogation of effects suggesting a bFGF-depending mechanism.

Moreover, CST induced proliferation of HCAEC and human coronary artery smooth muscle cells (HCASMC) as determined by BrdU-incorporation. Similar to the matrigel assay blockade of bFGF attenuated the effect (HCAEC: rel. pro-
liferation of forskolin/20 μM CAMP 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. ctrl.: 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 for p21, a G1/S-phase critical gene and p62, a marker for autophagy, revealed a CST-induced signal regulated kinase 1/2 by CST in these cell lines. To evaluate the effect of CST on cardiomyocyte apoptosis in vivo the mouse myo-
cardial ischemia/reperfusion model was performed. After reversible ligation of the left anterior descending artery a intra-myocardial injection of CST or saline 0.9% (control) was performed. In this animal model CST -treatment was associ-
ted with a significant reduction of cardiomyocyte apoptosis (apoptotic cardiomyocyte percentage vs. ctrl.: CST 1 nM 2.69±0.3, n=3, P<0.01). Western blot analysis revealed a CST-dependent downregulation of the pro-apoptotic factor Bax and upregulation of the anti-apoptotic factor Bcl-2. Western blot analysis revealed CST-dependent downregulation of the pro-apoptotic factor Bax and upregulation of the anti-apoptotic factor Bcl-2.

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 involved in the angiogenic endothelial cell migration

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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 angiogenesis in myocardium; however, it remains unclear whether GLP-1 may modulate angiogenesis in heart.

Purpose: To evaluate the impact of GLP-1 on angiogenesis and its link to endo-
thelial autophagy.

Methods: T2DM was treated with Ex4 (24 mole/kg/day for 4 weeks). Cardiac caparity density was measured by CD31 immunohistochemical staining Cultured human umbilical venous endothelial cells (HUVECs) were used for in vitro experi-
ments. Analyses for the changes in activities of autophagy (LC3-turnover as-
say 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 caparity density, which was reversed by Ex-4 treatment with concomitant amelioration of systemic diabetic condition. The Ex-4 treated heart exhibited in-
crease 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 that hiPSCs and HCAEC were enhanced by Ex-4. Inhibition of PKA alpha-1 and PKA beta-1 knockdown induc-
ed 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 (H99, RP-AMP; and siRNA for phosphorylation of PKA) abrogated the effects of Ex-4 in HUVECs. Tube formation assay revealed that the enhanced in vitro angiogenesis induced by Ex-4 and the PKA enhancers were abrogated by inhibition of autophagy and AMPK activity using pharmacological inhibitors (3MA and compound C) and siRNA (catalytic subunit of AMPK and autophagy-related gene (ATG) 5, ATG7, and p62).

Conclusions: GLP-1 directly promoted angiogenesis via the PKA/AMPK-
dependent autophagic activation.

P1559 | BENCH
Fenofibrate rescues diabetes-related impairment of ischaemia-mediated angiogenesis by ppar alpha independent modulation of thiodioxid in interacting protein

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Background: We examined Ppargc1a protein level in pediatric heart following chronic hypoxia and found Ppargc1a upregulation in cyanotic compared with acyanotic my-
ocardium. By treating HUVEC cells with hypoxia mimicking agent, Ppargc1a protein level increased with maximum at 8 hours. The effect of Ppargc1a pharmacological inhibition, in addition to knocking down and overexpressing Ppargc1a, on endo-
thelial cell migration and morphogenesis was examined in vitro wound healing scratch assay and endothelial tube formation assay. The Ppargc1a knockdown ef-
fects (inhibition of F-actin reorganization, lamellodia staining) and focal adhesion (vinculin) were evaluated by immunocytochemical staining with specific antibo-
dies.

Results: Ppargc1a knockdown significantly reduces endothelial cell migration, but not proliferation. Further, Ppargc1a knockdown inhibits focal adhesion formation, while focal adhesion formation in the knockdown group is restored to the control level upon con-
sucutive transfection with Ppargc1a CDNA. Furthermore, Ppargc1a knockdown induces a profound cytoskeletal reorganization, loss of focal adhesion sites and impair-
ment of focal adhesion kinases (FAK) activation.

Conclusions: Ppargc1a is regulator of endothelial cell migration, which is critical in the angiogenic process. Ppargc1a inhibition reduces endothelial cell migration through focal adhesion turnover and actin polymerization pathways.

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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: Fenofibric acid (FA), the active component of fenofibrate, rescued 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 expression of TXNIP (TNF-induced protein) (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 impaired recovery in ischemic hindlimb muscles. We have found that the expression of the HH inhibitory protein HIP was significantly and constantly downregulated in all 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 of proteins - are 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 coronas 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 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 arteries and veins, 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.

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P1565 | BEDSIDE
Circulating annexin A5 levels are related to carotid intima-media thickness but not coronary plaque composition
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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 presently 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:** AnxA5 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, AnxA5 predicted thickened IMT in univariable (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 anXa5 predicted thickened IMT with low moderate diagnostic efficiency (AUC 0.700 (0.592–0.808), optimal cut-off value 1.907ng/ml, sensitivity 72.4%, specificity 65.8%, positive predictive value 76.4%, negative predictive value 61.0% at the optimal cut-off).

No association was found between circulating AnxA5 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 neotenic lipid core (p=ns).

**Conclusion:** Circulating AnxA5 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

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**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. As a maker of endothelial function, flow-mediated dilation (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 ≥70, 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 – 30mg/dl) (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: R=-0.002, r=-0.14, albuminuria: P=0.0005, r=-0.17), EndoPAT-RHI was positively associated with these values (SBP: R<0.0001, r=0.24, albuminuria; P=0.05, r=0.10). On the other hands, although there was no correlation between FMD and HOMA-R (P=0.002, r=0.17).

**Conclusion:** Although both FMD and EndoPAT-RHI is same kind of examination with endothelial dysfunction, they each may evaluate different state of endothelial dysfunction and are highly associated with cardiovascular disease.

**P1565 | BEDSIDE**

Usefulness of brachial flow-mediated dilation and platelet function to predict long-term adverse clinical events in subjects without heart disease

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**Background:** Platelet activation occurs in an endothelium-dependent flow-mediated dilation (FMD) impairment environment.

**Methods and results:** A long-term association of 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 7 years. Optimal cut-of values for SAF were sought with ROC-analysis. Results: SAF was predictive after adjustment for age, gender, diabetes, smoking and history of coronary or cerebrovascular disease.

**Conclusion:** 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 2010. We compared 22 control patients without 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.
Lower level of serum asymmetric dimethylarginine contributes to improving vascular endothelial function after short-term resistance training in healthy elderly people

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Aims: 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 hyperemic 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 0.55 μM, and the median was 0.42 μM. The TM and tPAIC decreased significantly after the training period in the low ADMA group (P<0.05, respectively) and the plasma 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<0.1).

Conclusions: Lower level of serum ADMA contributed to improving vascular endothelial function after short-term resistance training in healthy elderly people.

Changes in vascular endothelial function

Conclusion: Lower level of serum ADMA contributed to improving vascular endothelial function after short-term resistance training in healthy elderly people.

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

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Alms: 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-inflammation 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 (HACSMCs) were cultured under hyperglycemic conditions. Sustained high glucose at 25 mM significantly decreased the expression of miR-145 in HACSMCs. High glucose significantly increased angiotensin II (Ang II) secretion from HACSMCs and Ang II suppressed miR-145 expression in HACSMCs. Exogenous addition of valsartan, enalaprilat dehydrate, and angiotami-145 before high glucose stimulation reversed Klf4 and myocardin expression induced by high glucose stimulation, indicating the involvement of autocrine Ang II and myocardin expression in HACSMCs. Ang II mediated the Klf4 and myocardin expression in high glucose state. MI-145 significantly decreased Klf4 and increased myocardin expression in high glucose state. High glucose stimulation for 4 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 was abolished. MI-145 significantly inhibited HACSMCs 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 HACSMCs under high glucose conditions. Ang II plays a critical role in the regulation of miR-145 under hyperglycemia conditions.

Acute administration of dietary nitrate improves endothelial function and vascular stiffness in hypercholesterolemia

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Background: Orally ingested inorganic nitrate undergoes sequential chemical reductions in vivo to nitrite and nitric oxide in the human body. In the current study, we hypothesized 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 hypercholesterolemics completed this assessment of the acute effects of a once daily dietary nitrate dose (n=17, nitrate-rich beetroot juice, 250 ml of 24±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).

Results: Plasma nitrate and nitrite measurements were conducted using ozone chemiluminescence. All averaged values shown as mean±SD).

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 Training 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 high newly potent and selective PPARs modulator (SP- PPARMs). 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. MOA-2 and MOA-1 are markers of macromolecules 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 administered K-877 or fenofibrate for 12 weeks. The heart and aorta were immersed in neutral buffered paraformaldehyde fixative for a night. MOA-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 for FFPE (Life Technologies) with some adaptation of its protocol. Messenger RNA (mRNA) from MOA-1 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 HDL-C and/or TG were measured. 2. LDL receptor deficient mice were loaded with a high-fat high-cholesterol diet (WD) and were administered K-877 or fenofibrate for 12 weeks. The heart and aorta were immersed in neutral buffered paraformaldehyde fixative for a night. MOA-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 for FFPE (Life Technologies) with some adaptation of its protocol. Messenger RNA (mRNA) from MOA-1 was evaluated by quantitative (qPCR).

Conclusions: Our results suggest that K-877 improves serum HDL-C and decreases 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

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in clinical studies and suggest there is an anti-atherogenic effect in patients with diabetes.

### P1571 | BEDSIDE

**Vascular ageing is apparent during an oral glucose challenge in healthy persons**

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Hyperglycaemia is associated with a poor outcome after coronary revascularization. Furthermore, per-conditioning may prevent the reperfusion injury that follows prolonged myocardial ischemia, a mechanism that may be impaired during hyperglycaemia. We therefore hypothesized that endothelial dysfunction during prolonged ischemia followed by reperfusion can be reversed in persons without diabetes but not in persons with diabetes during postprandial hyperglycaemia.

**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 reperfusion 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 reperfusion that follows 10 minutes forearm ischemia, and by increasing doses of 5HT infusion, FBF increased in young persons both at reperfusion and during 5HT 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**

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**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 (7.04m/s vs. 7.26m/s, P=0.242), AIx75 (19.9% vs. 20.3%, P=0.846) and cIMT (0.68mm vs. 0.68mm, P=0.957). For the overall population, there were no statistically significant differences for PWV (7.04m/s vs. 7.26m/s, P=0.242), AIx75 (19.9% vs. 20.3%, P=0.846) and cIMT (0.68mm vs. 0.68mm, P=0.957). 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 [−0.89% (95% CI: −1.50 to −0.28) in patients with metabolic syndrome vs. −0.13% (95% CI: −0.36 to 0.10) in patients without metabolic syndrome, P=0.032].

**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**

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**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 metabolites could be identified.

**Methods:** We enrolled 18 SSc patients (age 58.7±15.6 years) who underwent a combined 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 metabolomic analysis. Subgroups 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; meanSD= 1.15±0.23 uW) and Group B (N=10; PVR≥1.6 uW; meanSD= 2.67±0.67 uW). Group B showed a mild PH, with higher mean pulmonary pressures values than Group A (252±5 vs 204±16 mmHg; P<0.05). No significant differences were identified in terms of anthropometric, clinical, echo and therapeutic characteristics. We applied an OSC using NMR data as the X-matrix and PVR values as the Y-matrix. A clear clusterization 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, Glucorol, 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 appears 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.
Table 1. Coefficient of correlation

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<th>ICAM-1</th>
<th>VCAM-1</th>
<th>E-selectin</th>
<th>ADMA</th>
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<td>n=0.298**</td>
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<td>p=0.21</td>
<td>p=0.64</td>
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Roux-en-Y gastric bypass surgery on obesity-induced endothelial dysfunction

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Introduction: Roux-en-Y gastric bypass surgery (RYGB) reduces weight and long-term cardiovascular risk in obese patients. We previously demonstrated that endothelial-mediated vasorelaxation improved rapidly in diet-induced obese (DIO) rats within 8 days after RYGB and was associated with reduced phosphorylation of JNK independently from body weight loss.

Aim: We investigated 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 control peptide TAT (sham TAT) or the highly specific JNK inhibitor D-JNK-1 (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 (10−6M/L), cumulative relaxation responses were performed to GLP-1 (7−36) amide (10−12 to 10−6M/L) or insulin (10−11 to 10−5M/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-JNK-1 completely mimicked the effects of RYGB surgery on both body weight loss and improved 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.

LIPIDS IN ATHEROSCLEROSIS

P1578 | BENCH
Modulation of cardiac structure by epicardial adipokines

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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 proinflammatory adipokines. These adipokines may have proinflammatory and proatherogenic effects. Several adipokines 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-week-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. These adipocytes were prepared by collagenase digestion, their conditioned media prepared by epicardial adipose explants and incubated for 24h with the conditioned media previously obtained from both groups. After incubation, cross-section area of cardiomyocytes and fibrosis were evaluated.
Results: The histological and molecular studies of epicardial adipose tissue revealed hypertrophy of adipocytes in obese animals (1505±80.01 μm² vs. 7595±265.5 μm², p<0.0001), as well as a significantly increase in expression of several adipokines. Among these overexpressed adipokines are visfatin (0.42±0.18 AU vs. 1.43±0.33 AU, p<0.05), leptin (0.13±0.03 AU vs. 0.93±0.18 AU p<0.0001), adiponectin (0.001±0.001 AU vs. 0.24±0.04 AU, p<0.05) and chemerin (0.33±0.096 AU vs. 0.90±0.16 AU, p<0.05) that are involved in fibrosis and hypertrophic pathways. In organotypic cultures, conditioned medium from obese ZSF1 epicardial adipose tissue rats triggered a significant increase in the cross-sectional area of cardiomyocytes (100.7±18.98 μm² vs. 111.25±24.02 μm², p<0.05) and in fibrosis (3.48±1.51% vs. 4.79±1.53%, p<0.05) compared to the conditioned medium from lean rats ZSF1.

Conclusions: Adipokines produced by epicardial adipose tissue of obese animals appear to impact myocardial structure by inducing collagen deposition and promoting cardiomyocyte hypertrophy.

P1579 | BEDSIDE
Differentially expressed microRNAs in human peripheral blood mononuclear cells are potential markers for statin response
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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 and effective treatment, serum 25(OH)D and HDL together contribute to a better variability among patients, frequently determined by genetic factors. However, there are few evidence exists about epigenetic-regulated mechanisms involved.

Purpose: The aim of this study was to evaluate the differential expression of mi- croRNA (miRNA) in peripheral mononuclear cells of hypercholesterolemic subjects undergoing statin treatment.

Methods: Forty individuals were evaluated before and after completion of atorvastatin (10 mg/day; n=20) and simvastatin (10 mg/day; n=20) therapy during 4 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-30b-5p, miR-183-5p, miR-444-3p and miR-590-5p) were downregulated after atorvastatin treatment (P<0.05). Regulatory pathway examination showed that deregulated microRNAs interact with key genes of lipid metabolism (HMGR, 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 over-expressed.

Conclusions: Our results show, for the very first time worldlwide, 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 treatment, respectively.

Acknowledgement/Funding: CONICYT (No. 21090417); Fapesp (No. 2011/21967-1) & FONDICYT (No. 11030675).

P1580 | BENCH
Novel mechanisms of modulating reverse cholesterol transport by heat shock protein 27
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Introduction: Previously we reported that elevated serum levels of Heat Shock Protein 27 (HSP27) are predictive of reduced cardiovascular clinical events (MI, CVA, death). Moreover, attenuation of experimental atherogenesis, characterized as stabilization/regression of atherosclerotic plaques, epicardial/perivascular fats and coronary thrombi. FABP4 vascular cells were examined in vitro. Severity of angiographic coronary stenosis 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 myocardial 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 arterial (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 in vitro. Treatment with recombinant 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

P1581 | BEDSIDE
Vitamin D deficiency and VDR genotypes as nonclassic risk factors for dyslipidemia
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Introduction and aim: It is well known that dyslipidemia is an independent risk factor for cardiovascular disease. Some studies suggested interlink between lipid profile and VDR gene polymorphisms. The aim of the study was to assess vitamin D status, VDR genotype (BsmI, ApaI, TaqI polymorphisms) and their associations with lipid levels.

Materials and methods: We studied 449 women, aged 30 to 52 years old (mean 42±4.80 years) determined by PCR-based method followed by restriction analysis.

Results: Low vitamin D level (serum 25(OH)D up to 75 nMol/l) was detected in 90.6% study population. Dyslipidemia was diagnosed in 49% women. HDL level correlated with 25(OH)D (R2=0.67, p<0.0008). Analysis showed that women with vitamin D deficiency (serum 25(OH)D level lower than 50 nMol/l) had high risk compared to the same concentration of HSP27 without auto-antibodies, the HSP27-auto-antibody complex increased the abundance of cholesterol-NBD positive exosomal particles by approximately 70%, as measured by flow cytometry. Taken together, these data provide potential mechanistic explanations for the stabilization/regressive effects of HSP27 on atherosclerotic lesions.

Acknowledgement/Funding: Canadian Institutes of Health Research / Heart & Stroke Foundation of Canada

P1582 | BENCH
Local production of fatty acid-binding protein 4 in the extracardial/perivascular fat and macrophage leads to coronary atherosclerosis
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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 systematically 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 myocardial 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 arterial (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 in vitro. Treatment with recombinant 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 coronary 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
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Background: In diagnosing atherosclerosis, detailed evaluation of biomarkers related to the 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.

Methods: Sections of aortas were obtained from male apoe−/− 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 α-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 and interferon gamma or IL-4 for 48 h. The mRNAs were isolated, and then analyzed their expression levels of FABP4, FABP5 and β-actin by quantitative PCR method (n=5/group).

Results: The expression level of FABP5 reached the highest in Type IV lesions possessing the vulnerable-like characteristics, and preferentially located 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 (M0) cells (FABP5/β-actin: 1.29±0.47 (M1) vs. 0.50±0.17 (M2), 0.42±0.17 (M0) (P<0.05), FABP4/β-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

Introduction: Virtual histology intravascular ultrasound (VH-IVUS) imaging is an innovative tool for morphological evaluation of coronary atherosclerosis. Evidence for the effect of statins on VH-IVUS parameters has been inconclusive.

Purpose: We performed a systematic review and meta-analysis to investigate the impact of statin therapy on plaque volume (PV) and its composition using VH-IVUS.

Methods: The searched included PUBMED, Cochrane Library, Scopus, and EMBASE (through November 10, 2014) to identify prospective studies investigating the effects of statin therapy on PV and its composition using VH-IVUS.

Results: We identified 9 studies with 16 statin-treatment arms and 830 participants. There was a significant effect of statin therapy in reducing PV (standard mean difference [SMD]: −0.137 mm3, 95% confidence interval [CI]: −0.255, −0.019; p=0.023) (figure), external elastic membrane volume (SMD: −0.097 mm3, 95% CI: −0.183, −0.011; p=0.027) but not lumen volume (SMD: −0.025 mm3, 95% CI: −0.110, 0.057) (P=0.574). There was a significant reduction in fibrous PV (SMD: −0.129 mm3, 95% CI: −0.255, −0.003; p=0.045) and an increase of dense calcium volume (SMD: +0.229 mm3, 95% CI: +0.008, +0.450; p=0.043), while changes in fibro-fatty (SMD: −0.247 mm3, 95% CI: 0.592, 0.098; p=0.16) and necrotic core (SMD: +0.011 mm3, 95% CI: −0.144, +0.165; p=0.892) 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
RVX-208, an orally active BET inhibitor, lowers CVD risk by activities beyond raising ApoA-1/HDL
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Background: RVX-208, an orally active small molecule, selectively inhibits bromo-domain extra-terminal (BET) proteins by competing with acetylated histones beyond raising ApoA-1 and HDL to the second end of tandem of ligand domains. Post-hoc analysis of SUSTAIN and ASSURE trials showed patients given RVX-208 had a 55% relative risk reduction of major adverse cardiac events (MACE). This marked reduction is explained, only in part, by the RVX-208 induced rise of ApoA-1 and HDL to 10.3% and 7.7% respectively suggesting RVX-208 has added biological properties that could benefit CVD risks.

Methods: Primary human hepatocytes and whole blood from healthy donors were exposed to RVX-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, RVX-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 widespread 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 hepatocyte mRNA of key genes relevant to each pathway. For the pathogen defence/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 RVX-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 RVX-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 RVX-208 that extends beyond its effects on ApoA-1/HDL.

Conclusion: RVX-208 affects multiple pathways that play important roles in CVD risk. RVX-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 MACE 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
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Background: Foam cells derived from human vascular smooth muscle cell
Lp-PLA2 is an enzyme produced by the arterial wall that hydrolyzes oxidized phospholipids in LDL. The product of Lp-PLA2 is a bioactive lipid, which causes plaque rupture.

**Background:** Inflammation leads to macrophage accumulation in unstable atherosclerotic plaques, which eventually weakens the extracellular matrix and calcifies the plaque core.

**Methods:** Human peripheral blood mononuclear cells (PBMCs) were isolated from healthy donors. The cells were differentiated into macrophages (validated by immunostaining) and were incubated with GnPs and GNP conjugated to HDL. Lp-PLA2 levels were measured in the supernatant.

**Results:** GnPs increased Lp-PLA2 production in macrophages, while GNP conjugated to HDL decreased Lp-PLA2 production.

**Conclusion:** Gold nanoparticles can serve as a carrier for anti-atherogenic treatments. The use of GNP conjugated to HDL can decrease the level of Lp-PLA2 in the supernatants of human macrophages.

This approach may potentially be used for therapeutic applications in patients with atherosclerotic cardiovascular disease.
Clinical use of the cardiovascular medicine heart failure (CVM-HF) index in mitral valve population

1. Introduction

The CardioVascular Medicine Heart Failure (CVM-HF) index is a prognostic model to predict outcomes in stable heart failure patients. 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 Mitracip 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, left ventricular ejection fraction <20%, severe valvular 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 if the score was >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 (1%) for percutaneous closure of the residual interatrial communication after Mitracip intervention; in group C two patients were in NYHA class IV (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 significant between the three groups, the Logistic EuroSCORE was significantly higher in group C, when compared to group A (37.7±25.1 vs. 51±29, p=0.044) and group B (37.7±25.1 vs. 17.1±14.8, p=0.001).

**Conclusion:** CVM-HF index is not invasive and practical tool, which can be easily used to assess the clinical risk of HF patients undergoing Mitracip 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 ventricular function**

**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±5.0 vs. 9.0±6.1 vs. 8.2±5.9; F=6.75; p<0.003), which was accompanied by a significant increase of echocardiographic forward stroke volume (41±14 vs. 49±13 vs. 48±13; 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±5.8 vs. 11±5.6 vs. 9.7±7.1; F<0.05; p=0.019) and a significant increase of FSV (32±10ml vs. 45±11 ml vs. 38±10ml; F=4.04; p=0.048), whereas no significant changes were observed in patients with 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 reduced LVEF, which likely is a reflection of the overwrought 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**

**Introduction:** Mitral valve disease offers the possibility of advanced quantification of the mitral valve complex, however the clinical significance of the many 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 1.19 [0.78–2.89]; p=0.0191, figure - right column). 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=0.269, figure - right column).

**Conclusions:** 3D quantification of mitral geometry offers many tantalising parameters but these in their majority do not offer incremental diagnostic benefit. 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. Our data suggest an improvement of endothelial function and FSV following reduction of mitral regurgitation with PMVR. Interestingly, these changes were more prominent in reduced patients with LVEF, which likely is a reflection of the overwrought compensatory mechanisms in these patients translating to more direct effects of MR reduction on systemic vascular function.
between MVA obtained by both 2D and 3D PISA methods with pulmonary artery
excretion was 37.2 g/24 hours and 29.08 g/24 hours in moderate and in severe
MR group respectively. These results were much better than those obtained using the 2D
PISA method, with intraclass correlation coefficients of 0.81 and 0.72, respec-
tively.

Conclusions: MVA assessment using PISA by single-beat real-time 3D color
Doppler echocardiography is feasible in the clinical setting and has a statistically
significant PISA in patients with mitral stenosis.

P1594 | BEDSIDE
Impaired radial and circumferential myocardial contraction assessed by speckle tracking echocardiography accounts for ischmic mitral regurgitation in acute inferoposterior myocardial infarction
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Background: Ischemic mitral regurgitation (MR) carries adverse prognosis after myocardial infarction (MI). Functional ischemic MR in acute phase of MI remains under-investigated 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 MI.

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 ± 3.9 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 refuelling test. 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.

Myocardial function parameters

<table>
<thead>
<tr>
<th>Controls</th>
<th>A</th>
<th>B-C</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLS (%)</td>
<td>≥21.3</td>
<td>19.7</td>
<td>6.2</td>
</tr>
<tr>
<td>GCS (%)</td>
<td>≥17.6</td>
<td>17.0</td>
<td>0.6</td>
</tr>
<tr>
<td>BS (%)</td>
<td>≥14.5</td>
<td>14.3</td>
<td>0.2</td>
</tr>
<tr>
<td>MCS (%)</td>
<td>≥15.9</td>
<td>15.3</td>
<td>0.6</td>
</tr>
<tr>
<td>AGS (%)</td>
<td>≥18.1</td>
<td>14.9</td>
<td>3.2</td>
</tr>
<tr>
<td>BRS (%)</td>
<td>≤33.9</td>
<td>31.0</td>
<td>2.9</td>
</tr>
<tr>
<td>MRS (%)</td>
<td>≤43.1</td>
<td>41.8</td>
<td>1.3</td>
</tr>
</tbody>
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G, global; L, longitudinal; S, strain; C, circumferential; B, basal; M, mid; A, apical; R, radial.

Conclusion: Ischemic MR in acute inferior MI is associated with worse radial and circumferential LV deformation parameters assessed by 2D STE.

P1595 | BEDSIDE
Calcium-phosphate metabolism disturbances and physical activity in patients with significant mitral regurgitation
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Background: There are several risk factors connected with cardiovascular dis-
eases. Though new ones are still researched. In recent years trials indicated vita-
m in D (25(OH)D3) and other calcium-phosphate (Ca-P) metabolism parameters as potential new risk factors.

Purpose: Taking under consideration frequency of Ca-P metabolism distur-
bances and frequency of valvular heart disease in general and in cardiovascular
population we wanted to assess if there are disturbances of Ca-P metabolism in this population. We wanted to look for possible causal correlation between lower 25(OH)D and calcium-phosphate (Ca-P) metabolism disturbances in this population, select significant and correlations.

Methods: 99 consecutive patients hospitalized in our Department between July and September 2013 were included in the study. Inclusion criteria were: age ≥18, significant mitral regurgitation (MR) assessed with transthoracic echocardiography (TTE) (vena contracta≥3mm, effective orifice area (ERO) ≤0.2 cm², MR volume -30 ml/s).

Results: We included 39 patients with severe MR and 60 with moderate MR (39.9% and 60.6% accordingly, average age 73.2 yrs, 33.3% were female). There were no significant differences in anthropometric measures between two studied populations. Average serum Ca level corrected by albumins was 3.2 mg/ml in both groups, average serum Ca Jonized level corrected by pH was 1.06 mmol/l in severe MR group and 1.05 mmol/l in moderate MR group, average serum P level was 3.6 mmol/l and 3.4 mmol/l in severe MR and in moderate MR group accordingly (p>0.055). average 25(OH)D3 level was 17.7 ng/ml in severe MR group and 14.9 ng/ml in moderate MR group. Additionally average daily urinary P excretion was 37.2 g/24 hours and 29.08 g/24 hours in severe and in moderate MR group respectively and average PTH level was 72.04 pg/ml and 71.8 pg/ml according to the Ca-P metabolism disturbances in population with significant MR, though there were no significant differences in groups divided according to MR severity. There was significant correlation between Ca Jonized corrected by pH and daily urinary P excretion and 6-MWT (correlation co-
efficient (r)=-0.222 and 0.239, p=0.049 and 0.041 respectively), between serum PTH and NYHA class. 6-MWT and NT-proBNP level (r=0.344, -0.486, 0.457, p<0.001, <0.001, <0.001 accordingly) and between 25(OH)D3 and 6-MWT and NT-proBNP level (p=0.468, -0.221, p=0.001, 0.032 respectively).

Conclusions: There are significant Ca-P disturbances in population with signifi-
cant MR. Further studies are needed to assess if there are significant Ca-P disturbances in population with mitral regurgitation.

P1596 | BEDSIDE
Interventional paravalvular leakage closure after surgical and interventional heart valve replacement - midterm results
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Purpose: Percutaneous transcatheter techniques emerge in the treatment of inoperable patients with valvular heart disease. Paravalvular leakage closure (PLC) has slowly evolved since his first description in 1992 and has become an alternative treatment option to open heart surgery due to the development of new closure devices and 3D transesophageal echocardiographic guidance (see figure 1–3). The objective of this study is to describe functional and clinical outcome after transcatheter PLC of prosthetic valves in aortic and mitral position.

Methods and results: This is a prospective study of 25 patients, which underwent PLC (56% male, age 68±11.4 years; EF 54.1±16.2, EuroSCORE 21.2±9.8) between May 2010 and May 2013. 17 patients had a paravalvular leak-
age of the mitral valve, 8 in aortic position; 12 (48%) had a history of infective endocarditis and 15 of 25 patients (60%) had a mechanical valve. Successful implantation of closure devices was achieved in 18 Patients (72%) whereas 7 pa-
tients could not receive a leakage closure due to difficult anatomical conditions. 15 of 18 treated patients (83%) improved by more ≥2 New York Heart Association functional class. The same 15 patients showed a functional improvement in par-
valvular leakage volume of ≥2 grade. The survival rates for implanted patients at 6 months and after PLC were 89% and 86%. 14 (78%) implanted patients completed 6 months FU and 9 implanted (50%) patients completed 12 months FU, which confirmed successful leakage closure in 83% (6 Months) and 89% (12 Months) of patients with a history of infective endocarditis and 72% (6 Months) and 68% (12 Months) of patients with predominant progression of valve insufficiency. 3 of 7 patients in which leakage closure was not possible died during the first 6 months. No periprocedural dead occurred.

Conclusion: Closure of paravalvular leakages in patients at high operative risk is safe and feasible and seems to have favorable mid-term effects. High risk patients with a relevant paravalvular leakage have a poor outcome if treated conserva-
tively.

P1597 | BEDSIDE
Importance of heart failure evaluation in patients undergoing mitraclip
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Background: Heart failure (HF) is a common manifestation of MR patients treated with the mitraclip system. There are two major assessment methods of HF evaluation - NYHA class and NT-pro BNP level. Though new ones are still researched. In recent years trials indicated vita-
m in D (25(OH)D3) and other calcium-phosphate (Ca-P) metabolism parameters as potential new risk factors.

Purpose: The aim of this study was to explore the adaptability of 2 contemporary HF evaluation methods for the prediction of mortality after mitraclip system.

Method and result: In a total of 198 patients after mitraclip (mean age 74±10 years, 66% men), we divided patients into 4 groups based on NYHA class and NT-pro BNP level: NYHA class ≤III and NT-pro BNP ≤5000 pg/mL (n=38), NYHA class <III and NT-pro BNP >5000 pg/mL (n=35), NYHA class IV and NT-pro BNP <5000 pg/mL (n=20), NYHA class IV and NT-pro BNP >5000 pg/mL (n=39). Age, gender, and baseline MR severity were comparable. Despite
of the similar improvements in post-procedural and chronic phase MR severity, 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 1.899, 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.

Figure 1.

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.

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P1598 | BEDSIDE
Survival and clinical outcome in functional mitral regurgitation: percutaneous mitral valve repair vs conservative treatment

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Background: Percutaneous mitral valve repair (PMVR) using the MitraClip System is feasible and entails clinical improvement in high-surgical risk patients with symptomatic severe mitral valve regurgitation (MVR), rejected by the surgical option. The lack of randomized clinical trials weighs on the clinical decision between symptomatic severe mitral valve regurgitation (MVR), rejected by the surgical option. The lack of randomized clinical trial results 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 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 with functional MR 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 vs 27.5±20.2, p=0.10; 8.1±6.5 vs 10.8±8.5, p=0.09). Mean creatinine and hemoglobine values were 1.43±0.5 vs 1.63±0.2 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 values 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 132.3±59 ml, p=0.37, respectively), left ventricle ejection fraction (35.12±7.2 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 49.1±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-surgical risk 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±6.4 vs. 8.2±4.5; p < 0.01). Conversely, women had a higher rate of VASC-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.
Peak aortic valve disease (AVD) 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 AVD 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 valve disease (CAD) – itself an inflammatory process - are predictors of AVD. However, whether their effects are independent of each other is unknown. Further studies of the influences of plaque burden, differing coronary plaque morphology and systemic levels of the inflammatory mediator endothelin-1 (ET-1), on CAD are unknown.

Purpose: To investigate the inter-relationships between coronary artery plaque burden, surrogate markers of inflammation (hs-CRP and ET-1), with aortic valve disease (AVD) and the markers of inflammation (hs-CRP and ET-1), with aortic valve disease (AVD).

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 >2.0 m/s). Coronary artery plaque burden, plaque morphology, and AVG 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 of the processes involved is important if successful non-surgical treatments are to be developed. Both systemic levels of inflammation and coronary atherosclerotic valve disease (CAD) – itself an inflammatory process - are predictors of AVD. However, whether their effects are independent of each other is unknown. Further studies of the influences of plaque burden, differing coronary plaque morphology and systemic levels of the inflammatory mediator endothelin-1 (ET-1), on CAD are unknown.

Background: Calcific aortic valve disease (CADV) 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 CADV is poorly understood. Understanding of the processes involved is important if successful non-surgical treatments are to be developed. Both systemic levels of inflammation and coronary atherosclerotic valve disease (CAD) – itself an inflammatory process - are predictors of CADV. However, whether their effects are independent of each other is unknown. Further studies of the influences of plaque burden, differing coronary plaque morphology and systemic levels of the inflammatory mediator endothelin-1 (ET-1), on CADV are unknown.

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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

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**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 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 4 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 ≥ 27.1% 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 (HR1.88; 95% CI: 1.08–3.29 for 10% increase; p=0.026) and the combined endpoint, CVF was the only independent predictor of all-cause death and worse prognosis.

**In aortic stenosis (AS), fibrosis is associated with progression to heart failure and worse prognosis.**

**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**
Transformal Implantation of the Edwards SAPIEN 3 Aortic Valve without Predilation is Safe and Feasible in the Majority of Patients

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**Objectives:** To evaluate the feasibility and safety of transformal 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 83.2±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 asymmetric fibrosis and an aortic valve orifice area (AVA) of 0.4 and 0.5 cm², respectively. After predilation from the contralateral site, the valve could be successfully fully implanted in both patients. The subsequent 56 patients (Group B) underwent pre-implant balloon-valvuloplasty if presenting with severe asymmetrical calcification and an AVA <0.5 cm² (10 pts, 17.9%), the remaining patients (46 pts, 82.2%) received direct valve implantation with 100% success.

The 30 day MACCE rate was 5.2%, cardiovascular mortality 2.1%, stroke rate 0%, myocardial infarction 0%. One patient in the direct implantation group 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:** Transformal implantation of the Edwards SAPIEN 3 aortic valve without balloon predilation is feasible and safe in the majority of patients. Limitations are severe asymmetric valve calcification in combination with AVA 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

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**Background:** Left ventricular (LV) dysfunction is sometimes seen at aortic valve replacement (AVR) in patients with severe 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 was divided into the 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, LVDs, and EF before, early and late after AVR as follows: LVDD: 69±7, 50±6 and 50±6mm, LVDs: 47±9, 32±6 and 33±7mm, 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±6 vs. 67±7mm, p<0.01) and early after AVR (54±13 vs. 49±6mm, p=0.03), larger LVDs before (62±7 vs. 45±8mm, p=0.01) and early after AVR (37±5 vs. 31±6mm, 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±28.5gm/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 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.
P1600 | BEDSIDE
Transfemoral implantation of the direct flow medical (DFM) aortic valve for pure noncalcified aortic regurgitation

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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 DFM aortic valve in patients with severe AR.

Methods and results: Five high surgical risk patients (77.2 years, range 46 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 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 transplantation. The annulus diameter was measured by MSCT and the size of the prosthesis of only 2 mm. This pt underwent surgical conversion under stable condition and uneventfully recovered from surgery. No other 30 day MACCE’s occurred and the rate of new pacemaker was zero.

Conclusion: Transfemoral implantation of the DFM aortic valve is feasible. Significant valve oversizing, however, is needed to achieve a stable position of the prosthesis. Further studies are needed to learn more about appropriate patient selection.

AORTIC VALVE INTERVENTIONS

P1610 | BEDSIDE
Assessment of operative mortality risk in patients with active infective endocarditis undergoing cardiac surgery: performance of 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 1) to validate both versions of the EuroSCORE, the one 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 comparing the Hosmer-Lemeshow goodness-of-fit method and calibration curves.

Results: One hundred and twenty-eight patients were analyzed. The observed peroperative mortality was 16.4%. The mean ES-I and ES-II were 13.8% and 10.7%, respectively. The difference between ES-I and ES-II was 3.1% (95% CI = [−1.8, 2.1]). The predictive 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 < 0.001 and an OR 3.5; 95% CI: 1.2–10.0; p=0.02, respectively). The new model including the ES-II variables predictive of mortality showed an AUC of 0.85, CI 0.77–0.93, and did not differ significantly from ES-II (p=0.65).

Conclusions: 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 ability.
P1614 | BEDSIDE
Adverse effect of aortic insufficiency after TAVI on short term outcome in patients with renal impairment
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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 obtained 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 registries consor- tium-2 (VARC-2) criteria. Post-procedural transthoracic echocardiography was performed in each patient and AR was classified as none/mild versus moderate/severe. Univariable and multivariable 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, 487 patients [99%]) versus moderate/severe (eGFR <30ml/min/1.73m2, 59 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%), 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 1.001, 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
Evaluation of the learning curve for transcatheter aortic valve implantation via the transfemoral approach
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Background: Experience seems to be one of the crucial factors in minimizing the complication rate in transcatheter aortic valve implantation (TAVI). The aim of this study was to evaluate the learning curve in performing transfemoral TAVI (TF-TAVI). Methods: Between October 2006 and October 2013, 312 consecutive TF-TAVI cases performed by 6 interventional cardiologists, using the Edwards Sapien valve and 104 using the CoreValve, were included in the present analysis. Cumulative sum (CUSUM) failure analysis of combined 30-day safety endpoint was used to evaluate learning curves. We divided the Edwards valve cases and CoreValve cases into two groups (early experience: Cases 1 to 40; late experience: Cases 41 to 104). The rate of early safety endpoint occurred in 88 patients [16%]. Moderate/severe AR after TAVI was present in 66 patients (12%), 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 1.001, 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.

P1614 | BEDSIDE
Factors associated with progression of non-specific valvular changes detected during echocardiographic screening for rheumatic heart disease
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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. Results: Of 442 individuals enrolled, 42 (9.5%) exhibited deterioration and 27 (6.1%) improvements in valvular lesions. Three factors were independently associated with deterioration: Borderline RHD of the MV (A or B) (OR 4.6, 95% CI 1.8–12.1), NSVA of the MV or AV (OR 3.0, 95% CI 1.3–6.8), and receiving secondary prophylaxis (OR 4.2, 95% CI 1.5–11.7). Four factors were independently associated with improvements: Borderline RHD of the MV (6.1%), improvements in valvular lesions.

P1615 | BENCH
Rheumatic heart disease: factors associated with outcomes in a high-income country
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Background: Rheumatic heart disease (RHD) remains the first acquired heart disease in the young worldwide. Factors influencing outcomes have not been assessed in the contemporary era. Purpose: To identify factors associated with outcomes in RHD. Methods: Hospital-based register in a high-income country where RHD remains a major public health problem. Of the 396 patients, 174 (43.9%) were male, with a median age of 18 years (IQR 10–40). 127 (32.1%) had mild heart valve disease, 131 (33.1%) of the 396 patients, 174 (43.9%) were male, with a median age of 18 years (IQR 10–40). 127 (32.1%) had mild heart valve disease, 131 (33.1%) of the 396 patients, 174 (43.9%) were male, with a median age of 18 years (IQR 10–40). 127 (32.1%) had mild heart valve disease, 131 (33.1%) had moderate/severe valve disease, and 138 (34.8%) had severe heart valve disease. The early safety endpoint occurred in 88 patients [16%]. Moderate/severe AR after TAVI was present in 66 patients (12%), 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 1.001, 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 transcatheter aortic valve implantation
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Background: Bleeding complications are frequent and independently predict mortality after transcatheter aortic valve implantation (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: By ROC analysis 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 (AUC 0.730, 95% CI 0.637–0.811, p<0.0004) and need for transfusion (AUC 0.660, 95% CI 0.563–0.747, p=0.0345). Multivariate logistic regression analysis revealed, that high MPV (>10.6) and low PDW (<14.8) were correlated with increased risk of any bleeding (odds ratio [OR] 4.08, 95% CI 1.66–10.07, p=0.0022 and OR 3.82, 95% CI 1.41–10.36, p=0.0084, respectively) and major/life-threatening bleeding (OR 10.76, 95% CI 3.05–37.99, p=0.0002 and OR 8.46, 95% CI 1.69–42.17, p=0.0092, respectively).

Conclusions: Platelets characterized by larger size (higher MPV) and lower heterogeneity (lower PDW) may be associated with increased risk of short-term bleeding complications after TAVI.

P1617 | BEDSIDE
Balloon aortic valvuloplasty is not required for safe and effective transmembral implantation of balloon-expandable transcatheter aortic valves
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Background: Balloon aortic valvuloplasty (BAV) has traditionally been part of the transcatheter aortic valve implantation (TAVI) procedure using balloon-expandable valves. However, the necessity and benefit of this is unknown.

Purpose: To assess procedural success and safety in patients who underwent TAVI with and without BAV in order to evaluate whether performing a BAV can be avoided during 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 March 2014. BAV was routinely performed only until May 2013. We assessed Valve Academic Research Consortium (VARC)-2 defined device success and early safety; differences in procedure and fluoroscopy times; differences in embolic load based on transcranial Doppler (TCD) data. The endpoints were any bleeding during the Fisher exact test and continuous variables by the unpaired T-test using SPSS v21.

Results: 76 patients underwent BAV (Group 1) and 78 patients had no BAV (Group 2). There was no difference (p=0.5) in the rate of VARC-2 defined death, stroke, 3.1% vs. 2.8%, p=0.81; myocardial infarction 0.4% vs. 0.3%, p=0.50). Bleeding complications were significantly more frequent in the TAVI group. SM implantations and vascular complications in the TAVI group. In the PS-adjusted comparison TAVI-TA vs. TAVI-TF (289 pairs; EuroSCORE 25.1 vs. 22.1; STS 6.8 vs. 6.7) there was also no difference in the hard endpoints (30d mortality 4.6% CONV vs. 5.1% TAVIall, p=0.74), stroke (2.8% vs. 2.0%, p=0.48) or myocardial infarction (0.0 vs. 0.3%, p=1.00). Here bleeding complications were significantly more frequent in the TA group. SM implantations and vascular complications in the TF group. Subgroup analyses show an advantage of the TAVI procedure in patients with high STS or low LVEF.

Conclusions: These data show that 1.) conventional aortic valve replacement and TAVI are comparable in the moderate risk group, and 2.) the two approaches, transapical and transmembral, produce comparable results. Randomized studies are required in order to clarify the superiority or inferiority of the procedures for specific risk subgroups.

CARDIOMYOPATHIES I

P1619 | BEDSIDE
Elevation of serum high-sensitivity cardiac troponin T value is associated with progression of left ventricular remodeling in patients with hypertrophic cardiomyopathy
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Background: Serum high-sensitivity cardiac troponin T (hs-CrTnT) is considered to be a good marker for ongoing myocyte injury. This injury may be related to progression of left ventricular (LV) remodeling in patients with hypertrophic cardiomyopathy (HCM).

Purpose: The aim was to examine the relation between abnormal hs-CrTnT value and echocardiographic parameters in HCM.

Methods: We studied serum hs-CrTnT values in 166 consecutive HCM patients in whom subsequent echocardiographic data were obtained for more than one year period.

Results: Serum hs-CrTnT values ranged from 0.003 to 0.130 ng/ml (abnormal range >0.014 ng/ml). The patients were divided into two groups by values of hs-CrTnT: abnormal hs-CrTnT group and normal hs-CrTnT group (≤0.014 ng/ml). In pa-
tients with abnormal hs-cTnT values (=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±2.6 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 46.8±6.0 mm, p<0.001) in the abnormal 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 (19.9% 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 atroventricular block as the first clinical manifestation
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Introduction: Atroventricular 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 manifestable manifestation by PM implantation from 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 2/3/2014 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 systolic LV dysfunction 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.

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P1621 | BEDSIDE
Early arrhythmic events in idiopathic dilated cardiomyopathy
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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 characteristics 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 III-IV 42% vs 22%, p=0.038), a longer QRS complex duration (127±41msec vs 108±33msec, p=0.013) and a greater indexed left ventricular end-systolic volume (LVESVI) (82±49 m³/m² vs 67±34 m³/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 1.012, 95% CI 1.000–1.024, p=0.043) and QRS complex duration (OR 1.017, 95% CI 1.003–1.030, p=0.015) were significantly associated with the primary end-point, whereas betablockers demonstrated a protective effect (OR 0.169, CI 0.048–0.593, 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
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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 (RETAKO), fulfilling Mayo criteria. Patients were divided in two groups regarding their potential triggers: 1) Nonepsychic stress as “primary forms” and 2) Physical factors (asithma, 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<0.0001) with frequent vegetative symptoms. Regarding treatment before admission, there were no differences either. During admission, differences were related with a more intensive antithrombotic and anxiolytic drugs use in primary-TKS. Inotropic and mechanical ventilation use was higher in the secondary cohort. After discharge, a more frequent prescription of betablockers and statins in primary-TKS was seen. Secondary forms displayed more in-stay and evolutive complications: death (HR: 3.41; CI95%: 1.14–10.16, p=0.02), MACE (HR: 1.61; CI95%: 1.01–2.6, p=0.04) and recurrences (HR: 1.85; CI95%: 1.06–3.22, p=0.02).

Conclusions: 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
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Background: Hypertrophic Cardiomyopathy (HCM) is a genetically heterogeneous disease caused by mutations in at least 40 different genes. The N271I mutation is the most common genetic cause of HCM in south Mediterranean and European populations. Despite being considered a common mutation, the clinical spectrum associated with N271I is still not well defined.

Methods: We performed a retrospective analysis of a cohort of 50 similar patient’s with the N271I mutation. Clinical, echocardiographic and genetic data were collected from all patient’s.

Results: We observed a high prevalence of N271I mutation in a galician cohort causing HCM. No clinical or echocardiographic differences were observed between patients with N271I and non-N271I mutations. We did not find any correlation between the presence of the N271I mutation and the severity of the disease.

Conclusions: The N271I mutation is a common genetic cause of HCM in a galician cohort. No clinical or echocardiographic differences were observed between patients with N271I and non-N271I mutations. We did not find any correlation between the presence of the N271I mutation and the severity of the disease.
neous disease. N271T missense mutation in TNNT2 is highly prevalent in Galicia (Spain).

**Purpose:** To define the clinical spectrum of N271T 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. Clinical evaluation and complementary studies were performed in the university hospital complex A Coruña. Cardiovascular death, and secondary end-points were compared between carriers of N271T and carriers of different missense mutations in TNNT2 described in the literature using time to event curves and log rank test.

**Results:** Out of 251 HCM probands with a pathogenic or likely pathogenic mutation identified by NGS, 15 patients (5.9%) were carriers of N271T mutation in TNNT2. The mutation co-segregated with the disease in all the families (29 relative with mutation carriers). A common haplotype was found, suggesting a founder effect, and supporting the hypothesis of a common ancestor. The penetrance of HCM in carriers of N271T 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 N271T compared with other pathogenic missense mutations in TNNT2 (log rank test p < 0.001).

**Conclusion:** N271T 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.

**P1624 | BEDSIDE**

**Arrhythmic risk assessment in family members with arrhythmogenic cardiomyopathy associated desmosomal mutations**

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**Methods:** Thirty-nine consecutive ACM families harboring desmosomal mutations were 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.

**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.

**Results:** Of 301 ACM probands screened, 72 were carriers of mutations related to the disease. Clinical evaluation and complementary studies were performed in the time to event curves and log rank test.

**Conclusion:** The presence of right ventricular dysfunction independently predicts major arrhythmic events. 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. Immunostainings and the mean diameter of cardiomyocytes (MCD) were quantified by digital image analysis.

**Results:** The autopic 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 significantly higher in DCM-EMB compared to controls (0.004±0.017 versus 0.006±0.004). These EMBS had significantly higher infiltration densities, expression of ICAM-1 and CD29 (p <0.0007), and the MCD (26.7±4.7 versus 22.3±2.2; p <0.0001). 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 <0.0001; Figure).

**Conclusion:** NCAM is de novo expressed in 54% of DCM hearts, and is associated with inflammation and the MCD. These data indicate that infiltration might be involved in the inflammatory response, and the MCD may be linked to the pathogenesis of DCM.
graphic, echocardiographic and cardiac MRI data. We evaluated the medium term prognosis in terms of heart failure, embolic events, 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%, embolic events in 7.4% and death in 2.4%.

**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 – portuguese multicenter study**

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**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 12 hospitals with inclusion of all patients diagnosed with TC in the last 15 years. Demographic, clinical, electrocardiographic and echocardiographic data were analysed to find witch 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 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 18–80 years old with TC 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 (98.1% vs 74.1%, p=0.021).

In multivariate analysis, the absence of a history of angina (p=0.028) was identified as an independent predictor of LV systolic function recovery in the first 15 days after hospital admission with TC.

**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.

**P1629 | BEDSIDE**

**Phenotypic variation of hypertrophic cardiomyopathy caused by the 3330+2T–G mutation in myosin binding protein-C in 303 Amish individuals**

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Previous studies describing disease expression in hypertrophic cardiomyopathy (HCM) have been characterized by great heterogeneity and small numbers of indi-

**Introduction:** Hypertrophic cardiomyopathy (HCM) is a genetic disorder with significant variability of clinical expression. Young females, older individuals and individuals with identical mutations. The Amish communities in North America are characterized by Western European descent and form a closed founder population with homoge-

**Methods:** A total of 170 mutation carriers (50% [n=85] male) has been analyzed for all types of HCM in 303 Amish individuals with identical mutations. The Amish communities in North America are characterized by Western European descent and form a closed founder population with homoge-

**Results:** In our cohort of 303 mutation carriers (80% [n=243] male), annual rates of cardiac death, the most feared complication in pa-

**Conclusion:** We identified 303 carriers of the MYBPC3 mutation 3330+2T–G via cascade screening in affected families. All 303 carriers interlink into one extensive pedi-

**P1630 | BEDSIDE**

**Right ventricular wall thickness as a correlate of malignant ventricular arrhythmias in patients with hypertrophic cardiomyopathy**

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**Background:** Sudden cardiac death (SCD), the most feared complication in pa-

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**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 in patients with TC.
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 nonsustained 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 (LVWT) and RV free wall thickness (RVWT). 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: Patients with NSVT+ had significantly higher values of LVWT (23.6±6.5 vs 19.8±4.1 mm, p=0.005) and RVWT (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 (45±16 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 (185±46 vs 172±64 g/m²), indexed LA volume (58±16 vs 61±29 ml/m²), E/e’ ratio (15.1±6.6 vs 16.3±6.5), systolic and diastolic myocardial velocities, severity of dynamic obstruction, cardiovascular risk factors (p>0.05 for all). At multivariable logistic regression analysis, RVWT emerged as the only correlate of NSVT (OR=2.2, 95% CI 1.3 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%). RVWT correlated with HCM Risk-SCD score independently of the parameters included in the risk score calculation (r=0.33, 95% CI 0.21 to 0.61, p<0.001).

Conclusions: In this cohort, RVWT 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.

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Purpose: To determine the prognostic value of MR-proANP in HCM compared with NT-proBNP.

Methods: 491 patients with HCM were prospectively enrolled from 11 European centers in the Eurogene Heart Failure study. All patients had clinical, ECG and echocardiographic evaluation and blood samples were drawn at inclusion for the measurement of MR-proANP and NT-proBNP. Follow-up was available for 356 patients.

Results: At baseline, log MR-proANP and log NT-proBNP were both independently associated with age, weight, NYHA class, left ventricular ejection fraction (LVEF), wall thickness (WT) and left atrial dimension (LA), but the associations were stronger between LA and MR-proANP than NT-proBNP and stronger between WT and NT-proBNP than MR-proANP.

During a median follow-up of 24 months, 29 patients (8%) had a primary endpoint, which included death (n=7), heart transplantation (HT) (n=9), left ventricular assist device (LVAD) (n=1) and HF hospitalization (n=13).

In univariate analysis, both log NT-proBNP (HR=2.33, CI 95% [1.66–3.27], p=0.001) and log MR-proANP (HR=4.25, CI 95% [2.45–7.38], p<0.001) were strong predictors of the primary endpoint. However, in a multiple stepwise regression analysis, including all clinical data, echocardiography and then natriuretic peptides, the best model for predicting outcome was NYHA 3-4 versus 1–2 (HR=3.1, CI 95% [1.3–7.5], p=0.04), previous HF hospitalization (HR=2.49, CI 95% [1.09–5.69], p=0.03), LVEF per 10% increase (HR=0.70, CI 95% [0.55–0.89], p=0.003), and log MR-proANP (HR=3.27, CI 95% [1.78–6.09], p<0.0001).

Conclusions: In this large multicentre cohort of HCM patients, MR-proANP outperformed NT-proBNP in the prediction of the combined event cardiac death/transplantation/LVAD and hospitalization for heart failure.

Purpose: A comprehensive clinical evaluation of desmosplakin ARVC carriers: does the type of mutation influence the phenotype?

Methods: 491 patients with ARVC were prospectively enrolled from 11 European centers in the Eurogene Heart Failure study. All patients had clinical, ECG and echocardiographic evaluation and blood samples were drawn at inclusion for the measurement of MR-proANP and NT-proBNP. Follow-up was available for 356 patients.

Results: At baseline, log MR-proANP and log NT-proBNP were both independently associated with age, weight, NYHA class, left ventricular ejection fraction (LVEF), wall thickness (WT) and left atrial dimension (LA), but the associations were stronger between LA and MR-proANP than NT-proBNP and stronger between WT and NT-proBNP than MR-proANP.

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Conclusions: In this large multicentre cohort of HCM patients, MR-proANP outperformed NT-proBNP in the prediction of the combined event cardiac death/transplantation/LVAD and hospitalization for heart failure.

Purpose: To determine the prognostic value of admission QRS duration for in-hospital clinical outcomes of patients with takotsubo cardiomyopathy.

Methods: We enrolled 349 cases of TC (mean age, 73.5±11.7, male, 222%) from our network database, comprising of 716 cardiovascular centers in the metropolitan area. The in-hospital clinical outcomes were compared between patients with p-QRSd defined as QRS>0.12 s (p-QRS group, n=40) and normal QRS duration (n-QRS group, n=309).

Results: There were significant differences in age (69.8±12.5 vs 74.0±11.6, p=0.02), peak creatinine kinase level (1250±2344 IU/l vs 526±840 IU/l, p=0.04), brain natriuretic peptide level (1231±1881 pg/ml vs 512±888 pg/ml, p=0.001), and preceding physical or emotional stresses (82.1% vs 65.7%, p=0.02) between p-QRS group and n-QRS group.
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-QRSd was independent predictor of in-hospital mortality (hazard ratio, 10.29, 95% confidence interval: 3.599–29.433, p<0.0001).

Conclusions: In the database from our Network, patients with TC admitted with p-QRSd seem to be associated with poor in-hospital clinical outcomes. Aggressive intervention may be required to prevent further deterioration of clinical course in TD admitted with p-QRSd.

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 500 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.

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 onset symptoms 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 fibillation 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 tachycardia 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 unchanged in 77%, improved in 8% and got worse in 15%; intraventricular conduction worsened in 86%, improved in 7% and was worse in 7%. There were no significant changes in the ejection fraction.

When compared with LT recipients, the tafamidis group had superior rates of symptom improvement (p<0.04), lesser pacemaker dependence and similar mortality (p=0.1).

Conclusions: Overall, there were no major cardiovascular changes after 1-year treatment with tafamidis. This data supports the safety of tafamidis, particularly when compared to LT; nevertheless, a longer follow-up is mandatory.

P1635 | SPOTLIGHT
Comparative evaluation DDD pacing, alcohol ablation and surgical myomyotemy in patients with hypertrophic cardiomyopathy
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Objective: Surgical myomyotomy and transcoronary septal alcohol ablation have been successfully used to treat patients with hypertrophic obstructive cardiomyopathy (HOCM). Our previous studies showed efficacy of left ventricular apical transcoronary septal alcohol ablation in HOCM pacing in HOCM pts. The aim of this nonrandomized 15-th years cohort study was to compare subjective and objective outcomes in HOCM pts undergoing surgical myomyotomy, DDD pacing and alcohol septal ablation.

Methods: 183 consecutive pts with drug refractory HOCM were treated invasively (108 male and 74 female; age 48.7±9.2yrs). All pts were evaluated by cardiac catheterization. Systolic pressure gradient (SPG) on left ventricular outflow tract (LVOT) and functional mitral regurgitation (FMR) degree were assessed by eco- cardio- and left heart catheterization (LHC). FMR was assessed by Doppler in LHC in 54 pts (group1). In 46 pts with massive LV hypertrophy and its cavity obliteration extensive myomyotomy was performed (group2). In 82 pts with appropriate coronary anatomy transcoronary septal alcohol ablation was performed (group3).

Initial peak LVOT gradient was 98±45.9 mm Hg in group1, 107±5.8 mm Hg in group 2 and 93±7.9 mm Hg in group 3.

Results: Short-term results of DDD pacing with optimal atrio-ventricular delay (85–180 ms for atrium pacing and 45–120 ms for atrial sensing) brings dramatic decreasing LVOT SPG to 31, 7.6±5.8 mm Hg and FMR degree (p<0.01). After extensive myomyotomy we observed reducing LVOT SPG to 28±13.6 mm Hg and degree FMR (p<0.01). Septal alcohol ablation in group 3 brings LVOT SPG decrease to 22±5.4, 1 mm Hg (p<0.01).

But because of progression of the disease the long-term results of DDD pacing were not successful.

The long-term results (LVOT SPG) in group 1 (mean 125 month (from 175 to 12 months)) was 64 (7.3±5.6 mm Hg (p<0.05). 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 12 month)) was 29±5.4±6 mm Hg (p<0.01).

Conclusions: Short-term results of DDD pacing, alcohol ablation and surgical myomyotomy are comparable. But hemodynamic results of alcohol septal ablation and surgical myomyotomy have an advantage in long-term period. DDD pacing didn’t show significantly good, stable long-term results.

P1636 | BEDSIDE
Filamin C is a novel disease gene for familial restrictive cardiomyopathy
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Background: Restrictive cardiomyopathy (RCM) is characterized by increased stiffness of the ventricles, impaired diastolic filling with preserved systolic function. Currently, the limited genetic basis of RCM is a 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. Ex- planted heart tissue has been evaluated by histology and immunohistochemistry. Functional analysis of mutated 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 re- quiring 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.

Histo pathological identified minimal myofiber disarray and cytoplasmic inclusions in infiltrated FLNC protein as well as intracellular filament aggregation. FLNC specific aggregates were found. Further expression of mutant FLNC proteins in C2C12 and H9C2 cells showed perinuclear and cytoplasmic ag- gregates not observed in wild-type FLNC transfected cells. Western blot analysis showed reduced amounts of mutant soluble N-terminal FLNC protein compared to wild-type.

Finding of a second mutation in a different family with RCM leading to heart transplantation. Further genetic studies via NGS found a unique variant in FLNC (p.S1624L) segregating with the disease.

Conclusions: Mutations in FLNC are a novel cause for familial restrictive cardiomyopathy. FLNC mutations cause inherited RCM demonstrating 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
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Background: Fatal ventricular arrhythmia (VA) is an independent predictor of mortality in cardiac sarcoidosis (CS). However, clinical effects of corticosteroid therapy on VA in CS are still uncertain.

Methods: From a tertiary center between 1993 and 2014, we examined 102 pa- tients with CS. Patients were followed-up to determine adverse outcomes (sus- tained ventricular tachycardia (VT), appropriate ICD therapy, or all-cause death).

Results: We enrolled 78 patients who underwent corticosteroid therapy in the present study. Forty five 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 ventricu- lar ejection fraction (LVEF) between patients with Va at diagnosis and patients who didn’t have VA at diagnosis (39% vs. 47%, p<0.01). Patients with VAs at diagnosis were significantly worse than those without (log-rank p=0.001). On multivariate analysis, the presence of VA at diagnosis was a significant predictor on mortality after ad-
The presence of VAs at diagnosis was a significantly worse prognostic factor in patients with reduced EF (log-rank p<0.01), 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. Patients with VA and reduced EF should be considered aggressive anti-arrhythmic therapy such as ICD implantation and/or catheter ablation regardless of corticosteroid therapy.

P1639 | BEDSIDE
Percutaneous coronary artery interventions in paediatric population: a 15-years experience
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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 17/22 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 periprocedural 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
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Background: Percutaneous pulmonary valve implantation (PPVI) using bovine jugular vein (BJV) valved stent is safe and effective. However, infective endocarditis has been reported for unclear reasons.

Purpose: To assess the impact of PPVI procedural steps on valvular histology, selective bacterial adhesion and leaflet mechanical behaviour.

Methods: Three valved stents (BJV valved stent, homemade stents with bovine and porcine pericardial leaflets) 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 valve leaflets.

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.

Figure 1. S. sanguinis adhesion electron microscopy

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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 (16–73) 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 (45–9860) 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 cTnI 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-fold 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 (p < 0.0001 r=91121).

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 analyses (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 infarction 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 should also be considered for the transient supraventricular arrhythmias after transcatheter ASD closure.

Cardiac troponin-I release after transcatheter closure of the atrial septal defect are related with arrhythmias in the early follow-up

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 mmHg (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 atrioventricular valve regurgitation in Group 1. Logistic regression analysis revealed systemic right ventricle morphologic changes 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.

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 arterial and venous VM treated with percutaneous occlusion in pediatric and adult patients.

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 assessed. 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 predominantly 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 communications, 9 systemic venous communications, 6 peripheral arteriovenous fistulae, 5 Blalock–Taussig shunts, 4 coronary fistulae, 2 Fontan fenestrations and 2 renal artery aneurysms. Mean median size was 4.5 (2.0–16.0) mm. The 139 devices used (1:1±0.6/valv.) were selected according to the lesion anatomy and flow and included 75 vascular, 24 direct occluders, 22 duct occluders and 1 atrial septal defect occluder. Median device size/valve 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 hematoma after unsuccessful Blalock–Taussig shunt 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.
temporarily abnormal processes of myocardial excavation and endocardial tissue fenestration, contributing to the formation of papillary muscles and chordae tendineae. In support of this thesis, ICEF disappear when cardiac structures development is complete with no consequences on systolic-diastolic myocardial function and cardiac valve performance.

P1645 | SPOTLIGHT
Diagnosis and prognosis in nine fetuses with idiopathic constriction of the ductus arteriosus using fetal echocardiography
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Objective: Most constriction of the ductus arteriosus (DA) in fetuses are secondary to medication or structural lesions. Idiopathtic 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 echocardiographic 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 transthoracic 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 32.1±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 0.76±0.17m/s. And pulsatility index 1.23±0.61. Right heart diastolic 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±3.03mm, 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 4 fetuses (severe 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 transthoracic 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?
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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 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: 88/ (98.2%) FE were requested in absence of risk factors: 24.2% for a suspected CHD, 27% for inadequate visualization of cardiovascular 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 following validated risk factors: 6.8% for twin pregnancy, 1% for maternal chromosomal anomalies, 2.1% for maternal size and function on CMR. All results are presented in mean ±STD apart from differences (p<0.05). The gestational age had no significant correlation with the outcome.

Conclusion: The incidence of CHD increased from 0.04% in cases without any risk factor to 2.8% for cases with at least one risk factor. The risk factors associated with CHD are maternal age >35 years, parental history of CHD, male sex, twin pregnancy, family history of CHD, maternal use of cyclooxygenase inhibitors. These risk factors do not exclude CHD and are not predictive of a certain type of CHD. The prevalence of CHD in cases without any risk factor is very low, and is even lower in cases with at least one risk factor. The gestational age is not predictive of the outcome of the FE.

P1647 | BEDSIDE
Long-term outcome of ross procedure performed in childhood: a single centre cohort study in an adult congenital heart disease unit
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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 Ross Procedure were based on a variety of medical records, cardiac magnetic resonance imaging (CMR) and cardiopulmonary exercise testing (CPET) were reviewed. We examined right ventricular-pulmonary artery (RV-PA) conduit, aortic autograft function, biventricular size and function on CMR. All results are presented in mean ±STD apart from differences (p<0.05).

Results: 29 patients (86% males) with mean age at time of surgery of 10.5±5.3 yrs and median follow up of 14±3 yrs (range: 12 to 23 yrs) werereviewed. The mean age at latest follow up was 25.7±4.9 yrs. CMR findings revealed PV Vmax of 2.3±0.7 m/s, right ventricular regurgitant volume of 6.6±9.4 ml, pulmonary regurgitant fraction of 6.7±9.5%, left ventricular (end diastolic volume indexed [EDVI]: 91.1±23.3 ml/m2, end systolic volume indexed[ESVI]:31.6±16.2 ml/m2, ejection fraction[EF]:63.7±8.4%), 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±4.68 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
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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.
P1649 | BEDSIDE
Follow-up of 316 molecularly defined pediatric long QT syndrome patients - clinical course, beta blocker treatment and side effects
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Method and 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 final 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 included 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 ≤500 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.

Conclusion: 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
Reurrence and long-term follow-up for double-outlet right ventricle with biventricular repair
O. Villemain1, E. Belli2, M. Ladouceur1, L. Houy2, Z. Jalal1, M. Ly2, R. Roussin2, P. Vouhe1, D. Bonnet1, 1 M3C Necker, Congenital and Pediatric Cardiology, Paris, France; 2 Surgical 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 (Taussig-Bing Anomaly) in 32% (n=139), and 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).

Conclusion: Factors affecting the prognosis of DORV are anatomical and surgical factors. However, there is no difference between the main types of surgical strategy.

P1651 | BEDSIDE
Temporal trends in the incidence of acute myocardial infarction and sudden cardiac death in the general population: a 10-year population based study
M. Honna1, K. Tanaka1, R. Kom1, F. Tanaka1, K. Sato1, T. Sakai2, M. Onodera3, T. Onoda1, K. Sakata1, M. Nakamura4, J. Ikeda5, K. Kontula1, M. Ly2, E. Belli2, M. Haim1, M. Hoshen1, R. Balicer2, O. Reges1, Y. Rabi2, M. Leibowitz2, Z. Jakobishin1, D. Hasdai1, J. Rabin Medical Center, Beilinson Hospital, Petah Tikva, Israel; 2 Clalit Health Research Institute, Tel Aviv, Israel

Background: As the proportion of elderly in the Japanese population is increasing and aging along with major dietary changes, it may be assumed that the number of patients suffering from coronary heart disease is increasing. However, temporal trends of the incidence and outcome of acute myocardial infarction (AMI) and sudden cardiac death (SCD) in the general population remains unclear.

Methods: We conducted a population based survey of MI registration including unexpected sudden cardiac death (<24 hours; SCD) from January 2003 to December 2012 in a rural community (population = 27x10^5) in northeast Japan, which has a high proportion of elderly in the population and relatively poor access to emergency care. AMI was defined by the MONICA type 1 criteria (A = non-fatal AMI, B = fatal AMI, C = SCD).

Results: The incidence of AMI was compared across 5 terms (T1 = 2003–2004, T2 = 2005–2006, T3 = 2007–2008, T4 = 2009–2010, T5 = 2011–2012). The age-adjusted incidence (per 100,000 person-year) of hospitalized AMI (MONICA criteria; A+B) was found to decrease gradually and significantly across the time periods in both sexes (Fig-left). However, AMI presenting as SCD (MONICA criteria; C) was stable over time and remained relatively high in both sexes (Fig-right).

Conclusion: These temporal trends underscore the need to improve preventive strategies and prehospital care for reducing SCD in the community dwelling population.

P1652 | BEDSIDE
Estimated glomerular filtration rate within the normal or mildly impaired range and incident non-valvular atrial fibrillation in the general population
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Background: Lower estimated glomerular filtration rate (eGFR), in particular in the range of significant renal impairment (eGFR ≤ 60 ml/min/1.73m²), is associated with incident atrial fibrillation (AF). This association is less clear within the normal or mildly impaired range of eGFR.

Methods: Using the Chronic Kidney Disease Epidemiology collaboration (CKD-EPI) eGFR formula, we analyzed ambulatory adults (<22 years old) without rheumatic heart disease or prosthetic valves and with eGFR between 60–130 ml/min/1.73m² in their index visit, for incident, newly diagnosed AF. We analyzed both patients with and without prior cardiovascular disease (CVD).

Conclusion: These temporal trends underscore the need to improve preventive strategies and prehospital care for reducing SCD in the community dwelling population.

CLASSICAL AND NEW RISK FACTORS FOR CARDIOVASCULAR DISEASE

P1651 | BEDSIDE
Temporal trends in the incidence of acute myocardial infarction and sudden cardiac death in the general population: a 10-year population based study
M. Honna1, K. Tanaka1, R. Kom1, F. Tanaka1, K. Sato1, T. Sakai2, M. Onodera3, T. Onoda3, K. Sakata1, M. Nakamura4, J. Ikeda5, K. Kontula1, M. Ly2, E. Belli2, M. Haim1, M. Hoshen1, R. Balicer2, O. Reges1, Y. Rabi2, M. Leibowitz2, Z. Jakobishin1, D. Hasdai1, J. Rabin Medical Center, Beilinson Hospital, Petah Tikva, Israel; 2 Clalit Health Research Institute, Tel Aviv, Israel

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Conclusion: These temporal trends underscore the need to improve preventive strategies and prehospital care for reducing SCD in the community dwelling population.
Background: The recent EAS consensus paper on familial hypercholesterolemia (FH) [1] indicated a higher prevalence of elevated low density lipoprotein cholesterol (LDL-C) in FH patients with genetic factors including mutations in the LDL receptor (LDLR) and proprotein convertase subtilisin kexin type 9 (PCSK9) genes. A prospective analysis of the FH population in the US found that up to 30% of FH patients harbored mutations in FH genes [2]. The mechanisms of reduction in Lp(a) in patients with FH were not clear. We previously investigated the association between FH and lipoprotein(a) (Lp(a)) levels in a cohort of French patients, and demonstrated that FH patients had higher Lp(a) levels compared to non-FH controls, but no further studies have been conducted on the association between FH and Lp(a) levels. Here, we examined the association between FH and Lp(a) levels in a multi-center study of patients with FH.

Methods: We examined the association between FH and Lp(a) levels in a multi-center study of 3,129 patients with FH. Lp(a) levels were measured using an immunoturbidimetric assay (IDEXX Laboratories, Westbrook, ME). FH status was determined based on the presence of FH symptoms or signs or FH genetic testing results. Logistic regression analysis was used to determine the association between FH status and Lp(a) levels. The study was approved by the Institutional Review Board of each participating center.

Results: We found that FH patients had significantly higher Lp(a) levels than non-FH controls (median Lp(a) = 54.2 mg/dl vs. 24.3 mg/dl, p < 0.001). The odds of having a high Lp(a) level (≥30 mg/dl) were significantly higher in FH patients compared to non-FH controls (OR=2.74, 95% CI=2.12-3.55, p < 0.001). The association was independent of age, sex, and LDL-C levels. The association was also stronger in FH patients with FH-PCSK9 mutations than in those with FH-LDLR mutations (OR=3.39, 95% CI=2.23-5.18, p < 0.001 vs. OR=2.25, 95% CI=1.69-3.00, p < 0.001). The association remained significant after adjusting for age, sex, and LDL-C levels. The results were consistent across all centers.

Conclusions: Our study is the first to examine the association between FH and Lp(a) levels in a multi-center study of patients with FH. The results suggest that FH patients have higher Lp(a) levels than non-FH controls, and that the association is stronger in FH patients with FH-PCSK9 mutations than in those with FH-LDLR mutations. These findings may have implications for the management of FH patients with high Lp(a) levels.
P1656 | BEDSIDE
The association between serum apolipoprotein B and acute myocardial infarction is modified by plasma glycine
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Background: Hepatic cholesterol uptake and VLDL excretion depend on the availability of free plasma 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 73 (70–104) 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 may increase the life-span of circulating atherogenic 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
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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 population.

Purpose: To evaluate temporal trends of CAD severity in a rural population in Belgium.

Methods: To identify common variants associated with cardiovascular events by replication of SNPs derived from genome wide association study (GWAS) data in Koreans.

Methods: Two variants (rs1333049 located in bp21 and rs9508025 in FLT1 gene) that showed strong associations with coronary artery disease in prior GWAS were selected for candidate SNPs. Replication cohort was established by 2,814 high-risk patients withdrawn from a cardiovascular genome center, university and surrogate markers of vascular disease including carotid intima media thickness (c-IMT), carotid stiffness and carotid endothelial dysfunction and carotid vasoreactivity were measured by high-precision echotracking device in 6163 participants attending a health check up in a large health centre in France between 2008 and 2012 by three trained technicians certified in vascular echography. Participants were categorized as having poor, intermediate and ideal cardiovascular health if they had 0–2, 3–4 and 5–7 ideal health components (smoking, physical activity, body mass index, diet, blood glucose and total cholesterol, blood pressure). Multivariable linear regression analysis was performed to examine the relationship between carotid parameters and ICVH.

Results: Mean age was 59.4 (SD 6.2) years and 62% were males. Mean cIMT was 0.5 (12.2) mm in men and 0.6 (10.6) mm in women (75th percentile of the age and gender adjusted reference values). Poor, intermediate and ideal cardiovascular health was present in 48.9%, 43.7% and 7.3% of study participants. After multivariable adjustment and compared to poor ICVH, intermediate and ideal ICVH were associated significantly with lower c-IMT and carotid stiffness, and higher carotid endothelial dysfunction. The inverse association with c-IMT corresponded to 4 to 6 years of prolonged survival. All these associations existed and were consistent for each item of ICVH.

Conclusion: The current associations of ICVH with c-IMT, carotid stiffness and carotid endothelial dysfunction support the major importance of primordial prevention of cardiovascular disease.

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P1658 | BEDSIDE
Two-year-five trends in coronary artery disease in coronary artery disease in a population-based study
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Background: Coronary artery disease (CAD) remains a major health problem in developed countries.

Purpose: To evaluate temporal trends of CAD severity in a rural population in Belgium.

Methods: The Monaca-Bellux registry records the rate of CAD related events of inhabitants (inh.) of a Belgian province since 1986. We analyzed temporal evolution of incidence of acute myocardial infaracts as well as incidence, indications and results of coronary angiograms, and revascularization rates (both PCI and CABG) for stable and unstable CAD for the population aged 35–74 years between 1986 until 2011.

Results: From 1986 until 2011, the crude rate of acute myocardial infaracts 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
males in 2011. Consequently, the incidence of patients diagnosed with significant new CAD on first angiograms decreased from 592/100000 to 393/100000 male in. from 1995 until 2011 and 171/100000 to 108/100000 female in. aged 34–75 years. Also, rates of first revascularization by either PCI or CABG remained stable in females at about 125/100000 in. aged 34–75 years, while it decreased significantly in males from a peak of 426/100000 in. aged 34–75 years in 1996 to 358/100000 in. 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: 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. Those results provide new insights into the novel pharmacological target for ABCA6 and ABCA10.

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Methods: A large family with autosomal dominant, familial hyper HDL-cholesterolemia was identified. A well-known variant in CETP gene which has already been reported to raise HDL-C (rs742907, c.1321+1G>A) was identified only in some of the subjects with extremely high HDL-C, suggesting that other unknown pathogenic variants are co-segregated in this family (figure). Exome capture and sequencing were performed in 5 family members of 3 generations (4 affected, 1 unaffected). Shared variants were filtered for quality of the exome sequencing, rarity, and predicted functional significance.

Results: Although there were no variants co-segregated among all of the affected individuals in CETP gene, we found 132 shared heterozygous nonsense, missense, or splice site variants, of which 24 were rare (minor allele frequency <0.01 or not reported) in 1000 Genome (Asian population). Filtering manually against previous findings on each gene reduced the number of candidates to 3 (c.1331_1334delACAG and c.4515_4516delGA in ABCA10, and c.212T>C in ABCA6).

Conclusions: Whole exome sequencing identified deleterious variants in ABCA6 and ABCA10 genes possibly associated with hyper HDL-cholesterolemia. Those results provide new insights into the novel pharmacological target for ABCA6 and ABCA10.

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.

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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 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, external intact consistency was found on the global scale ($\alpha=0.92$) and the physical subscale ($\alpha=0.91$), and good internal consistency was seen on the emotional scale ($\alpha=0.87$). 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 misattribution of the questionnaire. Discriminative validity was confirmed with females reporting poorer global, physical and emotional scores, older patients reporting poorer global, physical and emotional scores and higher education also 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 patients 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.

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**

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**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 compelled cardiologists to face new demanding issues that may engender stress and affect work satisfaction. Physician distress impacts on the frequency of medical errors, patients’ compliance and health care costs.

**Purpose:** The IANUS survey was designed to determine the prevalence of job distress among a nationwide cardiologists sample and to assess the relationship between personal-professional characteristics and positive and negative experiences in cardiological practice.

**Methods:** 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% reported loss 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 management for their work and 52% work 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 inpatients and outpatient departments of patients 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

**The association between somatization and health care utilization in patients with non-cardiac chest pain**

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**Background:** Chest pain is one of the most common reasons for care-seeking, about 0.6 million patients are diagnosed with non-cardiac chest pain (NCCP). NCCP patients suffer from cardiac anxiety, defined as fear of cardiac-related stimuli and sensations, which is strongly associated with increased healthcare utilization. Research indicates that somatization, defined as report of somatic symptoms that have no pathological biological cause, is a risk factor for health care utilization.

**Purpose:** To describe the prevalence of somatization and its association with cardiac anxiety and healthcare utilization in NCCP patients.

**Methods:** Data in this cross sectional study was collected from 552 patients diagnosed with NCCP in four Swedish hospitals within one month from discharge. Patients had a mean age of 64±17 years, and 51% were women. Somatization was measured with the Patient Health Questionnaire-15 and cardiac anxiety with the Cardiac Anxiety Questionnaire. Healthcare utilization, i.e. number of health care contacts the year before study inclusion was self-reported by the patients. To determine the association between somatization, cardiac anxiety and health care utilization, a logistic hierarchical regression analysis was used with cardiac anxiety as an independent variable and somatization as a dependent variable in the first step, and anxiety inserted in the first block, and a variable where these two were multiplied in the third block.

**Results:** In total, 283 (51%) patients reported at least moderate levels of somatization and 229 (42%) patients reported cardiac anxiety. Of the total, 89 (16%) had both somatization and cardiac anxiety, 211 (38%) had only somatization and cardiac anxiety, 161 (29%) had only somatization and 164 (30%) had only cardiac anxiety. Somatization was strongly related to cardiac anxiety ($r=0.54$, $p<0.001$). About 26% of the patients reported 2–3 healthcare contacts and 14% reported more than 3 healthcare contacts due to chest pain. Both somatization ($r=0.37$, $p<0.001$) and cardiac anxiety ($r=0.46$, $p<0.001$) were significantly related to number of healthcare contacts. The logistic hierarchical regression showed that cardiac anxiety (OR=1.09, CI: 1.07–1.11, $p<0.001$) and somatization (OR=1.08, CI: 1.03–1.13, $p<0.001$) were associated with increased healthcare utilization. The multiplicative interaction term between these variables was not significant (OR=1.09, CI: 0.969–1.00, $p=0.901$).

**Conclusions:** Somatization was frequently reported by NCCP patients and associated with cardiac anxiety and increased healthcare contacts. Somatization may therefore be important to target with interventions.

P1666 | BEDSIDE

**Psychosocial consequences of venous thromboembolism in youth: A mixed methods study**

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**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

**Methods:** 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 controls were 4.7% and 18.3%, respectively). The confidence interval for the 5-year risk difference was 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 concerns of being alone, worries 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 preferably to seek help from health care professionals or emergency services. Women were more likely to have more intense and non-focal chest pain, as well as type of healthcare services, used by patients up to FMC. Logistic regression showed that females had lower odds of being transported by ambulance (OR 0.56, 95% CI 0.42–0.74) and were also more likely to be transported by family and friends (OR 2.13, 95% CI 1.68–2.71) than men. There were no differences between sexes in the type of transports utilized.

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 cardiovascular compensatory effects of other activities. Cardiovascular prevention strategies should include a range of occupational physical activities.

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 how they influenced the incidence of CVD over 10 years of follow-up.

Results: The incidence of CVD from time spent sitting or standing at work showed a U-shape relationship. The incidence of CVD was lower for those who spent 300–1200 mins/week sitting or standing at work halved the risk of CVD HR: 0.63 [0.42–0.94]; 0.48 [0.31–0.76], respectively. The risk was higher for men who routinely carried heavy objects when their jobs involved little or no time spent sitting or standing still at work, although this risk was decreased for men who spent >300–1200 mins/week sitting or standing still at work.

Conclusion: Sex differences in symptoms presentation and health care-seeking behaviour may influence an early diagnosis of acute coronary syndrome (ACS). This study aimed to evaluate sex differences in ACS symptoms presentation and health care-seeking behaviour.

Methods: Sex differences in symptoms presentation and health care-seeking behaviour may influence an early diagnosis of acute coronary syndrome (ACS). This study aimed to evaluate sex differences in ACS symptoms presentation and health care-seeking behaviour.

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 diagnosed with ACS were older than men (mean 69.4 years versus 62.1 years, p < 0.001). The median delay between symptoms onset to first medical contact (FMC) was 128 (IQR 55–422) minutes in women and 95 (IQR 50–325) minutes in men (p = 0.08). Most patients, both women and men, reported chest pain (95.4 vs. 97.5%, p = 0.123), however women had more intense and irradiated chest pain (63.1% vs. 39.4%, p < 0.001; 70.1% vs. 57.9%, p = 0.002; respectively). Symptoms other than chest pain were more often referred by women (83.4% vs. 69.9%, p < 0.001). A large proportion of patients, either women or men, did not perceive symptoms as cardiac (50.5% vs. 47.0%, p = 0.387). Regarding help-seeking behaviour, women were more likely to firstly seek help from relatives, friends or spouses (44.9% vs. 42.4%, p = 0.005), whereas men were more likely to firstly seek help from health care professionals or emergency services (45.5% vs. 35.2%, p = 0.009). There were no differences between sexes in type of transport, as well as type of healthcare services, used by patients up to FMC. Logistic regression analysis showed that pain irradiation, chest pain severity and type of help requested were independently associated with sex.

Conclusion: Women were more likely to have more intense and non-locally chest pain accompanied by other symptoms, and yet, they ask for help to nearby people preferably to seeking help from health care professionals or emergency services. This study reinforces the need of raising awareness of ACS symptoms as well as appropriate health care-seeking behaviour, particularly in women.
more of the maximal heart rate for age in 80% of the participants. Supra ventric- 
ular ectopic beats and paroxymal 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 vary 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
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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 
interest 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
(Functional Assessment of Chronic Illness Therapy – spiritual well being – FACIT - 
spirituality). All patients answered a self-administered questionnaire about 

depression (Functional Assessment of Chronic Illness Therapy – spiritual well being – FACIT - spirituality)

Results: 507 patients, 85% male gender and median age of 63 years. CAD man-
agement was 32.7% CABG, 32% PCI, 11.8% both and 23.5% 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%, 
q quintile 4 (sp4): 19.7%, quintile 5: 14.8% (sp5; most spiritualized group).

The prevalence of moderate or 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
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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 
and 30-day outcomes has 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 of 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 addres-
sive 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 
given in 500mg 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 
PS alone. In addition to ezetimibe, PS can counterbalance the increased 
sterol absorption besides improving lipid profile. Our study confirms the rele-
ance 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), INCIT-Fox (National Institute of Science and Technology 
Complex Fluids, Brazil)

P1674 | BEDSIDE

A Clinical Decision Support System can improves the quality of 
lipid-lowering therapy in coronary patients
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Introduction: Familial hypercholesterolemia (FH) is the most common inherited 
disorder of lipid metabolism, resulting in very high levels of LDL-cholesterol (LDL-
C) from birth and increased premature coronary disease. Underdiagnosed and 
undertreated, 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 
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TREATMENT STRATEGIES AND ADHERENCE: CAN WE DECREASE RISK?

P1673 | BEDSIDE

Plant sterol supplementation on top of lipid-lowering therapies in 
familial hypercholesterolemia
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Background: Familial hypercholesterolemia (FH) is the most common inherited 
disorder of lipid metabolism, resulting in very high levels of LDL-cholesterol (LDL-
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Acknowledgement/Funding: FAPESP (Foundation for Research of the State of 
Sao Paulo, Brazil), INCIT-Fox (National Institute of Science and Technology 
Complex Fluids, Brazil)
to recruit 8 patients. The physicians enrolled consecutive eligible patients with high 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. Researchers were asked to evaluate HTE-DLP with questionnaire QoE for applications 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 1 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 (3.8/5). The widespread use in Spain of HTE-DLP would mean in 2020 a reduction in fatal and nonfatal coronary events in the population of 35–74 years of between 5.4% and 7.4% in males and between 1.8% and 2.0% among women and a decrease in coronary heart disease health costs between 4.7% and 6.4% (between 24 and 32 million Euros savings to the healthcare system).

Conclusion: In clinical practice a specific CDSS it is possible to improve the management of dyslipidemia with a decrease in coronary heart disease and lowering healthcare costs.

Acknowledgement/Funding: The present project is a follow-up to the Observatory of Innovation Experiences in ICTs and Health in Catalonia (Fundació TIC Salut, Health Department, A. K. Gitt1, J. Ferriere2, G. De Ferrari3, M. Elissaf4, M. P. Hermans5, T. Kiernan6, R. Oganov7, D. Lautsch8, V. Ashton9, B. Ambegaonkar10 on behalf of DYSIS II Europe Investigators. 1 Stiftung Institut für Herzinfarktforschung and Herzcentrum Ludwigshafen, Med. Klinik B, Cardiology, Ludwigshafen am Rhein, Germany; 2 Toulouse University School of Medicine, Rangueil Hospital, Toulouse, France; 3 Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; 4 University of Ioannina School of Medicine, Ioannina, Greece; 5 Cliniques Universitaires St Luc, Brussels, Belgium; 6 University Hospital Limerick, Limerick, Ireland; 7 State Research Centre for Preventive Medicine, Moscow, Russian Federation; 8 Merck & Co., Inc., Kenilworth, United States of America.

Background: Current guidelines recommend a low-density lipoprotein cholesterol (LDL-C) target of <1.8mmol/l for coronary patients and the administration of high-intensity statin therapy. Purpose: Our study documents real word lipid target achievement, including distance to target, among patients with stable coronary heart disease (CHD) and patients surviving an acute coronary syndrome (ACS) event in Europe.

Method: The TDCC project is 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 for 12 months in intervention patients and 0–12 months prior to enrollment for CHD patients. Patients were on lipid-lowering therapy (LTT) ≥3 months and not participating in clinical trials involving medication. Patient characteristics, risk factors, treatment patterns, and laboratory values were collected. LDL-C target achievement was assessed based on ESC/EAS guidelines.

Results: 880 ACS and 2778 CHD patients currently on LTT were enrolled in Europe from 2012 to 2014. Only 23.2% (n=204) ACS and 29.6% (n=821) CHD patients achieved an LDL-C <1.8mmol/l, with median distance to LDL-C target in patients not at goal being 0.9 mmol/l (IQR 0.4, 1.5) in ACS and 0.6 mmol/l (IQR 0.3, 1.1) in CHD patients.

Mean lipid values and LDL

<table>
<thead>
<tr>
<th></th>
<th>ACS patients (N=880)</th>
<th>CHD patients (N=2778)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol (mmol/l)</td>
<td>4.4±1.2</td>
<td>4.1±1.0</td>
</tr>
<tr>
<td>LDL-C (mmol/l)</td>
<td>2.6±1.0</td>
<td>2.3±0.8</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.6±0.9</td>
<td>1.5±0.8</td>
</tr>
<tr>
<td>HDL-C (mmol/l)</td>
<td>1.1±0.3</td>
<td>1.2±0.4</td>
</tr>
<tr>
<td>Non-HDL-C (mmol/l)</td>
<td>3.3±1.2</td>
<td>2.5±0.9</td>
</tr>
<tr>
<td>Atoxasatin equivalent dose (mg/day)</td>
<td>2.2±1.7</td>
<td>27.5±0.9</td>
</tr>
<tr>
<td>Statin monotherapy</td>
<td>87.2%</td>
<td>79.8%</td>
</tr>
<tr>
<td>Statin + ezetimibe</td>
<td>6.4%</td>
<td>11.6%</td>
</tr>
<tr>
<td>Statin + other non-statin (fibrates, omega 3 fatty acids)</td>
<td>2.4%</td>
<td>6.7%</td>
</tr>
<tr>
<td>Non-statin monotherapy</td>
<td>3.8%</td>
<td>2.0%</td>
</tr>
</tbody>
</table>

Conclusion(s): Three out of four coronary patients did not achieve the recommended LDL-C target, even while being treated with LTT, primarily statin monotherapy. The most frequent LTT in the study was found in both patient cohorts, despite the high risk of our patient population and the need for more intense LTT (as stressed by our distance to target findings).

Acknowledgement/Funding: This study was funded by Merck & Co., Inc.
with suspected SI-1 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 38% 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 satisfactory address CV risk management in these patients.

Acknowledgement/Funding: This study was sponsored by Amgen Inc.

P1676 | 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” defined radical strategies for CKD 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 tapering 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: Total 53.3±15.9 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 1676.3±2089.86 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 32.8% of the group and the rest had regular lipid measurements at every 3 months. (30.9%), every 6 months (32.8%), every 12 months (18.9%) 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 status 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 atherosclerosis. 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: This 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 not received 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. Bays2, R.A. Braeckman3, S. Philip4, W.G. Stiranoff5, R.T. Doyle6, P.N. Soni7, R. Juliano8, I. Baylory College of Medicine, Houston, United States of America; 2Louisville Metabolic and Atherosclerosis Research Center, Louisville, United States of America; 3Consultant, Doylestown, United States of America; 4Amarin Pharma Inc., Bedminster, United States of America; 5Consultant, Mystic, United States of America

Background and introduction: Apolipoprotein C-III (ApoC-III) is a small protein that resides on various lipoproteins, inhibits lipoprotein/hepatic lipases, im-

patients hepatic uptake of triglyceride (TG)-rich lipoproteins (such as lipoprotein remnants), and generally promotes hypertriglyceridemia. Its increased activity is associated with resistance to lipoprotein lipase and generally promotes hypertriglyceridemia. Recent studies have shown that omega-3 fatty acid docosahexaenoic acid have suggested inconsistent effects on ApoC-III levels. Icosapent ethyl (IPE) is a high-purity prescription form of EPA ethyl ester approved to lower TG levels in adult patients with severe hypertriglyceridemia (TG > 500 mg/dl).

Purpose: To evaluate the effects of IPE on ApoC-III levels in patients from the MARINE and ANCHOR studies.

Methods: MARINE and ANCHOR were 12-week, phase 3, double-blind studies that randomized adult patients to IPE 4 g/day, 2 g/day or placebo. MARINE randomized 229 patients (TG >500 and <2000 mg/dl); ANCHOR randomized 702 patients at high risk for cardiovascular disease (TG >200 and <500 mg/dl) despite low-density lipoprotein cholesterol (LDL-C) control on statin therapy. This analysis assessed median percent change from baseline to study end in ApoC-III levels compared with placebo.

Results: 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 g/day (14.3%, p=0.0154, MARINE; 8.5%, p=0.0008, ANCHOR).

ApoC-III levels in patients from the MARINE and ANCHOR studies (IPE 4 g/day and placebo groups only)

ApoC-III Median baseline Median final Median change Median change from baseline%
MARINE IPE 4 g/day n=53 25.6 (11.6) 19.7 (10.5) -10.1 (27.1) -25.1 (-0.0001)
MARINE Placebo n=44 26.8 (17.3) 32.7 (14.6) 12.2 (21.5) -
ANCHOR IPE 4 g/day n=208 15.2 (4.76) 13.7 (4.80) -9.4 (29.5) -19.2 (-0.0001)
ANCHOR Placebo n=201 14.8 (4.48) 16.2 (5.57) 10.9 (30.0) -

Conclusions: 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 (DYSSIS) II MEA results

S.N. Al Sifri1, W. Al Mahmeed2, R. Azar3, M. Sobhy4, A.K. Gitt5, M. Horack6, V. Ashston7, R. Bradu8, B. Ambegaonkar9, S. Wajih1 on behalf of DYSSIS 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 für Herzinfarktforschung, and Herzcentrum Ludwigsafen, Med. Klinik B, Cardiologie, Ludwigshafen am Rhein, Germany; 6Stiftung Institut für 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 <1.8 mmol/l.

Purpose: DYSSIS 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: DYSSIS 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 DYSSIS 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 <1.8 mmol/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 mmol/l (IQR 0.2, 0.9) for CHD patients. Table 1 provides patient characteristics and LLT details. High intensity statin (atorvastatin 40–80mg/day equivalence) was not administered to more than half the patients (68.9% ACS and 55.4% CHD patients).

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.

**P1682 | BEDSIDE**

Predictors 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. Zhou1, A.J. Dalby3, J. Zhou1, A.J. Dalby3

Other LLT (no statin) 2% 3% 3% 4% 6% 5%
High-intensity statin 33% 13% 12% 6% 3% 7%
Moderate-to-low intensity statin 43% 54% 50% 58% 46% 50%
Ezetimibe (no statin) 1% 2% 1% 1% 1% 1%
Other LLT (no statin) 2% 3% 3% 4% 6% 5%
No LLT 22% 28% 34% 31% 45% 37%
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: A high potency statin regimen was shown to reduce CV events after ACS, but remains underscored 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 treated 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. Sandoe3, J. Chin1, K. Gray1, C. Benoit1, X. Khan2

Statin use included elevated cardiac biomarkers, PCI for index event, diabetes mellitus, peripheral arterial disease and statin treatment prior to the index event (Figure).

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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.

**P1684 | 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. Sandoe3, J. Chin1, K. Gray1, C. Benoit1, X. Khan2

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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.
Investigators.

Persistent lipid abnormalities and other key risk factors, such as hypertension and Acute coronary syndrome (ACS) and coronary heart disease, are important contributors to cardiovascular disease (CVD) risk. The Aspirin Randomized Intervention trial in secondary prevention for Outcomes (ARISTOTLE) study was 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 3–12 months prior to enrollment (CHD). Patients were on lipid-lowering therapy (LLT) with 63.3% (n=1142) and 91.7% (n=2570) currently on LLT respectively. Only 18.2% (n=203) and 5.8% (n=150) were on high-intensity statins.

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- statin 4.4%, 5.3%; and non-statin monotherapy 1.6%, 0.8%.

Material and methods: During 2005 to 2012 a total of 300 consecutive out-patients 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 Tropinin T in healthy controls is 14 ng/l. However, 9% of patients with psychosis had Tropinin T values > 15 ng/l. The upper normal values for BNP is 150 pg/l. Studies at an emergency unit have indicated the patient with BNP > 100 pg/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 Tropinin T was significantly but weakly related (r=0.21, p<0.01).

Conclusion: A surprisingly high percentage of stable patients with psychotinic disease have high levels of risk markers (Tropinin 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.

P1684 | BEDSIDE
LDL-C target attainment remains low among treated coronary patients in Asia-Pacific: the Dyslipidemia International Study (DYSIS) II AP results

J.P.S. Sawhney1, F.T. Chiang2, Y.S. Jang3, P.N. Venkati4, K.K. Poh5, W. Buddhari6, R. Sy7, M. Munawar2, B. Yan8, H.P. Balaji9 on behalf of DYSIS II Asia-Pacific Investigators; 1Kangla Ram Hospital, Kathmandu, Nepal; 2National Taiwan University Hospital, Taipei City, Taiwan, ROC; 3Severance Cardiovascular Hospital, Seoul, Korea, Republic of; 4Tam Duc Heart Hospital, Ho Chi Minh City, Vietnam; 5National University Heart Centre, Singapore, Singapore; 6King Chulalongkorn Memorial Hospital, Bangkok, Thailand; 7Cardinal Santos Medical Center, Manila, Philippines; 8Binawaluya Cardiac Center, Jakarta, Indonesia; 9The Chinese University of Hong Kong, Hong Kong SAR, People’s Republic of China; 10MSD International GmbH, Singapore, Singapore

Background: Acute coronary syndrome (ACS) and coronary heart disease (CHD) patients remain at high risk for subsequent cardiovascular events due to persistent lipid abnormalities and other key risk factors, such as hypertension and diabetes.

Purpose: Our study documented real world lipid target attainment and the prevalence of dyslipidemia 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 3–12 months prior to enrollment (CHD). Patients were on lipid-lowering therapy (LLT) 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 target, primarily being on moderate statin dose. Higher intensity LLT should be provided to these high risk patients.

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.
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 1. The score of consequence factors was not significantly different between two groups.

**Table 1: Scores of FSAS, triggers factor and consequence factor.**

<table>
<thead>
<tr>
<th>FSAS</th>
<th>Appropriate shock group</th>
<th>Re-shock group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.5 ± 5.4</td>
<td>16.0 ± 7.5</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

**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

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**P1689 | BEDSIDE**

**The effect of synthetic cannabinoids on P-wave dispersion: an observational study**

M. Sunbul¹, E.A. Sunbul², A. Terzi³, S. Cali⁴, E. Koca⁵, R. Biliçi⁶, S. Cikat⁷.

¹Marmara University, Faculty of Medicine, Department of Cardiology, Istanbul, Turkey; ²Erenköy Ruh Sinir Hastalıkları Hastanesi, Psychiatry, Istanbul, 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±4.4 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 = 0.09, p=0.026).

**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.

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**P1690 | BEDSIDE**

**A continuum in cocaine cardiotoxicity. From myocardial strain alteration to left ventricular dysfunction. A cardiovascular magnetic resonance strain/rate strain study**

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**Background:** Cocaine is a highly addictive drug with potentially cardiovascular lethal effects. We have previously showed 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. 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 global longitudinal, radial and circumferential strain (GLS, GRS, GCS), and 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
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
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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 before discharge, discharge and one year after discharge for depression improvement 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 as defined as LDL-cholesterol below 1.8 mmol/l or 50% decrease or use of high-intensity statins (atorvastatin 40 mg or rosvastatin 20mg 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; 5) intensification of physical activity and smoking cessation were as- sociated with improvement for smokers; 6) reporting using drugs for smokers; 7) reducing blood pressure; 8) reporting using drugs for those with more than 14 drinks per week 5) 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 ≥65 years of age (p<0.001) and anti-depressive drug users (p<0.001) and less likely to improve or persistent/new treatment.

Conclusion: Intensification of physical activity and smoking cessation were associated with improvement in depression in ACS patients.

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P1692 | BEDSIDE
Electrophysiological features in chronic alcoholics in their relation to the echocardiographic and clinical data
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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 activa- tion rate (VAR) was used in analysis. Collected data were analyzed by one way ANOVA, Post hoc t- test for independent samples, linear regression analyses using SPSS software version 19.

Results: There was a significant difference between groups in VAR as deter- mined 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 ejection fraction 0.8±2.2sec-1 vs. 0.99±0.1 cm, NS; LVedd 4.9±0.24 cm vs. 4.93±0.2, NS. In alcoholic 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, 95% CI=0.687, p<0.0001).

Conclusions: Electrophysiological remodeling of heart in alcohol heart dis- ease precedes morphological changes. In alcoholics with normal echocardio- graphic parameters alcohol consumption provokes cardiomyopathy 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 | DOPPLERT
Doppler and specific differences in cardiovascular disease risk factors between homeless people and general population- a representative survey
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Introduction: Cardiovascular diseases (CVD) in the homeless represent a se- rious medical, social and economic problem. However, in the socially-deprived groups of population there is a lack of appropriate studies.

Purpose: The aim of the study was to assess prevalence and control of car- diovascular 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 partici- pants’ BMI, blood pressure, fasting serum lipids concentrations, 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 then in NATPOL, study subjects. (54.9% F & 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±12mg/dl vs 197±11.7mg/dl and 133±22mg/dl vs 123±7±1.4mg/dl respectively). CRP concentration was also higher in homeless individuals. Factors associated with improvement of depression after acute coronary syndromes

Conclusions: CVD risk factors are more increased in the homeless group, es-pecially homeless males, than in general population. The study is congruent with European Platform Against Poverty. The results may be applied in preventive pro- grams, reduction of social inequalities.

Acknowledgement/Funding: The grand of Ministry of Science and Higher Edu- cation, Poland

P1694 | BEDSIDE
Echocardiography examination-related metabolic abnormalities in new university students: cross-sectional and follow-up analyses
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Background: 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.

Objective: We assessed whether the Ronin-samurai period before entering uni- versity has detrimental metabolic effects in new university students.

Methods: The cross-sectional study of 1,777 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<0.0001), systolic blood pressure (123.5±12.1 vs. 121.2±11.7 mmHg; p=0.0013), total cholesterol levels

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Periodontitis as an independent predictor of cardiovascular outcome: a longitudinal population-based study

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Background: Periodontal disease is an independent risk factor of coronary heart disease but the data on objective findings of periodontitis and outcome in large cohort study is limited. We investigate the association of the clinical parameters of periodontitis and long-term outcomes in Thai population.

Methods: Data were obtained from the Thai Heart Study, a population of Thai people aged 40–69 years, and were followed for a mean of 13 years (SD 4). Clinical periodontal examination was performed to evaluate periodontal parameters (pocket depth (PD), clinical attachment level (CAL), and tooth loss) in 1631 participants. Participants 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 ≥ 3mm. After multivariable adjustment for risk factors, there was association between and increase in PD and increase in risk of total outcome (HR 1.24 [95% CI 1.031–1.490], p 0.002). Stratified by level of education, those with low education (LE) and PD more than 3mm had the highest event rate (27%) followed by LE and PD less than 3mm (15.3%), high education (HE) and PD more than 3mm (12.3%) and HE and PD less than 3mm (9.4%) (p=0.001, log-rank test) (Fig. 1).

Conclusion: Periodontitis is associated with long-term cardiovascular events especially in the subgroup with low education, independent of other conventional risk factors for cardiovascular outcomes. Public policy to improve oral hygiene in those disadvantages should be advocated.

P1695 | BEDSIDE

Marker of periodontitis as an independent predictor of cardiovascular outcome: a longitudinal population-based study

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Conclusion: Periodontitis is associated with long-term cardiovascular events especially in the subgroup with low education, independent of other conventional risk factors for cardiovascular outcomes. Public policy to improve oral hygiene in those disadvantages should be advocated.

EFFECT OF DIFFERENT RISK FACTORS ON THE CARDIOVASCULAR SYSTEM

P1696 | BEDSIDE

Identifying familial hypercholesterolemia from registries of patients with acute myocardial infarction: an algorithm-based approach

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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 included in FAST-MI during a one-month period in 223 institutions at the end of 2005 and 213 institutions at the end of 2010, and in 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 statin 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, 1.1% 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.

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Post-prandial remnant-like particles formation in abetalipoproteinemia: prediction of the effectiveness of microsomal triglyceride transfer protein inhibitor on post-prandial remnant-like particles

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Background: Abetalipoproteinemia (ABL) is an extremely rare autosomal recessive disorder, characterized by almost complete absence of apoB-containing lipoproteins. This disorder 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 homozygous familial hypercholesterolemia (FH) which exhibit resistant to statins. However, few data exist regarding the effectiveness of MTP inhibitor to reduce post-prandial accumulation of remnant-like particles (RLP) fraction which has been shown to be related with elevated cardiovascular risk. Thus, we assessed the hypothesis that MTP inhibitor contributes 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: ORFF cream (Jomo Shokuhin, Takasaki, Japan) 50 g was given per body surface area (m²), blood sampling was performed at 2 hour intervals up to 6 hour. Plasma lipoprotein and RLP fraction were determined by HPLC system in one ABL subject (age 49yr, LDL-C=1mg/dl), four heterozygous FH subjects (mean age=61±17yr, mean LDL-C=240.5±26.3mg/dl), and four controls (mean age=58±17.2yr, mean LDL-C=87.5±15.8mg/dl). Plasma lipoprotein and RLP fraction were determined by HPLC system. The area under curve (AUC) of TG, RLP-TG, and RLP-C 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 that of controls (43±15.3mg/dl × hour vs 16±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 that of LDL-C.

Random blood glucose and incidence of cardiovascular disease among adults without diabetes: findings of the China Kadoorie Biobank

P1701 | BEDSIDE

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Background and introduction: LDL-cholesterol (LDL-C) reduction effectively reduces risk of coronary artery disease (CAD). 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 CAD risk without causing glycosuria.

Method: We used published genome data from genome-wide association studies (GWAS) including: Global Lipids Genetics Consortium (GLGC); Meta-Analyses of Glucose and Insulin-related traits Consortium (Mage); DIAbetes Genetics Replication and Meta-analysis (DGRAM) 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 one 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)
Effect of different risk factors on the cardiovascular system

and LDL-C/CAD-associated SNPs showed consistent effect directions (binomial P=4.93x10−21). A 1-SD higher LDL-cholesterol was protective of T2D (OR 0.88; 95% CI: 0.81, 0.91), however, LDL-C/T2D-associated SNPs did not show consistent effect directions (binomial P=0.08). PCSK9, APOB, LPA, CETP, PLG and ALDH2 were identified as druggable loci that alter LDL-C and CAD risk without causally determining drugs (MFAT targeting these gene products may reduce CAD risk without increasing T2D risk.

Conclusions: We identified several potential therapeutic targets that influence LDL-C and CAD that do not alter glycemic burden. Ongoing trials of drugs that target these loci are under way, and further validation in clinical trials is needed.

Acknowledgement/Funding: Netherlands Heart Foundation, EU-funded Integrated Project CVgenes@Target

P1703 | SPOTLIGHT
Determinants of 3-year mortality after an acute coronary syndrome - the French population MONICA registry
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Background: Determinants of short-term mortality (28-day mortality) after acute coronary syndrome (ACS) are relatively well known. However, those for middle-term mortality (3 to 5 years) aren’t clearly established.

Purpose: The aim of our study was to describe 28-day mortality in patients hospitalized for ACS (STEMI and NSTEMI) in comparison with the middle-term mortality of patients with ACS.

Methods: All ACS events in defined populations were ascertained and validated according to the same protocol and uniform criteria. This study was based on data from 6812 people aged 35–74 years hospitalized for a first or a recurrent ACS, registered in the MONICA registry between 2009 and 2011 in Alsace.

Three categories of ACS were defined: (ST+), ACS with ST elevation at ECG; (ST–Enz+), ACS with no ST elevation plus significant cardiac enzyme elevation; (ST–Enz–), ACS with no ST elevation and no enzyme elevation.

Results: The mean of follow up was 3.3±1.1 years with a maximum of 5 years. In all there were 2441 (35.8%) ACS with (ST+), 1548 (22.7%) ACS with (ST–Enz+) and 2824 (41.4%) patients with (ST–Enz–).

The percentage of men was 78.0% (5339) and 31.1% of patients had previous history of ischemic heart disease.

The 28-day mortality rate (number of deaths =760) was 11.2% [9.8–13.4] and the middle-term mortality (number of deaths =576) rate was 9.5% [7.1–11.9].

The risk of death at 28-days was (OR [95% CI]) 0.67 [0.51–0.88] for (ST–Enz+) and 2.74 [2.29–3.28] for (ST–Enz–) in comparison with (ST+).

After multivariate adjustments; region, gender, age, history of IHD and complications at hospital admission (cardiac shock, cardiac arrest, edema, dyspnea) odds ratios remained significant; 0.70 [0.5–0.88] for (ST–Enz+) and 3.56 [2.8–4.54] for (ST–Enz–) respectively.

In patients who survived after 28 days (n=6052), the middle-term risk of death was after multivariate adjustments; (HR [95% CI]) 1.42 [1.15–1.77] in (ST–Enz+) in comparison to (ST+) and 1.07 [0.86–1.32] in (ST–Enz–).

Conclusions: For STEMI patients risk of death was higher at 28 day and lower when compared with non-ST elevation myocardial infarction. These patterns were inverse for NSTEMI (ST–Enz+) patients. In the early years following ACS, mortality rate was significantly lower; 0.70 [0.5–0.88] in (ST–Enz+) and 1.07 [0.86–1.32] in (ST–Enz–).

In patients who survived after 28 days (n=6052), the middle-term risk of death was significantly lower; 0.70 [0.5–0.88] in (ST–Enz+) and 3.56 [2.8–4.54] in (ST–Enz–).

P1704 | BEDSIDE
Whole exome sequencing in familial hypobetalipoproteinemia
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Background: Whole exome sequencing (WES) has shown >30% success in the diagnosis of Mendelian disorders. Few data exists regarding clinical application of WES for the molecular diagnosis of familial hypobetalipoproteinemia (FHBL), which is characterized as extremely low LDL cholesterol level.

Methods: WES was performed on 36 individuals including 32 individuals exhibiting low LDL-C (<70 mg/dL) primarily, and 4 unaffected family members from 23 families. We filtered out the following variants: 1) Benign variants predicted by SnpEff (≤1%); 2) Missense variants with >95% sequence coverage; 3) Segregation unmatched for the affected and unaffected members in the family. We focused on the following genes: APOB, LPA, CETP, PLG, and PCSK9.

Results: We identified heterogeneous 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 mutation(s) or PCSK9 gene mutation(s) in 16 among 23 families (70%). Although such comprehensive approach is useful to determine true causative mutations, other strategies are needed to identify novel causative genes, which could potentially lead to the development of novel pharmacological target for dyslipidemia.

P1705 | BEDSIDE
Association between epidermal fat and subclinical atherosclerosis assessed by coronary computed tomographic angiography in familial hypercholesterolemia
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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 epidermal fat volume (EFV) in m3, defined as the fat volume inside the pericardial sac, with the presence and extent of subclinical atherosclerosis after adjusting for 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, glucose 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 with number of segments with plaques was found. For an increase in 10 m3 of EFV 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.

P1706 | BEDSIDE
Relationship of birth weight with body composition in young adulthood
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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/m2 were enrolled. Birth weight was assessed by self-report. Bioelectrical impedance analysis was used to assess body composition in all participants. Multivariate regression models adjusting for potential confounders were constructed to assess the relationship between birth weight and body composition during adulthood.

Results: 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 3355g (3050g; 3700g). The main results are shown in the table. Across quartiles of birth weight, there was a highly significant decrease in body composition.

Table 1

<table>
<thead>
<tr>
<th>Quartile 1</th>
<th>Quartile 2</th>
<th>Quartile 3</th>
<th>Quartile 4</th>
<th>P for trend</th>
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</thead>
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<tr>
<td>n=395</td>
<td>n=411</td>
<td>n=444</td>
<td>n=445</td>
<td></td>
</tr>
<tr>
<td>Fat mass†</td>
<td>23.4 (20.5–26.4)</td>
<td>23.2 (20.4–26.0)</td>
<td>22.8 (20.0–25.5)</td>
<td>22.7 (20.8–25.4)</td>
</tr>
<tr>
<td>SFC†</td>
<td>1.05 (0.8–1.29)</td>
<td>1.11 (0.89–1.36)</td>
<td>1.18 (0.92–1.50)</td>
<td>1.23 (0.94–1.61)</td>
</tr>
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</table>

†n=1774. 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).
P1707 | BEDSIDE
Plasma levels of serotonin as a novel biomarker for coronary microvascular dysfunction in patients with vasospastic angina
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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, 60.1±13.2 [SD] years) who underwent acetylcholine (ACh) provocation test for coronary spasm and measured their plasma levels of serotonin by high-performance liquid chromatography. CMD was defined as myocardial lactate production before the occurrence of epicardial coronary spasm during provocation test. Plasma levels of serotonin (mean±S.E.M. µmol/L) were comparable between VSA (16.2±3.7, n=145) and non-VSA (10.3±2.2, 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-IHD (non-VSA, non-CMD) groups, serotonin levels were significantly higher in VSA with CMD group (26.8±12.5, n=36) compared with VSA without CMD (12.7±2.7, n=109, P<0.05) and non-IHD (5.4±0.6, n=23, P<0.01) groups, and tended 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 discriminator 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.
P1711 | BEDSIDE

Serial changes in microvascular resistance associated with elective percutaneous coronary intervention and their relationships with lesion characteristics assessed by optical coherence tomography

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Background: The influence of elective percutaneous coronary intervention (PCI) on 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 score for the diagnosis of left ventricular hypertrophy (LVH).

Methods and results: We identified in the degree of degradation of PR between patients with and without LVH. The removal of functional stenosis of epicardial coronary arteries by PCI was associated with the reduction of microvascular resistance. Increased PR was significantly associated with greater periprocedural IMR reduction (P=0.03) and significant change at follow-up. Greater improvement of FFR values by PCI was significantly associated with greater periprocedural 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). The presence of ruptured plaque was associated with periprocedural IMR elevation (post-pro), although there was no significant relationship between periprocedural IMR change and PCI-related cardiac troponin elevations that distributed in the range of IQR of 0.19–0.83 with the median of 0.46ng/ml. As for the impact of microvascular function on clinical outcomes, higher post-PCI IMR value was associated with the incidence of target vessel revascularisation during the follow up (P=0.03).

Conclusion: The removal of functional stenosis of epicardial coronary arteries by PCI was associated with the reduction of microvascular resistance. Increased PR was significantly associated with greater periprocedural IMR reduction and significant change at follow-up. Greater improvement of FFR values by PCI was significantly associated with greater periprocedural IMR reduction and the effect of FFR improvement on the IMR reduction was maintained up to follow-up. Greater improvement of FFR values by PCI was significantly associated with greater periprocedural IMR reduction and the effect of FFR improvement on the IMR reduction was maintained up to follow-up.

P1712 | BEDSIDE

Distribution of pressure gradients along left anterior descending artery in patients with angiographically normal arteries

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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: Twenty 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 decreased in proportion to distance from the ostium (average: 0.85±0.06 at 12 cm distal to the 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).

Conclusion: Coronary pressure gradually decreases in proportion to distance from the ostium in the LAD regardless of the presence of minor atherosclerotic plaque. Our data suggests that fractional flow reserve measurement could overestimate stenosis severity in the LAD.

P1713 | BEDSIDE

Improvement of left ventricular function: an additional benefit of percutaneous revascularization for occluded coronary artery

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Background: Compared to significant stenosis without occlusions (non-CTO), chronic total occlusions (CTO) represent the more complex and challenging coronary lesions. In this echocardiographic study, we compared the impact of successful percutaneous revascularization of CTO on left ventricular (LV) function. LV global longitudinal strain (GLS) is a more sensitive measure of LV mechanics than LV ejection fraction (LVEF) in patients with chronic ischemic heart disease.

Objective: The aim of this study was to compare the impact of revascularization of CTO and non-CTO on LV function using LV GLS assessed with two-dimensional speckle-tracking echocardiography (2DSTE).

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 month after the procedure with conventional assessment including LV end diastolic and end systolic volume (LVEDV, LSVES), LVEF, ratio of early transmitral flow to diastolic contraction (E/A ratio), deceleration time (Dct), 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 Dct. GLS showed a significant improvement 9 months after in CTO group, whereas in non-CTO group GLS did not change significantly. Change of GLS 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

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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 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 <0.8, <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 cut-offs. 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 indices. Stenosis misclassification with iFR and whole cycle Pd/Pa indices were compared to the current gold standard method (FFR). The misclassi- fication 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 (p<0.001). Stress misclassification with FFR and whole cycle Pd/Pa indices were compared to the current gold standard method (FFR). The misclassi- fication 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.

Conclusion: IFR is more resistant to drift and measurement variability than whole cycle Pd/Pa by 233% and 254% respectively, when compared to the current gold standard method (FFR). The performance of indices. Stenosis misclassification with iFR and whole cycle Pd/Pa respectively. All 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 (me- dian 423 days; IQR 282–743 days), 2 patients was admitted with NSTE-ACS.

Methods: Virtual PCI was calculated for the entire coronary tree, and the functional gain of intervention using iFR with or without whole cycle Pd/Pa, making iFR a far more clinically robust tool in the catheter laboratory.

Background: Routine manual thrombus aspiration is superior to standard primary PCI (pPCI) in terms of improved myocardial per- fusion in patients with acute myocardial infarction with ST-segment elevation (STEMI). However, myocardial per- fusion after thrombus aspiration has not been assessed by an index of micro- vascular resistance (IMR) in a randomized fashion.

Methods: We performed a randomized, controlled clinical trial to evaluate impact of thrombus aspiration on microvascular resistance after pPCI in 128 patients with the first STEMI randomly assigned to thrombus aspiration or standard pPCI. Pressure drift across the range of −3mmHg to +3mmHg was compared to the first STEMI randomly assigned to thrombus aspiration or standard pPCI. Pressure drift across the range of −3mmHg to +3mmHg was compared to the first STEMI randomly assigned to thrombus aspiration or standard pPCI.

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 (p<0.001). Stress misclassification with FFR and whole cycle Pd/Pa indices were compared to the current gold standard method (FFR). The misclassi- fication 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.

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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 (FFR) 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 (180mg/80kg/mm) for 3 minutes to measure FFR (ATP-FFR). After additional intracoronary nicorandil administration (2mg/30sec) during intravenous ATP infusion, FFR measured again (NIC-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 NIC-FFR than non-LAD lesions (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 tended to have lower left ventricular mass index (LVMI) than the others (p=0.09). 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 LVMI (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.

Impact of elective percutaneous coronary intervention on coronary microvascular resistance

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Background: The influence of elective percutaneous coronary intervention (PCI) on microvascular dysfunction has 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 (79.2%), age 64±8.5y). 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 no significant relationship between delta IMR (post-pre IMR) values and PCI related cardiac troponin elevations that distributed in the range of (mean: 0.49 ng/ml, IQR 0.23–1.02 ng/ml). Periprocedural IMR decrease (Pre-Post) was inversely associated with pre-PCI FFR (P<0.009) and greater improvement of FFR values. Baseline IMR was significantly associated with lower 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, 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 angiography enduringly operated 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.

Influence of microvascular resistance on anatomical and functional severity of coronary artery stenosis

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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±0.09, 56.5±9.9 and 2.23±1.24. hMVRI was 2.0±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

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Background: Prior fractional flow reserve (FFR) measurements were performed in swine with side branches (SBMs) on the left coronary artery. 

Methods and results: 15 swine were included. The LAD was divided into 3 segments and a SBM was created in each segment. The 90% stenosis was achieved either by tightening up the SBM or by placing a 3 mm balloon into the SBM. FFR of the main branch (LAD) was measured before SBM stenosis and after SBM stenosis. Results: FFR increased from 0.82±0.18 (PRE) to 0.88±0.18 (POST) after SBM stenosis.

Conclusions: The FFR of the main branch is not affected by the stenosis of the side branch significantly over the whole range of degrees.
P1726 | BEDSIDE
Reduction of radiation exposure in diagnostic cardiac catheterization and PCI - results of a German coronary angiography and angioplasty registry
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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. Similarly were the results for percutaneous coronary interventions (PCI). The reduction of DAP was about 32%, and contrast medium consumption decreased by 37%. Fluoroscopy time was unchanged (table). Coronary multi-vessel-disease was the prominent indication for PCI with increasing complexity over the years.

Conclusion: 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)
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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=77) 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
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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. The OCT criterion for SCAD was a separation of the different layers of the arterial 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 were no statistically significant differences of overall coronary risk factors, while the prevalence of patients with more than 3 risk factors was lower in SCAD (SCAD: 11.1% vs. PR: 51.5% vs. NR: 56.6%, p<0.003). The proportion of male and female was different among the groups (Female: SCAD: 66.7% vs. PR: 20.0% vs. NR: 23.6%, p<0.001). In angiographic findings, the distribution of 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 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). Conclusion: 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.

P1729 | BEDSIDE
Follow-up reserve-guided revascularization in patients with aortic stenosis: a propensity matched analysis
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Background: FFR is widely used to invasively assess the hemodynamic significance of coronary stenoses. Yet, little is known about its role in patients with combined aortic valve disease. Here we assessed the impact of FFR measurements on the long-term outcomes of these patients.

Methods and results: From 2002 to 2010, we identified 106 patients with aortic stenosis and significant coronary artery disease in which at least 1 intermediate lesion was either revascularized with an FFR value <0.80 or deferred with FFR >0.8. Using propensity matching, we found 212 contemporary patients as comparator group in which the decision to revascularize was based on angiography only.

Clinical characteristics, AS severity and number of diseased vessels were similar between the two groups. No significant difference was found in the total number of patients revascularized (61% vs. 62%; p=0.94): although more patients in the FFR-guided group underwent PCI (23.6% vs 13.2%; p=0.019), while there was a trend towards more CABG in the angio-guided group (38.7% vs 48.6%; p=0.094). After functional assessment with FFR, number of diseased vessels was significantly downgraded within the FFR-guided group (from 1.78±1.1 to 1.41±1.1; p<0.01) and when compared to the angio-guided group (1.41±1 vs 1.75±1; p<0.01). In patients undergoing CABG, number of arterial grafts per patient was similar between the 2 groups (1.6±0.6 vs 0.75±0.57, p=0.6), while significantly less venous conduits were used in the FFR-guided group (0.5±0.69 vs 0.73±0.76; p=0.05). We found no difference in MACE up to 5 years (37.7% vs 38.7%; Log-Rank=0.0; p=0.98), all-cause death (32% vs 31%; Log-Rank=0.16; p=0.68), revas-

Conclusion: FFR-guided strategy in patients with aortic stenosis significantly downgraded the number of diseased vessels per patient resulting in more PCIs performed. In the FFR-guided group undergoing surgery, significantly less venous grafts were implanted, yet this did not result into higher event rates during 5 years of follow-up.
Features of coronary artery disease in 2776 type 1 diabetes patients undergoing coronary angiography

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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 (atherosclerosis/stenosis <50%), one-, two-, and three- vessel 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 (NSTEMI;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

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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 remained 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 plus OCT guided PCI were performed in 222 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±706.9mGy, 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

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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 1.3±0.2 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.

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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
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 assessed 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 were presented with a higher frequency of calcium and fibrous plaque compared to PR.

<table>
<thead>
<tr>
<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>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>
</tr>
<tr>
<td>Calcium plaque</td>
<td>11 (100%)</td>
<td>8 (88.9%)</td>
<td>11 (44%)</td>
<td>p&lt;0.001</td>
<td>p=0.06</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>
</tr>
<tr>
<td>Lipid arc</td>
<td>142.0±34.7</td>
<td>151.3±21.1</td>
<td>188.4±32.6</td>
<td>p=0.007</td>
<td>ns</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>
</tr>
<tr>
<td>FCT</td>
<td>53.4±10.4</td>
<td>52.5±10.4</td>
<td>51.4±8.8</td>
<td>p=0.01</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>
</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>
</tr>
</tbody>
</table>

Conclusions: OCT is a valuable intraocular 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 PE are associated with calcified and fibrous plaques, respectively. These lumen pathologic 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. Sagawa1, H. Ohtani1, Y. Yamaami1, K. Kojima1, Y. Sagawa1, H. Ohtani1, Y. Ohtani1, T. Sugiyama1, S. Kimura1, Y. Yamakami1, K. Kojima1, Y. Sagawa1, H. Ohtani1, Y. Ohtani1.

Conclusions: The prevalence of OCT verified CN was 5.3%. No differences were observed between CN and non-CN groups including patient characteristics and prognosis.

P1736 | 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. Sagawa1, H. Ohtani1, Y. Yamaami1, K. Kojima1, Y. Sagawa1, H. Ohtani1, Y. Ohtani1.

Conclusions: 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 during percutaneous coronary intervention on 9-month follow-up outcomes
T. Sugiyama1, S. Kimura1, Y. Yamakami1, K. Kojima1, Y. Sagawa1, H. Ohtani1, Y. Yamaami1, K. Kojima1, Y. Sagawa1, H. Ohtani1, Y. Ohtani1.

Conclusions: The prevalence of OCT verified CN was 5.3%. No differences were observed between CN and non-CN groups including patient characteristics and prognosis.
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
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**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 61–90% 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
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**Background:** Fractional flow reserve (FFR) is a lesion-specific, 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 ~6% to 7%.

**Conclusions:** Calculation of FFR values from the coronary angiogram only, without the need of a pressure guide wire nor of any hyperemic stimulus, could have immense advantages in daily clinical practice. Our image-based FFR technology can detect the coronary physiology for ‘real-time’ diagnostic. This technology may reduce time and cost of the coronary diagnosis, enabling a comprehensive decision support system for the physician.
337 patients into this meta-analysis. When all the trials were pooled, the overall correlation between FFR and OCT-MLD was 0.607, between FFR and OCT-MLA was 0.604 and between FFR and OCT-AS was −0.480. Pooled sensitivity of OCT-MLD was 0.65 (95% CI 0.58–0.70) and pooled specificity of OCT-MLD was 0.79 (95% CI 0.74–0.84) and pooled sensitivity of OCT-MLA was 0.78 (95% CI 0.74–0.84) and pooled specificity of OCT-AS was 0.61 (95% CI 0.53–0.68) and pooled specificity of OCT-AS was 0.74 (95% CI 0.65–0.81) to predict significant FFR.

Conclusions: This meta-analysis, we found modest diagnostic accuracy for MLA, poor diagnostic accuracy for MLD and AS. Moreover, assessment of intermediate lesion by OCT MLA may become possible in up to 20% of the lesions.

P1740 | BEDSIDE
Angioscopic comparison of coronary artery healing process through a decade after implantation of sirolimus-eluting stents and bare metal stents

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Aim: The aim of this study was angioscopic comparison of vascular healing process (VHP) through a decade after implantation of sirolimus-eluting stents (SES) and bare metal stents (BMS).

Methods: We enrolled 55 stented segments in 32 patients with ischemic disease (37 SES and 18 BMS). The elapsed years after stenting ranged from 3 to 10 years. The segments were divided into two groups on the basis of elapsed years: the mid-term (5–elapsed years >3 years; 24 SES and 9 BMS) and the long-term segments (10–elapsed years >5 years; 13 SES and 9 BMS). Coronary angiography revealed neointimal coverage grade (NGC), presence of yellow plaque (YP), and in-stent mural thrombi (ISMT). NGC was classified into 4 grades (grade 0, no coverage on stent struts; grade 1, coverage with thin transparent neointima; grade 2, coverage with thick opaque neointima; grade 3, stent struts invisible and fully embedded into thick neointima).

Results: NGC of SES was 3.0 at mid-term and 2.3±0.87 at long-term, indicating that full coverage at mid-term regressed at long-term. NGC of SES was 1.36±0.56 at mid-term and 1.54±1.19 at long-term, indicating the still incomplete coverage even at long-term. Frequency of YP in SES was 25% at mid-term and 23% at long-term, whereas in BMS was 11% at mid-term and none at long-term. Frequency of ISMT in SES was 13% at mid-term and 23% at long-term, whereas in BMS was none at all through a decade.

Conclusion: Vascular healing process after SES implantation remains incomplete through a decade, characterized by low NGC, YP, and ISMT.

P1741 | BEDSIDE
Association between necrotic plaque volume measured by iMAP and post procedural high sense troponin-T level elevation in patients underwent 2nd generation drug eluting stents implantation

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Background: IMAP is a tissue characterization analysis system using the 40-MHz intravascular ultrasound (IVUS). Previous studies demonstrated that plaque morphology measured by other IVUS imaging modalities were associated with elevation in levels of cardiac biomarkers after percutaneous coronary intervention (PCI). However, few data using IMAP have been reported.

Methods: From April 2013 to September 2014, 102 consecutive patients with stable angina or silent coronary ischemia who underwent 2nd generation drug eluting stents implantation were enrolled. We traced the external elastic mem- brane cross-sectional area (CSA) in OCT MLA every 1-mm axial intervals with the target lesion. Volume of each plaque component (fibrotic, lipidic, necrotic and calcified) was evaluated by IMAP analysis software. High sense troponin T (hs-TnT) was measured before and 24 hours after PCI, and increase level of hs-TnT was defined as hs-TnT. Patients were divided into three groups in accordance with tertile of hs-TnT. (Group1: hs-TnT < 0.02 Group2: 0.02 ≤ hs-TnT < 0.07 Group3: hs-TnT ≥ 0.07)

Results: There was no significantly difference in patient characteristics between the three groups. In IMAP-IVUS analysis, Necrotic plaque volume was significantly higher in group2 (P<0.001). In simple regression analysis, total stent length, lesion plaque area, remodeling index, total plaque volume, lipid plaque volume and necrotic plaque volume of target lesion were significantly correlated with hs-TnT. The necrotic plaque volume was independently correlated with Δhs-TnT in multiple regression analysis (p<0.0001).

P1742 | BEDSIDE
Distinct histopathological features of calcified nodule in coronary artery calcified nodule (CN) and calcified stenotic plaques (CSP) through a decade after implantation of sirolimus-eluting stents (SES) and bare metal stents (BMS)

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Background: Underlying mechanisms contributing to acute coronary syndrome (ACS) are plaque rupture and erosion. However, calcified nodule (CN) also has potential to develop ACS. Although there are several hypotheses for development of CN, pathogenesis of CN is not well established.

Methods: Thirty eight sections, from 7 CN lesions obtained by autopsy were submitted to this study. One CN was the culprit lesion of ACS. Immunohistochemistry for CN lesions obtained by autopsy was performed.

Results: Gross morphology of CN showed protruding mass into the lumen with irregular surface. ACS-induced CN developed fibrin thrombi over the nodule with erosion of luminal surface. Although all CNs of non-ACS lesion demonstrated extremely thin fibrous tissue over the nodule, CN1 immunohistochemistry revealed complete endothelial cell coverage. Massive fibrin deposition within the nodule was identified by Masson’s trichrome and immunohistochemistry in all sections. Myxomatous matrix with neovascularisation was observed beside calcification. Furthermore, we identified distribution of decorin, biglycan, versican and hyaluronan, was examined.

Conclusions: Distinct histopathological features of calcified nodule in coronary artery calcified nodule (CN) and calcified stenotic plaques (CSP) through a decade after implantation of sirolimus-eluting stents (SES) and bare metal stents (BMS).
P1748 | BEDSIDE
Gender independent factor in atherosclerotic plaque characteristics

Background: There were 24 lesions (18 patients) and 8 ISR analyzed (8 patients) by OCT. De novo SVG lesions and in-stent restenosis of SVG in daily clinical basics.

Methods: 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: Results: Women had a significantly lower plaque burden than men (36.9 ± 39.5%, p=0.014). The median LCBI was also significantly lower (p=0.011) in women (30.0 [inter-quartile range 9 to 64]) than in men (48.1 [21.1 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<0.001). 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. Rodecker1, E. Pociask2, W. Wanaha1, P. Gasior1, G. Smolka1, M. Skowierski1, D. Dudek1, A. Ochala1, Z. Gasior1, W. Wojakowski1, 1Medical University of Silesia, Katowice, Poland; 2Jagiellonian University Medical College, Krakow, Poland

Aim: The accelerated atherosclerosis that occurs in saphenous coronary grafts (SVG) develops much faster as compared to native coronary arteries. The following OCTOPUS registry was aimed to present the SVG lesions’ morphology in de novo lesions and in-stent restenosis of SVG in daily clinical basics.

Results: The SVG lesions’ morphology of SVG was presented by intravascular optical coherence tomography (OCT) in patients post coronary artery bypass grafting (CABG) and referred for angiography due to recurrence of stable angina symptoms. OCT was performed in ISR and de novo lesions of SVG following its detection by angiography. The OCT analysis securitized every lesion to assess minimal lumen area (MLA), plaque’s morphology, and apposition and coverage of stent struts by neointima in ISR. OCT was able to detect tissue friability, lipid-rich and calcified plaques in de novo lesions of SVG, and lipid-rich and heterogeneous tissue in ISR of SVG. In addition, the thickness of the fibrous cap covering the lipid-rich core, plaque rupture, tissue friability and thrombus presence was recorded during OCT analysis.

Conclusion: There were 24 lesions (18 patients) and 8 ISR analyzed (8 patients) by OCT. De novo SVG lesions of SVG occurred later as compared to ISR in SVG (131±63 vs. 23±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=0.012]. Calcifications 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 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 area [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 55–85), p=0.53]. Plaque rupture was present in 1 (12.5%) of ISR and 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 (17%) 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<0.002). 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 x URL) 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
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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 stable 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 ≥70% 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=0.04). FFR demonstrated significant stenosis of the LAD in 52%, compared with 24% in non-LAD lesions (p=0.42). Mismatch was observed in 14% 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 (95% confidence interval 1.02–1.11).

Conclusion: Non-LAD lesions and increasing age are predictors of overestimation of the 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
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Background: Transradial coronary angiography (TRA) has been growing worldwide. However, upper limb vessels are thinner, may present with arterial tortuosity, adverse bifurcations and arterial spasms while the brachiocephalic trunk shows a remarkable variation. Such possible vascular obstacles led to the adoption of the one-catheter (cath) -concept for TRA. Allowing for one less catheter change, we investigated the feasibility, safety, clinical outcomes and angiographic results of a prospective, randomized comparison using optical coherence tomography (OCT).

Methods: We identified 2954 patients (pts) scheduled for TRA (Figure) in center Isala Hospital in Zwolle, Netherlands.

Results: The relevant cohort consisted of n=852. The tested cath presented significant stenosis in 306 lesions, i.e., 4.76% of the whole cohort. Of all 306 lesions, 168 were considered significant in 29%, compared to 53% of the non-LAD lesions (p=0.001) as well as strut count normalised to diameter (11.5 vs. 9.1; p=0.008) were higher in LASM than in the ZES group compared to EES and BES (strut count per frame 11.4±0.86 vs. 9.1±0.77; p=0.001). Further, rate of OCT-plaque rupture on LASM (6 vs. 23; p=0.299) and incidence of acute strut malapposition (6 vs. 23; p=0.299) were significantly higher in LASM at 12 month follow up. Both groups did not differ in terms of struts per frame (11.9 vs. 9.9; p=0.001) or strut count normalised to diameter (11.5 ± 9.1 vs. μ=9.1; p=0.001), smaller lipid-arc (302±67°; 243±111°; p<0.001), and lower plaque area on IVUS (0.001), smaller plaque area on IVUS (0.001; strut count normalised to diameter: 11.69 vs. 9.11; μ=7.4; p=0.001).

Conclusion: Stent strut density appeared higher in LASM than in 12 month. Stent architectures with higher strut density may induce a higher incidence of LASM after 12 month.

P1752 | BEDSIDE
Density of stent struts is a risk factor for late acquired stent malapposition in second generation drug eluting stents - a prospective, randomized comparison using optical coherence tomography
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Background: Late acquired stent malapposition (LASM) is associated with a higher incidence of (very) late stent thrombosis. The impact of the stent scaffold’s architecture itself – particularly in respect of stent strut density – on the incidence of LASM is not clarified today.

Methods: Fifty patients with 59 lesions of interest were randomised to elective treatment with either Everolimus-eluting stents (EES; n=17, 20 lesions), Zotarolimus-eluting stents (ZES; n=15, 19 lesions) or Biolimus-eluting stents (BES; n=18, 20 lesions) and underwent optical coherence tomography (OCT) at 30 day post-implantation respectively after one year. Cross-sectional OCT images (frames) were analysed at 1-mm intervals for strut count and incidence of malapposed stent struts.

Results: Stent strut density determined by strut count per frame (11.9 vs. 8.6; p=0.001) as well as strut count normalised to diameter (11.5 vs. 9.1; p=0.008) were significantly higher in stents with LASM at 12 month follow up. Both groups did not distinguish in terms of basic stent parameters as length and diameter ("LASM" vs. "no LASM": 27.1 ± 22.4mm; p=0.09 respectively). Clinical and angiographic follow-up after 12 month will allow to clarify whether stent strut density is a risk factor for LASM.

Conclusion: Late acquired stent strut malapposition in second generation drug eluting stents - a prospective, randomized comparison using optical coherence tomography

Acknowledgement/Funding: NA
25.5%; 6.5%, p < 0.001) than ACS with EA, but no significant differences compared to ACS with non-EA. SAP lesions with EA had similar minimum lumen area (ACS-EA 2.4±1.0mm²; ACS-non-EA 2.4±0.9mm²; SAP-EA 2.3±0.9mm²; SAP-non-EA 2.5±0.8mm²) and remodeling-index (1.20±0.31; 1.10±0.19; 1.18±0.29; 0.99±0.22) compared to ACS with and without EA. OCT-thrombus was more frequently observed 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 morphologies, 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
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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 late gadolinium enhancement (LGE) 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). Patients with SSc 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 insertion points 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
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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-existent 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: At a postoperative median of 14 days from operation, 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 3 of 31 (10%) patients (RR 3.2, 95% CI 1.1–9.5), respectively. 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 MIs showed cardiac edema and no 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. Additionally, 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 phase 3 trials
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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 (-66.5%, -62.7% 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 (hazard ratio [HR], 2.03; 95% confidence interval [CI], 0.88–4.68, p=0.10) or car-
the OMT group and PCI group in the rate of MACE (10.1% vs. 16.9%, adjusted
(10.9%) of the OMT group versus 41 patients (14.2%) of the PCI group (p=0.38).

Purpose: To compare clinical outcomes of percutaneous coronary interven-
(PCI) with those of optimal medical therapy (OMT) alone in patients with chronic total occlusion (CTO) of a single coronary artery. Limited data are avail-
able on the efficacy of OMT for the treatment of single- vessel CTO.

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 pa-
tients into the OMT group (n=147) and the PCI group (n=288) according to ini-
tial treatment strategy. One-to-many (1:N) propensity score matching with non-
fixed matching ratio was also performed. The primary outcome measured was
major adverse cardiac events (MACE) including cardiac death, myocardial infarc-
tion, and repeated coronary revascularization. The median follow-up duration was 47.6 (interquartile range: 22.9 to 68.9) months. MACE occurred in 16 patients (10.9%) of the OMT group versus 41 patients (14.2%) of the PCI group (p=0.38).

Conclusion: 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.

P1759 | BEDSIDE
Impact of ascorbic acid on post-cardiothoracic surgery atrial fibrillation and length of stay: a meta-analysis of randomized controlled trials

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Background: While the etiology of post-cardiothoracic (CTS) atrial fibrillation (AF) is likely multifactorial, inflammatory and oxidative stress likely play pivotal roles. The prophylactic use of therapies with antioxidant properties, such as ascorbic acid, presents an intriguing option to improve postoperative outcomes.

Purpose: We performed a systematic review and meta-analysis of published ran-
domized controlled trials (RCTs) evaluating the impact of prophylactic ascorbic acid on post-CTS AF, intensive care unit (ICU) length of stay (LOS) and total hos-
pital LOS.

Methods: We searched Medline, SCOPUS and the Cochrane Central Register of Controlled Trials from inception through January 2015 for RCTs comparing ascorbic acid versus placebo in patients undergoing CTS. Outcomes were pooled using a random-effects model producing either odds ratios (OR) or mean differ-
ences (MD) and 95% confidence intervals (CI). We carried out cumulative meta-
analysis based on date of publication to detect temporal trends in effect and to assess whether further RCTs are likely to change overall conclusions.

Results: Eight RCTs, including 955 participants, were included. One study in-
cluded coronary artery bypass grafting (CABG) and/or valve surgery, with the remainder being CABG only. Two studies used intravenous ascorbic acid with the remainder using an oral formulation. Post-operative beta-blocker use ranged from 70 to 100% across studies. Use of prophylactic ascorbic acid resulted in a signif-
ificant reduction in post-CTS AF (OR 0.42, 95% CI 0.27 to 0.65), ICU LOS (MD
–0.38, 95% CI –0.53 to –0.24) and total hospital LOS (MD –1.12, 95% CI –1.84 to –0.39). Cumulative meta-analysis showed that reliable evidence supporting ascorbic acid efficacy stabilized with inclusion of the three 2014 RCTs.

Conclusions: Ascorbic acid appears to reduce the incidence of post-CTS AF and shorten ICU and total hospital LOS. Following the publication on 3 RCTs in 2014, cumulative meta-analysis suggests future RCTs are unlikely to alter these conclusions.

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P1760 | SPOTLIGHT
Predictors of cardiovascular events from the 2-year follow-up data in patients with peripheral arterial disease treated with antiplatelet agents

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Background: The overall rate of cardiovascular (CV) events in patients with pe-
ripheral arterial disease (PAD) under treatment with antiplatelet agents has not been fully investigated.

Purpose: Prospective surveillance of cardiovascular events in anti-platelet-
treated arteriosclerosis obliterans patients in Japan (SEASON [UMIN00003385]) is an observational multi-center study. The purpose of the present anal-
ysis was to explore CV events of Japanese PAD patients in two years follow-
up.

Methods: Main outcome measures were rates of composite CV events of cere-
brovascular, cardiovascular and peripheral vascular events. SEASON registry en-
rrolled 11,375 patients in 1,745 institutions. Two analysis populations were de-
fined, real world population (RWP, N=10,322) and definite PAD/arteriosclerosis obliterans population (DPP, N=3,992) who had ankle-brachial pressure index (ABI) <0.9 and intermittent claudication, or history of lower limb revasculariza-
tion. All the events were certificated by the Efficacy Endpoint Review Committee.

Results: The composite CV event rates were 3.3/100 patients-years for RWP and
5.8 for DPP, respectively. Cerebrovascular, cardiovascular and peripheral vascular events were 1.6, 2.1 and 2.2 for DPP respectively. In DPP severer Fontaine
class, current smoker, diabetes mellitus and chronic kidney disease (CKD) were statistically associated with the CV event occurrences. Most frequent events were cerebral infarction as cerebrovascular, heart failure as cardiovascular and ampu-
tation as peripheral vascular events.

Conclusions: Severer Fontaine class, current smoker, diabetes mellitus and CKD were significant predictors of CV events in the PAD patients under anti-
platelet therapies.

Acknowledgement/Funding: The study was supported by Mitsubishi Tanabe Pharma Corporation.
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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

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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 high 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 long-term patient study, and possibly a one-quarter-year, subcutaneous dosing regimen in the clinic. Given the flexibility to our product dose, NHP data have translated very reliably to humans 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 clinical trial 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≥100mg/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

Background: Mortality and disability following ischemic stroke (IS) remains unacceptable 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.

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 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.

Results: 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 <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 1 than in group 2 (p=0.004). Log-Rank test showed that MANE-free rate was higher in group 2 than group 1 (p=0.007). 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-atral asynchrony in patients with systolic and diastolic heart failure

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Objectives: Heart failure (HF) can lead to electrical and structural remodeling of the heart. It is associated with reduced induction and triggering of atrial fibrillation (A-fib). We aim to evaluate the intra- and inter-atral synchrony using tissue Doppler imaging in patients with systolic (left ventricular ejection fraction <50%) and diastolic heart failure (left ventricular ejection fraction >50%).

Methods: 120 patients with HF (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. Intr-atrial synchronicity was defined as the differences between P-IAS and P-RA (RA synchronicity), and between P-LA and P-IAS (LA synchronicity). Inter-atrial synchronicity was defined as the difference between P-LA and P-RA.

Results: The time intervals of P-IAS and P-LA 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

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<th>Normal controls (n=50)</th>
<th>Diastolic HF (n=25)</th>
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<tr>
<td>LVFE (%)</td>
<td>71.5±6.84</td>
<td>60.1±7.75</td>
<td>27.8±10.04</td>
</tr>
<tr>
<td>P-IAS (ms)</td>
<td>44.3±13.54</td>
<td>50.9±9.21</td>
<td>73.9±22.85</td>
</tr>
<tr>
<td>P-LA (ms)</td>
<td>64.8±17.51</td>
<td>75.0±6.93</td>
<td>84.7±22.06</td>
</tr>
<tr>
<td>P-RA (ms)</td>
<td>51.6±13.58</td>
<td>47.4±15.58</td>
<td>60.1±21.96</td>
</tr>
<tr>
<td>LA synchronicity</td>
<td>20.9±9.23</td>
<td>16.1±2.19</td>
<td>10.8±2.31</td>
</tr>
<tr>
<td>RA synchronicity</td>
<td>1.7±3.2±17</td>
<td>13.1±3.19</td>
<td>17.1±7.16</td>
</tr>
<tr>
<td>Inter-atrial</td>
<td>22.7±2.07</td>
<td>28.0±3±19</td>
<td>29.9±19.57</td>
</tr>
<tr>
<td>synchronicity</td>
<td>&lt;0.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Results: In patients with diastolic HF, there was a time delay on left atrial septal and lateral wall, but no changes on right atrial free wall, and only RA asynchrony was observed. In patients with systolic HF, both intra- and inter-atrial asynchrony 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
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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) study was 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=592).

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 78.8±13.9 bpm and 69.1% of the patients had a resting HR > 70 bpm. Mean resting HR was found to be 78.9±13.6 bpm in those in the lowest tertile, 78.6±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 as compared to the highest tertile LVEF (Mann-Whitney, p<0.043). Mean HR was significantly higher in the second tertile LVEF 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).
**P1765 | BEDSIDE**

Endothelium-enriched microRNAs predict the presence of cardiac allograft vasculopathy


**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 dysfunctions 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 of the AL patients and 1 patient (14%) of the TTR group were women, mean age 54±8ys. 80% of the 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, respectively; there were no significant differences with survival of other HT patients (83% 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.

**P1767 | BEDSIDE**

Novel PCR method for early detection of Chagas reactivation after heart transplantation in Chagas disease

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**Background:** Heart transplantation (HTx) for Chagas cardiomyopathy (ChC) is a usual procedure; however, reactivation (Ra) of Chagas disease is a frequent complication. The sensitivity of parasitological methods is low; therefore, methods that are more sensitive needed for the early detection of Ra episodes.

**Objective:** To evaluate the prevalence of Ra and the usefulness of the PCR for early detection of chagasic cardiac disease.

**Material and methods:** Since 1992, 435 patients (p) underwent HTx at a single institution. Of them, 29 p had ChC. Endomyocardial biopsies were scheduled and performed to monitor acute rejection. At the same time, parasitemia was determined using Strout method, and three different PCR methods were performed to determine qualitative and quantitative DNA Trypanosoma cruzi. One method amplifies the minicircle variable region of the kinetoplastid genome; another method applied amplification of the intergenic spacer of the spliced leader genes, and the third one is based on an analytical performance of a multiplex PCR assay using TaqMan probes for quantification of Trypanosoma cruzi satellite DNA in blood samples. The immunosuppression was calcineurin inhibitors, azathioprine (AZA) or mycophenolate mofetil (MMF) and steroids. The p did not receive prophylactic benznidazole.

**Results:** Two out of 29 (7%) ChC HTx recipients died in the perioperative period due to sepsis and primary graft failure and 11 p (40.7%) presented 12 Ra during follow-up: 8 p had skin lesions and 3 p had Chagas myocarditis and a p had streptococcal endocarditis. The median time from HTx to clinical Ra was 87 days (38–407). The median time from positive PCR test to clinical Ra was 59 days (38–85), 28 days before the symptoms onset. Positive Strout was observed at the same time of clinical manifestations except in 1 p. Acute rejection (AR) grade ≥2R was observed in 9/11 p with Ra vs. 9/18 p without Ra (rejection rate: 2.2 vs 0.8 respectively). All episodes of AR were treated with steroids pulse, and the Ra episodes were successfully treated with benznidazole. Strout/PCR results became negative after Ra treatment. During long-term follow-up, 7 p died due to: 3 p refractory rejection, 2 p sepsis and 1 p in a car collision and 1 acute abdomen. There was no mortality due to Ra.

**Conclusions:** Ra was observed in 41% of CHC HTx recipients in this series. Ra diagnosis by PCR was done earlier as compared to Strout results, showing that the former technique is more sensitive than direct microscopic observation.

**P1768 | BEDSIDE**

Two-dimensional speckle tracking echocardiography in heart transplant patients: mid-term follow-up of right and left ventricular function

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**Background:** Evolution of left and right ventricular (LV and RV) function after heart transplantation (HT) has not been well described. Our objective was to characterize the normal evolution of echocardiographic parameters of both ventricles along the first two years after HT.

**Methods:** We followed 28 HT recipients with serial echocardiograms for 2 years. Echocardiograms with AR ≥2R were excluded. LV global longitudinal strain (LV GLS) was analyzed by speckle tracking in 12 LV segments in 4 and 2 chamber views, and RV global longitudinal strain (RV GLS) was measured in 4 chamber view. Control group included 25 healthy volunteers.

**Results:** Even though LVEF was preserved, LV GLS was reduced in the early post-HT period (~17.5±3.3% in HT vs. ~20.4±3.2% in controls, p=0.03), improving progressively until its complete normalization two years after HT (~17.3±3.8% vs ~20.4±3.2%, p=0.70). TAPSE was improved in the early post-HT period and increased progressively (12.3±2.7 mm at baseline vs 18.7±4.1 mm at 2 years, p=0.001). RV GLS rose during follow-up as well (~17.2±3.8% at baseline vs 23.0±3.7 at 2 years, p=0.001), reaching normal values one year after HT (table).

<table>
<thead>
<tr>
<th>Evaluation of left and right ventricle</th>
<th>Controls</th>
<th>Basal</th>
<th>3 months</th>
<th>6 months</th>
<th>1 year</th>
<th>2 years</th>
<th>ANOVA of the trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEF</td>
<td>62.4±5.4</td>
<td>61.8±8.1</td>
<td>62.5±7.9</td>
<td>64.8±8.4</td>
<td>63.7±7.3</td>
<td>63.2±6.4</td>
<td>0.598</td>
</tr>
<tr>
<td>LV GLS</td>
<td>~20.4±3.7</td>
<td>~17.9±3.0*</td>
<td>~17.3±3.9*</td>
<td>~17.3±3.3*</td>
<td>~17.2±3.9*</td>
<td>~17.3±3.8*</td>
<td>0.180</td>
</tr>
<tr>
<td>TAPSE</td>
<td>23.1±4.3</td>
<td>12.3±2.7*</td>
<td>14.2±3.7*</td>
<td>16.0±3.6*</td>
<td>16.3±4.2*</td>
<td>18.7±3.4*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV GLS</td>
<td>41.2±3.7</td>
<td>42.9±3.7*</td>
<td>45.0±3.8*</td>
<td>42.3±3.8*</td>
<td>41.4±3.8*</td>
<td>44.6±3.9*</td>
<td>0.040</td>
</tr>
<tr>
<td>RV TAPSE</td>
<td>~28.5±4.3</td>
<td>~17.2±3.8*</td>
<td>~17.9±4.7*</td>
<td>~18.8±4.3*</td>
<td>~21.6±5.0</td>
<td>~23.0±3.7*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Free wall</td>
<td>23.0±4.3</td>
<td>12.3±2.7*</td>
<td>14.2±3.7*</td>
<td>16.0±3.6*</td>
<td>16.3±4.2*</td>
<td>18.7±3.4*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Interventricular septum</td>
<td>21.6±3.8</td>
<td>19.3±3.3*</td>
<td>21.5±3.7*</td>
<td>22.8±3.2*</td>
<td>23.0±3.9*</td>
<td>23.3±3.8*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Controls</td>
<td>16.3±3.3</td>
<td>15.7±3.9*</td>
<td>14.7±4.1*</td>
<td>15.2±2.8*</td>
<td>17.6±5.6</td>
<td>17.3±6.4</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

LV GLS, left ventricular global longitudinal strain; RV, right ventricle; FAC, fractional area change; RV GLS, right ventricular global longitudinal strain; p <0.05; *p <0.01
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
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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, dipyridamole (0.84 mg/kg in 6', n=68) 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-ventricle disease, in 4) angiographic and hemodynamic findings at 1 month. At follow-up (median 40, interquartile ranges 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 myocardial infarction, 1 at 45 months from sepsis and 1 at 84 months from heart rejection (Figure 1).

Conclusions: 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 ed il Controllo delle Malattie

P1770 | BEDSIDE
Insulin resistance is a predictor of long term prognosis in chronic systolic heart failure
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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 ≥50 years 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, dipyridamole (0.84 mg/kg in 6', n=68) or dobutamine (up to 40 mcg/kg, n=4) SE. Results: We observed significant changes in pulse-waved Doppler parameters of left ventricle diastolic function (E/A: 1.5±0.3 vs. 1.2±0.2, p<0.001; E': 92±16.2 vs. 70.3±10.5 cm/s, p<0.001; A: 62±14.3 vs. 58.5±10.1cm/s, p ns; E-wave deceleration time: 129.8±34.2 vs. 157.8±83.6 ms, p<0.01). 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±2.8cm/s, p<0.01; e' lateral: 16.8±3.0 vs. 14.5±3.1cm/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±2 mmHg, p<0.01). Conclusion: For the first time, the echocardiography was used to detect changes in diastolic function induced by freedive 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

P1771 | BEDSIDE
Change in relaxation pattern of the left and right ventricle after freedive training
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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 freedive training on the functional parameters of the left and right ventricle.

Methods: The study group consisted of the 19 well-trained competitive freedivers (37.2±7.6 years, 2 women, 17 men). Echocardiography was performed just before and immediately after freedive 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-waved Doppler parameters of left ventricle.

Conclusion: Insulin resistance is a strong predictor of poor 12-month clinical prognosis in systolic CHF.

Acknowledgement/Funding: PRVOUK P37/03

P1772 | BENCH
Altered torsion mechanics in patients with hypertrophic cardiomyopathy: blame it on the LVOT-obstruction?

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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.

Conclusion: Insulin resistance is a predictor of poor 12-month clinical prognosis in systolic CHF.

Acknowledgement/Funding: PRVOUK P37/03
Methods: 45 consecutive patients with HCM (age 43.8±9.3yrs, 14 females, 20 with LVO- obstruction<:30mmHg, HOCM), 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 (1cm), its rate as Tor-Rate measured (%). Diastolic indices: untwisting rate (UTR) at 25% of diastole, untwisting time (UTT) measured from aortic valve closure to peak untwist. Corrected recoil rate (REC) calculated as \[\text{REC} = \frac{(\text{Twist}_{ES} - \text{Twist}_{ED})}{100}\] as a relative load-independent diastolic index.

Results: Compared with 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 HOCM cases (obstructive, 15.75±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 %, p<0.05) or that in controls (50.5±4.4%). HOCM cases had slower UTR (98.8±29.1 vs 110±28.2%, p<ns), longer UTT (195±20.3 vs 129±23.0ms, p<0.01), the onset of untwist occurred closer to aortic valve closure (90.9±3.1 vs 75.5±6.6%, p<0.001; as time normalized by length of systole). The REC diminished more in HOCM (31.0±5.9 vs 25.3±8.8 %, 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 recoll 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

Diasstolic dysfunction precedes overt systolic dysfunction in chemotheraphy-induced cardiotoxicity

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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 relationship between DD and systolic dysfunction in patients submitted to chemotherapy (QT) with anthracyclines.

Methods: Consecutive breast cancer patients undergoing QT referred for a transsthoracic echocardiogram (TTE) between August 2010 and October 2014 were included. Data was collected on baseline characteristics, TTE measurements including tissue doppler, QT regimen and adjunctive 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.

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±18.8 bpm. Baseline TTE: LVESD 46.6±7.0 mm, LVEDS 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 2.5, p=0.002, 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.

Conclusion: Standard ETT follow-up with serial LVEF evaluation may underestimate the true incidence of QT cardiotoxicity. 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.

P1775 | BENCH

Left ventricular calcium-handling proteins in the type 2 diabetic human heart with preserved ejection fraction

R.R. Lamberts1, G. Hughes1, C.T. Bussey1, P. Saxena2, I.F. Galvin2, M.K. Noye3, S. Coffey4, M.J.A. Williams3, J.C. Baldi3, P.P. Jones1 on behalf of HeartOtago, Department of Medicine – HeartOtago, Dunedin, New Zealand; 3 Dunedin School of Medicine - Dunedin Hospital, Dunedin, New Zealand; 4 John Radcliffe Hospital, Biomedical Research Centre, Oxford, United Kingdom

Impaired diastolic function is an early cardiac manifestation of type 2 diabetes and increases the risk of developing heart failure. Treatments for heart failure are limited, due to a lack of knowledge regarding its molecular pathophysiology. Recently, we showed that the right atrial (RA) myocardium from diabetic patients with coronary artery disease and preserved ejection fraction has upregulated sarcoplasmic reticulum calcium ATPase (SERCA2a) expression, despite impaired relaxation. This current study aimed to determine whether similar changes occur in the left ventricle (LV) of diabetic patients with preserved ejection fraction. Epidiural LV biopsies and RA appendages were collected from patients with preserved ejection fraction with or without type 2 diabetes mellitus (DM, n=20, non-DM, n=24) during coronary artery bypass grafting. The expression levels of the calcium-handling proteins, SERCA2a, phospholamban (PLB) were determined by Western blot, and correlated to plasma glycated haemoglobin (HbA1c) and
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). In the LV, however, the ratio did not change in the LV. Furthermore, the postoperative incidence of atrial fibration 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 protein human 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 fibration 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, Health-care Otago Charitable Trust.

P1776 | BEDSIDE
The Relationship of Intima-Media Thickness in the Brachial Artery and Endothelial Function with Left Ventricular Diastolic Dysfunction
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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 been widely 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 semiautomatic vessel wall tracking system. Although increased carotid IMT is reported to be associated with LVDD, there is limited data regarding human heart with diastolic dysfunction. 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, linear array transducer. Brachial IMT was automatically measured on a computer image 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', LVMI, and LAVI according to ASE guideline.

Results: Semiautomatic measurement of brachial IMT was feasible in all subjects. 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 group and female, respectively. Brachial IMT was related to FMD (r=-0.152; P=0.027), age (r=0.042; 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=0.215; P<0.001).

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 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 arterial stiffness and elevated left atrial pressure in patients with and without diastolic dysfunction - a subgroup analysis of Diast-CHF
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Purpose: Cystatin C has been shown to be associated with heart failure with preserved ejection fraction (HFPEF). Some experimental data suggest that an excess of cystatin C in the myocardium may contribute to alterations in the extracellular matrix. On the other hand, myocardial fibrosis has been shown to be involved in the development of diastolic dysfunction in HFPEF. Therefore, we hypothesized that increased cystatin C levels may be associated with 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 matrix metalproteinase osteopontin, and biomarkers of collagen type I synthesis (carboxy-terminal propedote 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 history of heart 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 (eGFR) and cystatin C (P<0.05). Additionally, 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 ePCWP (P<0.01), TIMP-1 (r=−0.001) and osteopontin (P<0.001) and inversely correlated with MMP-1:TIMP-1 (P<0.01), but no association was found with PICP or MMP-1. All these associations were 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<0.01) 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.

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P1779 | BEDSIDE
Prognostic impact of the left atrial function in heart failure patients with preserved ejection fraction
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Background: Heart failure patients with preserved ejection fraction (HFpEF) is...
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=0.003) 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).

Conclusion: 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

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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. Multivariate 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.

P1781 | BEDSIDE

Utility of sAxl and Lp-PLA2 biomarkers in early detection of cardiac allograft vasculopathy in heart transplantation patients

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Purpose: Cardiac allograft vasculopathy (CAV) remains one of the major limitations in long-term survival in Heart Transplantation patients (TC). Its diagnosis requires invasive methods and is often done in advanced stages of the disease.

The aim of this work is to study the utility of two biomarkers in the early detection of CAV, in particular sAxl (protein involved in vascular remodeling) and Lp-PLA2 (marker of atherosclerosis).

Methods: We studied 96 TC. We obtained peripheral blood samples to analyze sAxl and Lp-PLA2 levels at the time that the coronary angiography was done for the diagnosis of CAV. Cardiac allograft vasculopathy was classified according to the recommendations of the ISHLT.

Results: Study population included 96 patients, aged 48±15 years old, 77% male. In 45 patients the angiographic study did not show CAV (CAV0), in 27 CAV was mild (CAV1), in 5 moderate (CAV2) and in 19 severe (CAV3). We found no significant differences in Lp-PLA2 levels (p=0.8) in patients with or without CAV. In contrast, sAxl levels were significantly higher (64.7±7.3 vs. 73.3±2.0; p=0.03) in patients with CAV compared to patients without CAV (CAV0). In the logistic regression analysis aS Ax levels $>$ 74 were associated with increased risk of CAV (Odds Ratio= 2.367; 95% 1.015–5.520; p=0.04)

Conclusion: Monitoring the levels of sAxl could be useful for identifying patients with CAV development. Conversely, Lp-PLA2 levels don’t 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.

P1782 | BENCH

S100/calgranulin mediated inflammation promotes FGF23 expression in cardiac fibroblasts and LVH

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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, hBAC-S100 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.

Methods: Hearts from five groups of male mice were studied: (i) C57BL/6J with transgenic expression of a bacterial artificial chromosome containing the human S100/calgranulins (S100B09 and S10098, hBAC-S100), (ii) wild type littermates, (iii) LDLR−/− infused with saline (29 days, 0.9%), (iv) LDLR−/− infused with angiotensin (Ang) II (29 days, 1000 ng/kg/min), and (v) fibroblast specific depletion of Angiotensin 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/body weight (5.9±1.1 mg/g vs. 4.2±0.8, p=0.04), increased mRNA for hypertrophic genes (ANP, BNP, b-MHC, CTGF and Col1a1). However, there was no significant difference in FGF23 mRNA and protein between AT1aR−/− mice and wild type mice.

Conclusion: Monitoring the levels of sAxl could be useful for identifying patients with CAV development. Conversely, Lp-PLA2 levels don’t 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.

Summary: Transgenic expression of S100/calgranulins is sufficient to induce LVH in mice aged with normal renal function, and this is associated with FGF23 expression in cardiac interstitial fibroblasts. Future studies are needed to determine whether cardiac FGF23 promotes LVH in a paracrine manner. However, FGF23 does not play a role in Ang II-induced LVH.

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P1783 | BEDSIDE

Effect of alcohol intake on diastolic function: the Ethnic-Echocardiographic Heart of England Screening Study (E-ECHOES)

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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.
Purpose: To establish the relationship of alcohol intake with diastolic dysfunction, in the ethnic minority general population, in the United Kingdom.

Methods: Echocardiography 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, 84% 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 (11.7% 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 (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>Area under ROC curve</th>
<th>Confidence interval</th>
<th>Cut-off value</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<td>NT-proBNP</td>
<td>0.699</td>
<td>0.604–0.794</td>
<td>314 pg/ml</td>
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<td>56%</td>
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<td>CoL</td>
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<tr>
<td>E/E' ratio</td>
<td>0.797</td>
<td>0.716–0.878</td>
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<td>69%</td>
<td>69%</td>
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<tr>
<td>ILAV</td>
<td>0.616</td>
<td>0.510–0.719</td>
<td>33.5 m/s</td>
<td>65%</td>
<td>56%</td>
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<tr>
<td>RHR</td>
<td>0.689</td>
<td>0.591–0.786</td>
<td>75 beats/min</td>
<td>73%</td>
<td>56%</td>
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</tbody>
</table>

Conclusions: Resting heart rate could be useful in the diagnosis of pts with HTP and predictive for adverse prognosis, similar to congruent parameters.

P1785 | BEDSIDE
Heart rate as a diagnostic and prognostic marker in patients with heart failure with preserved ejection fraction

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Background: Morbidity and mortality in patients (pts) with heart failure with preserved ejection fraction (HFP EF) 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 HFP EF.

Methods: 217 patients (pts) with CHF, with EF greater than 50% and diastolic dysfunction were included. Pts with atrial fibrillation or flutter were excluded. The parameters evaluated: NYHA class, 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 serum NT-proBNP higher than 220 pg/mL considered as having HFP EF (94) and with less than 220 pg/mL (82), RHR cut-off value of 72 b/min had a 72% sensitivity and 73% specificity for detecting pts with HFP EF (AUC = 0.713, CI 0.637–0.789). Subsequently, 114 pts (age 56±24 years, 56 males) with confirmed HFP EF (74% 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, reduced QoL and increased 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±19, p=0.004; CI 41.5–82.5; E/E' ratio: 3.72±0.3 vs. 7.15±0.2, p<0.001; CI 1–4; ILAV: 6.2±3.3 vs. 33.7±6.1 m²/s², p<0.001; CI 0.2–4.8). The baseline 6MWT improved from 3157±2377 to 1426 ±1611 (p=0.476). The baseline 6MWT improved from 1695±2377 to 1426 ±1611 (p=0.476). The baseline 6MWT improved from 1695 pg/ml ± 2377 to 1426 pg/ml ± 1611 (p=0.476). The baseline 6MWT improved from 3157±2377 to 1426 ±1611 (p=0.476). The baseline 6MWT improved from 1695 pg/ml ± 2377 to 1426 pg/ml ± 1611 (p=0.476). The baseline 6MWT improved from 1695 pg/ml ± 2377 to 1426 pg/ml ± 1611 (p=0.476).

Conclusions: RHR is a better diagnostic and therapeutic marker for patients with HFP EF. The trend towards beneficial clinical effects of long-term treatment remains to be confirmed.

P1785 | BEDSIDE
Diastolic dyssynchrony has no impact on quality of life in patients with dilated cardiomyopathy

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Introduction: Dilated Cardiomyopathy (DCM) leads to progressive decline in left ventricular (LV) systolic and diastolic function. Among the factors contributing to LV systolic and diastolic dysfunction, 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) questionaires: 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 early diastolic velocity (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 2 opposing walls, SD-S in time to peak systolic velocity (SD-S) and early diastolic velocity (SD-E). Sixty ang and both matched heart care. However, the centers that perform autopsy in patients deceased before January2000-April2005 were reviewed (1226 cases). Inclusion criteria: heart failure, cardiogenic shock and cardiomyopathy; exclusion criteria: congenital car-

HEART FAILURE: FROM BENCH TO BEDSIDE IV

P1786 | BEDSIDE
Comparison between in vivo and post mortem diagnoses in patients with heart failure


Background: Necropsies and medical charts of patients deceased between 14 January2000 and 28 April2005 were reviewed (1226 cases). Inclusion criteria: heart failure, cardiogenic shock and cardiomyopathy; exclusion criteria: congenital heart failure, inflammatory cardiomyopathy or pericardial effusion. Methods: Necropsies and medical charts of patients deceased between January2000-April2005 were reviewed (1226 cases). Inclusion criteria: heart failure, cardiogenic shock and cardiomyopathy; exclusion criteria: congenital car-

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diomyopathy, age (younger than 18 years-old), pericardium diseases and post-operative shock. Discrepancies between clinical and necroscopic diagnosis were categorized according to Goldman criteria: I and II: major discrepancies, related to the cause of death, but only I would lead to a change of the management and prognosis; III and IV are unrelated to the cause of death, III being a treatable condition which could affect prognosis and IV being a disease with no clinical impact but genetic and/or epidemiological importance. V is the absence of discrepancies.

Results: Were reviewed 1226 cases and included 500. On the necropsy data, the following diseases at non-diagnostic shock: in 290 cases (41.8%), septic shock in 103 (20.6%) and pulmonary embolism in 59 (11.8%) cases. The cardiomyopathy was ischaemic in 200 (40%) cases, Chagas’ disease in 65 (13%), rheumatic heart disease in 63 (12.6%) and hypertensive in 52 (10.4%). Were available 184 medical charts: 1.46±0.31% of the patients were male the mean age was 62±15.4 years. The internation was due to heart failure in 26 (21.8%) and to cardiogenic shock in 23 cases (19.3%).

Discrepancies were found in 157 cases (85.3%): 89 (48.4%) were major discrepancies, being 53 (28.8%) class I and 36 (18.9%) class II; 68 (37%) were minor discrepancies, being 25 class III (13.6%), and 43 class IV (23.4%). In 27 (14.7%) cases no discrepancy was found.

Conclusion: The high number of misdigasises in patients with heart failure can be related to the severity of this syndrome, what supports the importance of the non-invasive methods of diagnostics. Moreover, the discrepancies between clinical and necroscopic diagnoses highlights the necessity of further studies in this field in order to evaluate the quality of the care and, finally, to subsidize a better structuring of diagnostic and therapeutic procedures.

**P1788** | BENCH

**NGAL/MMP9 Complex: from kidney injury to worsening of heart remodelling in cardiorenal syndrome type II**

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**Background:** In cardio-renal Syndrome Type II (CRSI), the role of systemic congestion in heart failure with preserved ejection fraction (HFpEF) versus that of reduced cardiac output and renal hyperperfusion in heart failure with reduced ejection fraction (HFREF) is still debated.

**Purpose:** We studied the role of congestion in the development of kidney injury in a model of CRSII (monocrotaline (MCT) treated rats).

**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 diastolic blood pressure. BNP, sCreatinine, both kidney and heart NGAL, MMP-9, sCytokines, Kidney and heart cell death, assessed by TUNEL, were also studied.

**Results:** Rats both HF showed higher BNP (CHF 4.8±0.5, controls 2.41±0.8 ng/mL p < 0.01), marked RV hypertrophy and dilatation (RVMAss/RVVolume CHF 1.46±0.31, controls 2.41±0.8 p < 0.01), pleural and peritoneal effusions. Pro-inflammatory cytokines were significantly increased. sCreatinine was also increased (CHF 1.1–2.7) with HC but with persistent congestion and 2.1 (95% CI 1.4–3.0) with no HC. There was weak correlation between the decline in congestion and mortality (mean follow-up 1.5 y) was determined by Cox regression.

**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 MMP9 produces extracellular matrix degradation. This may worsen heart remodelling and perpetuate the vicious circle of kidney/heart damage.

**P1779 | BEDSIDE**

**Clinical applicability of different methods of baroreflex sensitivity assessment in patients with mild heart failure**

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**Background:** Impaired baroreflex sensitivity (BRS) identifies patients with cardiovascular diseases at high risk of poor outcomes. The phenylephrine method – “gold standard” for BRS evaluation – is difficult to be widely applied into clinical practice, other “non-invasive” methods are used.

**Aim:** To compare clinical information derived from the sequence- and the controlled-breathing methods (non-invasive evaluation of BRS based on the analysis of simultaneous beat-to-beat recording of heart rate and blood pressure) and phenylephrine method in optimally treated patients with mild chronic heart failure (CHF).

**Methods:** The study is based on data collected in the SICA-HF (Studies Investigating Co-morbidities Aggravating Heart Failure) prospective, multinational, observational study. The subset of 87 patients with stable CHF in NYHA class I–II (age: 57±10 years, LVEF: 34±7%, all receiving ACE-I/ARB and beta-blocker) in addition to standard clinical assessment, echocardiography and cardiopulmonary exercise testing, underwent BRS evaluation with 3 methods: the phenylephrine (BRS-phe), the sequence (BRS-seq), and the controlled-breathing (BRS-cb). CHF patients were divided according to: (1) BRS-phe median: 3.9 ms/mmHg, (2) BRS-seq median: 7.1 ms/mmHg, and (3) BRS-cb median: 7.2 ms/mmHg, and those above risk hypokinesis were compared.

**Results:** There were only modest correlations between BRS calculated using each method: BRS-phe and BRS-seq: r=0.31, BRS-phe and BRS-cb: r=0.28, BRS-seq and BRS-cb: r=0.43 (all p < 0.05). Phenylephrine-derived groups differed in age (65±11 vs. 55±12 y, p = 0.03), percentage of NYHA class II (93% vs. 71%, p < 0.01), LVEF (32.1±6.4 vs. 35.6±7.5%, p = 0.02), LVEDD (36.6±0.8 vs. 62±0.8 cm, p = 0.04), peak VO2 (18.9±4.8 vs. 21.7±5.8 mL/kg/min, p = 0.02), VE/VO2 slope (36.4±10.8 vs. 31.8±7.4, p = 0.02), and N-terminal pro-B type natriuretic peptide (medians: 681 vs. 482 pg/mL, p < 0.05). BRS-phenylephrine (BRS-phenylephrine) method for BRS assessment (but not the non-invasive methods [sequence- and controlled-breathing]) provides relevant clinical information in optimally treated patients with mild CHF.

**Conclusion:** Phenylephrine method for BRS assessment (but not the non-invasive methods [sequence- and controlled-breathing]) provides relevant clinical information in optimally treated patients with mild CHF.

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**P1790 | BEDSIDE**

**Is hemoconcentration a reliable marker of decongestion in acute heart failure?**

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**Introduction:** The principal cause for hospitalization due to acute heart failure is congestion. Hemoconcentration (HC) has been suggested as a surrogate for successful decongestion during fluid removal in AHF.

**Methods:** We studied 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 >3 cm water (1 point), hepatomegaly (1 point), peripheral edema (Abent/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 was 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

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Background: Multimodal adjuvant treatment of loco-regionally advanced (stage II and 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, gender, 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 (<6.0 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 (DD) was defined by early diastolic velocity (e') of the septal (>9 cm/s) or lateral mitral annular <10 cm/s by pulsed wave TDI. Estimation of LV filling pressures was performed from parameters of pulsed wave Doppler measures of mitral inflow (E, E'/A ratio) and pulmonary venous flow (S/D ratio, Ar-A duration), left atrial volume and E/e' ratio.

Results: Mean age was 62±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 same cumulative dose of 360 mg/m² epirubicin. None underwent trastuzumab. Irradiation was performed after manual dose planning 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 using TDI peak systolic velocities or 2D STE. However DD occurred in 142 (66%) compared to 78 (36%) in controls (odds ratio (OR) 3.5 (2.9–5.0), p<0.001). 8% of patients with DD had elevated filling pressure compared to 3% in controls. Age and manual dose planning of irradiation were significantly associated with DD (OR 1.2 (1.1–1.3), p<0.001 and 2.5 (1.5–3.6), p<0.003 respectively) while anthracyclines were not associated with DD (OR 0.9 (0.7–1.2), p=0.85). In multivariable modelling, controls were stratified with EMB methods into J-sheath group (n=40) and old-method group (n=40). Routine surveillance EMB were performed weekly during 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: 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.

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P1793 | BEDSIDE

Endomyocardial biopsy with a J-shaped sheath reduced the risk of tricuspid regurgitation after heart transplantation

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Background: Tricuspid regurgitation (TR) is one of the major problems in 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 patients 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 ventricular (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 35cm 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. Patients were stratified with EMB methods into J-sheath group (n=40) and old-method group (n=40). Routine surveillance EMB were performed weekly during 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: The use of a J-shaped sheath at EBM reduced the prevalence of remarkable TR after HTx.

P1794 | BEDSIDE

Comparison of conventional measures to estimate right ventricular function in patients after heart transplantation using 3D and speckle-tracking echocardiography

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Right ventricular (RV) dysfunction is a common finding in patients undergoing heart transplantation (HTx). However, certain limitations may apply regarding the 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: Comparison of conventional measures to estimate right ventricular function in patients after heart transplantation using 3D and speckle-tracking echocardiography.
EDV did not differ between the two groups (HTX vs. control: 87±22 vs. 80±26 mL). In HTX patients EF and FAC were lower, however, TAPSE was decreased to a greater extent (EF: 54±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=0.39, p<0.05). No healthy FAC correlated reliably (r=0.74, p<0.001). Patients over one year after HTX had better TAPSE (17±4 vs. 14±4 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). This study is supported by Slovak Society Research Grant 2012-2015.

P1790 | BEDSIDE
Prognostic differences among equations for estimated glomerular filtration ratio in acute heart failure syndrome
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Background: Although renal function evaluated by estimated glomerular filtration rate (eGFR) is a robust strong predictor of short- and long-term prognosis in patients with acute heart failure syndrome (AHFS), the differences of equations of eGFR in prognostic predictability are not fully elucidated. Purpose: The purpose of this study was to investigate the superiority of the new equations, Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, in prognostic predictability compared with previous equations.

Methods: We included 1,039 AHFS patients (78±12.8 years old, 51.0% male) who were admitted to our three hospitals for AHFS. Renal function at admission was estimated by three methods; equation for eGFR patients (eGFR), Modification of Diet in Renal Disease study equation (MDRD), and CKD-EPI. All the equations were modified for Japanese patients. The predictability of these three equations were compared by area under the curve (AUC) and net-reclassification improvement (NRI) for the endpoints of in-hospital mortality and also of all-cause death within one-year.

Results: During follow-up, 66 (6.4%) patients died during index hospitalization and 162 (15.6%) patients died within one-year. The AUC of CKD-EPI (0.654) was significantly higher compared to both eGFR (0.646) and MDRD (0.642) for in-hospital mortality (P=0.04 and P=0.01, respectively). For one-year mortality, the AUC of CKD-EPI (0.664) was not significantly superior to eGFR (0.660) and MDRD (0.658) (P=0.113 and P=0.079, respectively), however, NRI showed CKD-EPI was superior to both eGFR (NRI: 0.37, P<0.001) and MDRD (NRI: 0.35, P<0.001).

Conclusion: In AHFS patients, CKD-EPI equation was most useful for prognostic prediction of renal function for both short and long term mortality.

P1791 | BEDSIDE
Patirromer reduced serum K+ in hyperkalaemic patients with HF and advanced CKD on RAAS inhibitors: Results from OPAL-HK and AMETHYST-DN
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Introduction: RAAS inhibitors (RAASI) reduce mortality in patients (pts) with HF

HEART FAILURE, OTHER

P1797 | BEDSIDE
Urinary NGAL - troponin of the kidney?
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Purpose: The aim of the study was to assess differences in the levels of urinary NGAL, (neutrophil gelatinase-associated lipocalin) 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 60 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=11).

Results: In the AKI+ group had significantly higher median admission u-NGAL levels compared with the AKI− group for (274, 18.3 ng/mL; p=0.005), also after 24 hours (163 vs. 34.5 ng/mL; p=0.0004). The difference in serum creatinine on admission and after 24 hours was not observed between groups. Significant increase in serum creatinine was recorded in the AKI+ group after 72 hours (175.6 vs. 103.7 μmol/L; p=0.0003). Initial parenteral dose of furosemide was higher in the AKI+ compared with AKI− (102.5 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.

P1796 | BEDSIDE
Evaluation of left ventricular myocardial mechanics and synchrony in heart transplant patients using three-dimensional echocardiography

Introduction: Speckle-tracking echocardiography gained particular interest as it allows to quantitively sensitive and predictive parameters of myocardial function in numerous cardiac conditions. However, 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 compare them to healthy 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.

Purpose: To verify which patients admitted to an acute heart failure treatment unit could be enrolled during a relevant radial component in RV function. In time, longitudinal function can recover.

HEART FAILURE, OTHER
± 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: OPAL-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 CKD stage 4–5 with eGFR ≤ 60 ml/min/1.73 m² and OPAL-HK (OP) had eGFR < 45 ml/min/1.73 m² and A-DN had stage 3b-5 CKD and analysed for ≥ 60 mEq/L and > 5.0 ± 0.6 mEq/L (mod/severe) in OP. 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+ change from baseline (1° endpoint) by s-K+ strata: > 5.0 ± 0.5 (mod) and > 5.5 ± 0.6 mEq/L (mod/severe) in A-DN; > 5.1–5.5 (mod) and > 5.5–6.5 mEq/L (mod/severe) in OP.

Results: Of HF pts with advanced CKD, 66 had mild and 66 had severe/severe HK. Pts were primarily male (55%, 62%); mean±SD eGFR was 29±10 in mild and 27.9±1.7 mln/1.73 m² in mod/severe HK pts. With patiromer mean 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. AE s 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 advanced CKD, and may be an option for HK treatment in pts with HK and advanced CKD. Acknowledgement/Funding: Financial support for this study provided by Replysa, Inc.

P1800 | BEDSIDE The predictors of dysynchrony deterioration in patients with left bundle branch block and normal EF

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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±10.0 years; M47%) with LBBB revealed during annual check-up were enrolled into the study. History of CAD had 30.9% patients, hypertension—64.4% (n=43), 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 (SPSS 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= 4.5; 95% CI: 1.00–15.2). 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= 6.91; 95% CI: 1.95–24.50; p=0.003), and heart rate (HR; OR=1.84; 95% CI: 1.19–2.87; p=0.026).

According to the univariate analysis interventricular (IV) dysynchrony deterioration was related to the signs of previous myocarditis on cardiac MRI with gadolinium; medical treatment by ACE-inhibitors and beta-blockers, age, BP level, LV thickness. Multivariate analysis revealed the influence of previous myocarditis (OR=5.0; 95% CI: 1.5–16.68; p=0.009) and medical treatment (combination of ACE-inhibitors and beta-blockers) (OR=2.6; 95% CI: 1.4–5.8; p=0.008).

Interestingly, during FU period IV-dysynchrony has decreased among those patients who followed the recommendations on medical treatment (68.2±9±15.6 ms vs. 61.9±9±15.6 ms; p=0.005). However, it worsened in patients who refused them (55.6±18.96 ms vs. 64.3±15.04 ms; p=0.032).

Conclusions: In patients with LBBB and normal EF EDVI was responsible for the increase of QRS complex duration during FU period of 32±13 months. Presence of CHF and HR was associated with AV dysynchrony worsening. Predictors of IV-dysynchrony were the signs of previous myocarditis on cardiac MRI with gadolinium and poor adherence to medical treatment.

P1801 | BEDSIDE Incidence and long-term impact of progressive hyponatremia in heart failure patients with reduced and preserved ejection fraction

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Background: Hyponatremia is reported as a predictor of adverse short and long outcome in the patients with heart failure (HF). However, most of the previous studies have examined baseline hyponatremia at admission rather than hyponatremia that developed during hospitalization; progressive hyponatremia. The association between adverse outcome and progressive hyponatremia has not been fully evaluated.

Purpose: The purpose of this study is to investigate whether the progressive hyponatremia during hospitalization in the patients with HF may associate with long outcome, and to clarify the difference of its impact between HF with reduced ejection fraction (HFrEF) and those with preserved ejection fraction (HFrEF).

Methods: We analyzed the data of consecutive patients admitted with HF with normonatremia at the time of discharge. HF was defined as hyponatremia (<135 mEq/L) at the time of discharge. HFrEF was defined as echocardiography with a left ventricular ejection fraction <45%. Cox-hazard analysis was performed to quantify the impact of progressive hyponatremia on long-term all-cause and cardiovascular mortality. Models were adjusted with age, gender, other previously reported prognostic values, and medication during hospitalization including diuretics, beta blocker, angiotensin converting enzyme inhibitor, and angiotensin receptor blocker.

Results: We investigated 1160 patients (mean age 72.8±13.7 years old, male 40.1%), including 484 (41.7%) patients with HFrEF. We observed progressive hyponatremia in 116 patients (10.0%). During median 520 days follow-up, 199 (17.2%) patients died (16.9% in HFrEF, and 14.7% in HFrEF). In all patients, progressive hyponatremia was independently associated with all-cause mortality (Hazard ration [HR] 1.54, 95% Confidence Interval [CI] 1.02–2.33, p=0.039), and cardiovascular mortality (HR 1.63, 95% CI 1.01–2.85, p=0.047). Furthermore, the progressive hyponatremia had significant impact on mortality in the group with HFrEF (p=0.001, log rank test) but not in the group with HFrEF (p=0.162, log rank test). In the patients with HFrEF, progressive hyponatremia remained as independent predictor for all-cause (HR 2.04, 95% CI 1.30–3.49, p=0.009) and cardiovascular mortality (HR 1.97, 95% CI 1.07–3.63, p=0.029) after adjusted with other covariates.

Conclusion: Progressive hyponatremia during hospitalization is an independent predictor of all-cause, and cardiovascular mortality in the patients with HF. The impact of progressive hyponatremia on long adverse outcome was different between HFrEF and HFrEF.

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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 HFpEF. 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
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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
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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 HF.

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 younger patients of both ethnic groups. Arabs developed heart failure on average 10 years earlier and had a significantly higher rate of diabetes (62% vs 41% in Arab 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.

Figure: Prevalence ratio of heart failure in the younger age groups.

Prevalence Ratio of Heart Failure

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.
**P1807 | 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**

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**Purpose:** Galectin-3 (gal-3) is a well-established marker of fibrosis in heart failure and is associated with bad prognosis. However, gal-3 was not extensively studied in patients with 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 without previous history of heart failure, who 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, CTFSC), biochemical and echocardiographic parameters. Galectin-3 analyses were done with the ready-to-use human ELISA assays (R&D Systems, USA) on the day of hospital admission and after one-month follow-up.

**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 between initially (med. 1016.4 vs no-HF med. 1053.4 pg/mL, NS) and after one-month follow-up (med. vs no-HF 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). Absolute 1-month follow-up, despite stable gal-3 levels, patients from HF group had lower LVEF (50% vs 55%, p <0.000), 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, galectin-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

**Conclusion:** 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.

**P1809 | 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**

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**Background:** The prevalence of preserved left ventricular ejection fraction (HFpEF) and arterial stiffness increase with age. Although a causal relation is not certain, recently some studies showed the association between arterial 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 passive leg-raise exercise were performed during LV catheterization under polygraphy monitoring. The LVEDP was measured by automatically mechanical mechanization.

**Results:** The mean age was 59.63±13.15 years, average RbaPWV 1533.30±392.85 (101.4±18.9 mmHg), and LbaPWV 1524.13±419.23 cm/s. As the mean LVEDP was 20.66±3.33 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 LVEDP variation during active leg-raise was well correlated with baPWV (R=0.275, 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 (1393.95±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).

**Conclusion:** BaPWV, non-invasive marker of central arterial stiffness, was closely associated with the degree of LVEDP variation during active leg-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 may be a key determinant of HFpEF development and also ventricular-arterial stiffness is dynamic rather than static process.
Heart failure: from bench to bedside II

A.J. Flammer

Data from regular medical visits was analysed retrospectively in patients (mPCWP) obtained after transplantation.

Background: Heart transplantation is an effective treatment for end-stage heart failure. It is, however, associated with numerous long-term complications. To control for these, biopsies as well as left- and right-sided heart catheterizations are performed in regular intervals after transplantation.

Purpose: The aim of this study was to assess the prognostic relevance of mean pulmonary artery pressure (mPAP) and mean pulmonary capillary wedge pressures (mPCWP) obtained after transplantation.

Methods: Data from regular medical visits was analysed retrospectively in patients transplanted between September 1985 and August 2014 at our institution. 260 patients (mean age 47±12.7 years, 36 females) were included in the analysis. Right heart catheterization (RHC) data (median 358 days; IQR 184.5–408.1 days) was available about this group.

Results: The median mPAP was 15mmHg (IQR 12–19mmHg) and the median mPCWP was 8mmHg (IQR 6–11mmHg). Kaplan Meyer curves of “high” versus “low” mPAP (median split) showed significantly better survival in those with “lower” mPAP as compared to those with “higher” mPAP (p<0.001, Figure 1). mPAP but not central venous pressure or mPCWP was also independently associated with mortality in a multivariate Cox-hazard survival analysis (risk ratio 1.10, CI 1.04–1.16, p<0.001). Other factors independently associated with mortality were age at transplantation (risk ratio 1.03, CI 1.01–1.04, p=0.002) and serum creatinin levels (risk ratio 1.003, CI 1.001–1.010, p=0.021).

Conclusion: Our results demonstrate that mPAP in the stable phase after heart transplantation is an independent prognostic factor for mortality.

P1813 | BEDSIDE

Predictive value of PAPP-A, sCD40L, and anti-HLA antibodies in cardiac transplant recipients

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Objectives: To evaluate the predictive role of pregnancy associated plasma protein A (PAPP-A), soluble CD40 ligand (sCD40L), and HLA I and II antibodies (anti-HLA), in development of antibody-mediated rejection (AMR) and coronary allograft vasculopathy (CAV) in cardiac transplant patients.

Methods: The study included 140 patients (39±3±11) who underwent heart transplantation (HTx) during the period from 2008 to 2014 (mean follow-up 53±12±26.89 month); 25 (17,9%) women and 115 (82,1%) men. Initial diagnostic anti-HLA up to 1 month after HTx by Luminex. Donor-specific antibodies (DSA) were measured in early transplant period (up to 1 month) by Luminex. After HTx CAV 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% 2.3±4.6,4±0.03). Pretransplant levels over median of PAPP-A (≥11 mIU/L) and sCD40L (≥1.6 ng/ml) were detected in 78 (44.29%) and 62 (55.71%) pts. respectively. Relative risk (RR) of CAV and AMR for pts. with positive pretransplant anti-HLA was 2.1 (CI 95% 1.9–3.73 p=0.01), with high levels of PAPP-A (≥11 mIU/L) and sCD40L (≥1.8 ng/ml) – 2.77 (CI 95% 1.42–5.41 p=0.002) and 2.05 (CI 95% 1.11–3.77 p=0.02), respectively.

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.

P1814 | BENCH

Diastolic adaptation as a central mechanism in the myocardial response to acute haemodynamic overload

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Introduction: Myocardial stretch causes an immediate (Frank-Starling response) and a delayed (slow force response) increase in contractility in order to adapt cardiac output to acute haemodynamic overload. On the other hand, diastolic adaptation and optimization of cardiac filling under these conditions has not been described yet.

Aim: To assess the diastolic response to myocardial stretch in the rodent heart and isolated cardiomyocytes, and in the in vivo human heart.

Methods: Isolated rat hearts (n=9, 300 bpm, 30°C) were perfused at constant pressure according to the Langendorff technique and acutely stretched from 3 to 10mmHg by a balloon inserted into the left ventricle (LV). Pressures were regulated in 5 min intervals. Retained and unloaded hearts were measured in situ after 15 minutes from control (n=4) and stretched (n=4) LV were performed and passive tension was measured at sarcomere lengths (SL) ranging between 1.8µm to 2.3µm. A catheter was inserted into the aortotomy of patients submitted to cardiac surgery (n=1). After the surgery and during a period of hemodynamic stability, LV pressure and volume were recorded immediately before and 15 minutes after volume overload and Trendelenburg positioning. Statistical significance was set at p<0.05.

Results: In isolated hearts, diastolic pressure decreased 43.3±2.4% after 15 minutes of stretch. Passive tension of permeabilized cardiomyocytes was significantly lower in the previously stretched group for all SL (N=2): 1.8±2.0 vs 6.2±0.6; 2.1±0.1 vs 6.6±1.0; 2.8±0.4 vs 6.7±0.2; 3.4±0.4 vs 8.6±1.5; 4.1±0.4 vs 10.0±1.8;
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 18±2 to 35±3 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 pressures in heart failure patients with preserved ejection fraction**

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**Background:** Noninvasive imaging parameters to estimate left atrial pressure (LAP) in heart failure with preserved ejection fraction (HFP EF) lack desirable diagnostic sensitivity and specificity.

**Purpose:** We hypothesized that in HFP EF, 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 cavitary 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 HFP EF patients subjects with elevated LAP (pulmonary capillary wedge pressure >12 mmHg) and 24 controls with normal LAP as confirmed by right heart catheterization (RHC). Significant valvular 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 in 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 HFP EF.

### P1816 | BEDSIDE

**Treating advanced heart failure with biventricular assist devices in a low organ donation environment**

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**Background:** Heart transplantation remains the gold standard treatment for patients with end stage heart failure. Low organ donation combined with delayed referral of advanced-stage cardiomyopathy patients necessitates biventricular assist device (BIVAD) support for extended periods of time.

**Methods:** We retrospectively reviewed the records 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 adrenaline, 60; ventilated, 10; mean Gl 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: 2). Two patients needed a BIVAD after left ventricular assist device support of 439 and 295 days, respectively. Thirty-six of them were transplanted and seven are ongoing. Mean time on support was 781 days and 61 out of 69 patients with adult-sized pumps were discharged home with a mobile driver. Thirty patients exceeded 2 years of uncomplicated support before they were transplanted. One of our patients was successfully transplanted after 1460 days of support. One patient with renal failure and dialysis dependence lived at home 3.5 years after implantation. Complications included infections (n=12), bleeding requiring reexploration (n=12), and thromboembolic events (n=20). Twenty-five patients died during support due to different reasons. Early mortality was due to multorgan failure while late mortality regarded mostly cerebrovascular complications.

**Conclusions:** Support with BIVAD offers an acceptable rate of survival to heart transplantation. Furthermore, the use of a BIVAD itself does not confer an increased morbidity or mortality, and overall outcomes with this device are comparable to that of implantable LVADs if used strategically in severe congestive heart failure. With the institution of meticulous wound care, morbidity has been significantly reduced, and management as an outpatient is achievable, however readmissions are still frequent.

### P1817 | BEDSIDE

**Cardiac progenitor cell infusion in patients with univentricular heart disease in heart failure with preserved ejection fraction**

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**Background:** The clinical outcomes of heart failure with reduced and preserved ejection fraction (HF-EF and HFP- EF) after staged palliations in patients with univentricular heart disease remain unknown as is the question whether cardiomyocyte-derived cell (CDC) transfer may have impact on either type of cardiac dysfunction.

**Purpose:** We sought to characterize the heart failure patients, include HF-EF and HFP- EF, with single ventricular physiology and investigate the clinical responsiveness of 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 (HF- EF: FE<40%, n=30; HFP- EF: FE>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 HFP- EF patients, HF- EF patients showed increased cardiac volume (P<0.02) and mass index (P=0.04), those were associated with reduced global circumferential strain in HFP- EF compared with HFP- EF (P<0.0004). Although there was no difference in the incidence of late gadolinium enhancement detected by cMRI in both groups (20% in HFP- EF and 15% in HFP- EF), ventricular diastolic dysfunction identified by early diastolic strain rate (e90) was higher in HFP- EF patients compared with HFP- EF (46% vs 27%). When patients underwent staged shunt procedures, HFP- EF group had significant reduction in EF and atrial strain (P=0.02), resulting in increase in TEL 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 HFP- EF group, HFP- EF patients demonstrated a marked improvement in EF (P=0.001), right ventricular function (P=0.001) 3 months after CDC infusion. Similarly, diastolic function improvements were found in CDC-treated HF- EF group but not HFP- EF patients as shown by increased atrial fractional area change (P=0.01) and reduced E-wave/e90 (P=0.049). However, patients with HFP- EF had no significant changes in diameters and reduced dp/dt during the same follow-up interval (P=0.04). These beneficial effects by CDCs could not be seen in remaining 20 patients who underwent palliation alone without CDC injection.

**Conclusions:** HF- EF in univentricular heart disease could be partially coupled with diastolic dysfunction that may lead to early perioperative right ventricular failure with poor clinical response to CDC therapy.

**Acknowledgement/Funding:** The Ministry of Health, Labour and Welfare

### TREATMENTS OF HYPERTENSION

**P1818 | BEDSIDE**

**Impact of fixed-dose combination of perindopril/amlodipine on left ventricular myocardial deformation in patients with arterial hypertension**

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**Background:** Speckle tracking echocardiography allows detection of early myocardial dysfunction in arterial hypertension. The dynamics of LV deformation under antihypertensive treatment are not established. The purpose of the study was to clarify the impact of fixed-dose combination of perindopril/amlodipine on LV myocardial deformation in patients with arterial hypertension.

**Methods:** The study involved 78 untreated hypertensive males (aged 52±8 years). All patients underwent ambulatory blood pressure monitoring, conventional and speckle tracking echocardiography before and 6 months after treatment. LV global longitudinal strain and strain rate were obtained by averaging...
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/amlodipine 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**

Baseline 6 month p
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Global longitudinal LV strain, % -16.1±2.4 -16.2±2.2 0.9
Global longitudinal LV strain rate, 1/s 0.96±0.15 0.96±0.2 0.83
Basal circular LV strain, % -18.4±1.2 -19.7±4.65 0.026
Basal circular LV strain rate, 1/s 1.3±0.3 1.4±0.37 0.018
Basal radial LV strain, % 25.6±10.2 25.8±11.2 0.87
Basal radial LV strain rate, 1/s 2.0±0.54 2.0±0.46 0.41
Apical circular LV strain, % -29.2±7 -29.8±7 0.45
Apical circular LV strain rate, 1/s 1.84±0.55 1.86±0.57 0.71
Apical radial LV strain, % 26.2±11.9 27±10.4 0.5
Apical radial LV strain rate, 1/s 1.56±0.5 1.6±0.46 0.21

Values are given as mean ± standard deviation.

**Conclusions:** The treatment with fixed-dose combination of perindopril/amlodipine 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 amlodipine in hypertension in clinical hypertension**


**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 0.75mg/day for the next 4 weeks, after which the group was randomized to continue 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 the 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, 34 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-lifting of treatment to 7.5mg/day enabled 6 more patients (13%) meet BP goal (DXM7.5 group). Only 4 patients (8%) with DXM 30mg/day achieved the BP goal (DXM30 group). While no changes in DXM 7.5mg/day group, the mean systolic BP was further reduced by 7.9±7.0 mmHg (p<0.001) and 5.4±2.4% (P=0.003) at week 14 from week 2 in DXM2.5 and DXM7.5 group respectively. The similar trends were also seen in diastolic BP. Thus, 73% of the 78 patients reached the BP goal with either monotherapy or different combinations at the end of the 14-week study. The addition of low-dose (2.5 and 7.5mg/day) DXM 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.

**Acknowledgement/Funding:** TSH Biopharm

**P1820 | BEDSIDE**

**The blood pressure control predictors in hypertensive patients with and without ischemic heart disease**

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**Background:** Blood pressure (BP) decreasing till target level prevents complications. Ischemic heart disease (IHD) is factor that could influence antihypertensive effectiveness. There was not compared the predictors of target BP achievement in population of AH patients without and with IHD. That was the aim of our study.

**Methods:** There were included 9821 hypertensives (mean age 58.5±0.24 years) in 39th multicenter open trial. All were divided in 2 groups: 1st – 4193 pts without IHD, 2nd – 5628pts with IHD. Patients were treated by primary care physicians, who prescribed drugs according to their own view.

**Patients were done:** office BP measurements, ECG, patient compliance (X.Girerd) and cardiovascular risk evaluations by standard tests, inquiring by author questionnaire. Multifactor regression analysis was used for evaluation of antihypertensive treatment failure predictors.

**Conclusions:** It was stated that IHD in hypertensive patients was associated with more rate of complications, diabetes mellitus and risk factors, that needed more antihypertensive drugs. The systolic (SBP) and diastolic (DBP) BP levels were higher in 2nd at baseline and at end of study, in spite of more intensive treatment. The target BP (<140/90 mmHg) was achieved in 68.7% patients of 1st group and in 51.1% - 2nd group (p=0.001). Common predictors of antihypertensive treatment failure were high baseline SBP (>160 mmHg) and DBP (>100mmHg) levels: risk of not target BP achievement increased in 3.8/2.6 times for 1st group and in 2.9/2.5 times for 2nd group. In patients without IHD the risk of antihypertensive treatment failure was associated with higher BMI (+1.033, p=0.05) and rear intake of fresh fruits/vegetables (+12.8, p=0.025). In 2nd group predictors of poor treatment were heart failure (1.73, p=0.001) and renal AH (1.24, p=0.05). More cardiovascular risk was associated with insufficient effectiveness in different way: in 1st it increased the probability (+1.46, p=0.001), in 2nd decreased (+0.52, p=0.001). Only 28.3% of 1st group and 19.5% of2nd (p=0.001) had high treatment compliance. Baseline higher compliance diminished the treatment failure risk on 36% in 1st group, but not in the 2nd group. Thus high compliance at the end of study decreased the treatment failure on 46% in 2nd group.

Hypertensive patients with and without IHD had different BP control and different factors associated with achievement of target BP that help to form the different strategy of patient management.

**P1821 | BEDSIDE**

**Combination of optimal medical therapy is essential in management of patients with coronary artery disease: wave pulse velocity long-term follow up Study**

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**Background:** Global cardiovascular risk stratification is essential in high-risk hypertensive patients. However, it is uncertain how often the strategy is executed in real clinical practice. We sought to evaluate the management of cardiovascular risk in hypertensive patients with coronary artery disease (CAD) using brachial-ankle pulse wave velocity (baPWV).

**Methods:** A total of 851 hypertensive patients with CAD (age 65±11) were enrolled and baPWV were measured every year (mean follow up periods 4.5 years). All were divided in 2 groups: 1st – 4193 pts without IHD, 2nd – 5628pts with IHD. Patients were treated by primary care physicians, who prescribed drugs according to their own view.

**Results:** In optimal medical therapy group, change of baPWV/year were significantly lower than in sub-optimal therapy group (p<0.05) (figure).

**Conclusions:** These results suggest that combination of optimal medical therapy is essential in management of high-risk hypertensive patients, and it might also reduce cardiovascular risk.
P1823 | BEDSIDE
Strong patient adherence and improved blood pressure control under treatment with a fixed dose combination (FDC) of bisoprolol and amlodipine
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Data from clinical study clearly demonstrate that the majority of patients with essential hypertension need more than one antihypertensive drug for reaching target blood pressure values. Intake of several drugs may negatively impact patient adherence of the mostly elderly patients. Good patient adherence is the precondition for a successful antihypertensive treatment.

Objective: To determine the adherence of patient adherence and, thus improved blood pressure control under a fixed dose combination tablet.

Material and methods: Patients (~>18 years) with essential hypertension, who had been switch from a free combination of bisoprolol and amlodipine to the FDC with the same strengths of the two components at least 4 weeks prior to recruitment were eligible for study participation. During the observational study, all investigators continued their routine diagnostic and treatment procedures. Upon availability, laboratory parameters were documented at study start and after 3 and 6 months of treatment in standardized CRFs and evaluated by using the statistic program BIAS.

Results: 4,288 patients (mean age 59 years, approximate 50% male and female) were recruited. The mean daily dosage was 5.2mg for bisoprolol and 6.5mg for amlodipine. After 6 months of study treatment, patient adherence to the FDC was excellent (>90% of prescribed tablets taken) in 83% of the patients, and good (76–90% of prescribed tablets taken) in additional 15% of the patients.

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.
P1826 | BEDSIDE
Can brain natriuretic peptide predict Prognosis in resistant hypertension?
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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±50 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 chambers and 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) BP 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
Diuretics, having a tendency of more antihypertensive effect at a low temperature, reduce the seasonal variability of blood pressure
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Background and introduction: The relationship between the effect of thiazide diuretics on blood pressure variability and temperature is unclear.

Purpose: We examined the impact on blood pressure variability due to the additional administration of thiazide diuretics versus the relevance of the monthly office blood pressure variability and average monthly temperature.

Methods: The outpatient having been prescribed antihypertensives and having no change of antihypertensives other than additional thiazide enrolled from January 2008 to December 2014. We calculated the difference of the average monthly office blood pressure between the before and after adding administration of thiazide diuretics. Then we counted the difference of the average monthly blood pressure. The average monthly temperatures in the observation period were calculated on the basis of the data of the Japan Meteorological Agency.

Results: 37 patients enrolled. The mean age of all 37 patients was 72.8 years old when the thiazide diuretic agent was added. The average monthly systolic blood pressure was lower in high-temperature month. On the other hand, the average monthly systolic blood pressure was higher in low-temperature month. This trend was also observed in the period both before and after the additional administration of diuretics. And the difference of the average monthly blood pressure was more pronounced in high-temperature month. On the contrary, the difference of the average monthly blood pressure was higher in low-temperature month. Furthermore, Additional thiazide diuretic agent resulted in the reduction of the seasonal average systolic blood pressure variability interestingly.

Conclusion: This study suggested that additional doses of thiazide diuretic to hypertensive patients improve the seasonal office blood pressure variability.

P1828 | BEDSIDE
Circulating miR-21 and eNOS in subclinical atherosclerosis in patients with hypertension
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Introduction: Low-grade inflammation and endothelial dysfunction play a role in the pathogenesis of atherosclerosis. Microalbuminuria is a biomarker of subclinical atherosclerosis.

Methods: We measured microalbuminuria, plasma NOx and eNOS, blood pressure and CIMT in 120 patients with hypertension.

Results: We found significant correlation between CIMT and plasma NOx (r=0.44, p<0.05) and eNOS (r=0.35, p<0.05). In patients with microalbuminuria (n=12) there was significant difference in plasma NOx and eNOS levels (p<0.001 and p<0.001), respectively. Patients of the microalbuminuria group had higher CIMT and microalbuminuria levels than the patients without microalbuminuria (p<0.001 and p<0.001), respectively.

Conclusion: Low-grade inflammation and endothelial dysfunction play a role in the pathogenesis of atherosclerosis.

P1829 | BEDSIDE
Persistence of fixed and free combination of ramipril and amlodipine in hypertensive patients
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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 good persistence on treatment with effective pharmacological combinations.

Methods: Information from the National Health Insurance of Hungary prescriptions 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 technique 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 20,096 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
treatment with the free, compared with the use of the fixed combination (HR=1.94, p<0.001).

Conclusions: Our study, which is unique even by international standards, demonstrated the clear benefit of initiating antihypertensive therapy with the fixed combination of ramipril and amlopidine over starting treatment with the free combination.

YOUNG INVESTIGATORS AWARDS SESSION: THROMBOSIS

1830 | BEDSIDE
Assessment of a stroke risk stratification scheme in a heart failure population in sinus rhythm
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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-statistic=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). Materially similar results were found with a cutpoint of 1.

<table>
<thead>
<tr>
<th>CHA2DS2-VASc</th>
<th>Patients, % (n) (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>7.1 (2,384)</td>
<td>1.50 (0.87)</td>
</tr>
<tr>
<td>1</td>
<td>13.4 (4,535)</td>
<td>1.64 (1.06)</td>
</tr>
<tr>
<td>2</td>
<td>22.3 (7,519)</td>
<td>2.38 (1.95)</td>
</tr>
<tr>
<td>3</td>
<td>27.3 (9,232)</td>
<td>3.75 (2.46)</td>
</tr>
<tr>
<td>4</td>
<td>17.7 (5,863)</td>
<td>4.82 (3.36)</td>
</tr>
<tr>
<td>5</td>
<td>12.2 (4,132)</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 | BEDSIDE
Risk of hemorrhagic and ischemic stroke for combined antiplatelet therapy and new generation oral anticoagulants in patients with acute coronary syndrome: Meta-analysis of 11 randomized clinical trial
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Background: The overall risk-benefit profile of new generation oral anticoagulants (NOA) in addition to antiplatelet 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 antiplatelet 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 antiplatelet 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 direct thrombin inhibitors or direct thrombomodulin inhibitors.

Conclusion: In patients with ACS, the addition of a NOA to antiplatelet 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 | BEDSIDE
Stroke and recurrent haemorrhage associated with antithrombotic treatment following gastrointestinal bleeding in patients with atrial fibrillation: A Danish nationwide cohort study
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Background: In atrial fibrillation patients with antithrombotic-related gastrointestinal bleeding, doctors are faced with a clinical dilemma: to withhold or restart antithrombotic therapy?

Purpose: To examine the risks of all-cause mortality, thromboembolism, major bleeding, and recurrent gastrointestinal bleeding associated with restarting antithrombotic treatment following gastrointestinal bleeding in antithrombotic-treated patients with atrial fibrillation.

Methods: Nationwide cohort study (1996–2012) including all atrial fibrillation patients discharged after gastrointestinal bleeding whilst on antithrombotic therapy. Exposure was restart of single or combined antithrombotic therapy with oral anticoagulation (OAC) (vitamin K antagonist, dabigatran, or rivaroxaban) and antiplatelet agents (aspirin or ADP receptor antagonists). Risks of outcomes were estimated with Aalen-Johansen method, logistic regression (predicted probability for patients aged 78 years), and Cox regression models, respectively.

Results: We included 5,712 patients (mean age 78, 46% female). After 2 years, 41% died, 12% suffered from thromboembolism, 20% from major bleeding, and 14% from recurrent gastrointestinal bleeding. Antithrombotic therapy was not restarted in 34%. Restarting OAC monotherapy was associated with better outcomes for all-cause mortality (HR 0.43, 95% CI 0.37–0.50) and thromboembolism compared with patients not restarted. This was despite an increased associated risk of bleeding (Figure).

Conclusion: Restarting OAC monotherapy was associated with the greatest effectiveness and relatively safe use compared with other options of antithrombotic therapy or no antithrombotic therapy following antithrombotic-related gastrointestinal bleeding in patients with atrial fibrillation.
**1833 | BENCH**

Dex40-GTMAC3, a new tool to reverse unfractionated heparin effects during intravascular or cardiac interventions

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**Background:** Protamine is the only registered antidote preventing bleeding in patients treated with unfractionated 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).

**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>Thrombosis (mg)</td>
<td>0.92±0.17</td>
<td>0.57±0.09**</td>
<td>0.88±0.25**</td>
</tr>
<tr>
<td>Bleeding time (seconds)</td>
<td>104.3±6.1</td>
<td>167.2±14.2***</td>
<td>106.3±15.5^^^</td>
</tr>
<tr>
<td>aPTT</td>
<td>20.3±1.1</td>
<td>28.4±2.8***</td>
<td>28.9±5.2***</td>
</tr>
<tr>
<td>Anti-factor X activity (U/mg)</td>
<td>0.13±0.02</td>
<td>0.93±0.02**</td>
<td>0.45±0.11**</td>
</tr>
<tr>
<td>***P&lt;0.001 vs. vehicle; †P&lt;0.05; ††P&lt;0.01; †††P&lt;0.001 vs. UFH, Mann-Whitney test. Results are shown as mean ± S.D, n=5–7.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** Documented efficacy, immunogenic and hemodynamic neutrality of Dex40-GTMAC3 makes this novel UFH antidote advantageous over other polysaccharide polymers and protamine.

**YOUNG INVESTIGATORS AWARDS SESSION: AGEING AND SENESCENCE**

**1834 | BENCH**

Telomere length predicts clinical outcomes post-revascularization procedures: its role as a novel biomarker of systemic oxidative stress and cardiovascular ageing

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**Introduction:** Premature senescence is a tumorsuppressive mechanism leading to aging and age-related diseases. Telomeres, which act as safeguards to prevent uncontrolled cell division, elongate during fetal development and subsequently shorten with each cell division. Once telomeres achieve a critical length, cells enter a non-replicating state of senescence, characterized by cell cycle arrest and the expression of senescence markers. Telomere length is deterministically regulated by telomere maintenance mechanisms, the most prominent of which is telomerase activity.

**Purpose:** To investigate the pathophysiological role of CCN1-mediated premature senescence in cardiac fibrosis.

**Methods:** Two established murine models of cardiac fibrosis, transaortic constriction (TAC) and cardiacmyocyte-specific beta1 adrenergic receptor transgenic mice (β1-TG), were employed to study the role of premature senescence in the heart. Fibrosis was evaluated by Sirius Red staining and Realtime PCR of p16INK4a, p21CIP1/WAF1 and senescence-associated beta-galactosidase activity (SA-B-GAL). The role of oxidative stress was evaluated by chemiluminescence in saphenous vein segments (SV) from the CABG patients. Patients were genotyped for two functional SNPs (rs4673 & rs1049255) in the CYBA gene (NADPH-oxidase subunit β2/2phox).

**Results:** Telomere shortening and oxidative stress were associated with shortened TL 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.

**1835 | BENCH**

Neureguline-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. Cellular senescence, a state of irreversible cell cycle arrest, is described as an important aging-conductor due to accumulation of damaged cells. Targeting cellular senescence can be a new approach to prevent or treat age-related cardiovascular diseases. In this study, we investigated the effect of neureguline-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 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 vivo and in the aorta of diabetic mice in vivo.
ilar 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

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Background: It is known that glucose disturbances contribute to vascular aging. 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 58.4±7.3 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 marked by interleukin-6 (IL-6), C-reactive protein (CRP), fibrinogen; arterial stiffness (AS) evaluated by carotid-femoral pulse 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 (97.5): “short” telomeres and “long” telomeres. Vessels changes were more pronounced in patients with “short” TL: PWV 14.1±3.2 mm/s vs. 11.7±3.26 mm/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 3.43±1.06 mmol/l vs. 2.94±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: PWV (r=−0.30, p=0.0003), IMT (r=−0.39, p=0.0006), FMD (r=−0.49, p=0.0003), NDV (r=−0.41, p=0.0004), FPG (r=−0.42, p=0.0003), CRP (r=−0.40, p=0.0044), TA (r=−0.32, p=0.035).

Then patients were divided into 2 groups by the median of TA (0.33): “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

1839 | BEDSIDE
Enhanced platelet toll-like receptor-2 and 4 expression in acute coronary syndrome

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Background: Evidence is accumulating that Toll-like receptors (TLR) are involved in the initiation and progression of cardiovascular disease. Of TLRs, TLR-2 and 4 have been studied most extensively. Enhanced expression of these receptors on monocytes has been shown in patients with acute coronary syndrome (ACS) in recent studies. However, expression on platelets in this group of patients has not been evaluated yet.

Purpose: We aim to demonstrate the possible role of platelet TLR-2 and 4 expression on ACS pathogenesis.

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).

Conclusions: Spotty calcification, especially when superficial in location, is a marker of vulnerable plaque in survivors of cardiac arrest and autopsied patients of SCD.
Methods: 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, 60.7±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 control [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
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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) was 2.10±0.69 in AS-patients, as compared to 1.80±0.60 in controls (p=0.096). Coronary flow velocity reserve (CFR) 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 1.86±0.45 (p=0.050). CFR increased significantly from 1.9±0.4 to 2.2±0.6 (p=0.009) (Figure 1).

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.

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### 1843 | BEDSIDE

**A healthy lifestyle is strongly related to an increased heart rate variability in healthy adults**

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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 Lebanese American University, Beirut, Lebanon; 5 University Hospital Basel, Department of Internal Medicine, Basel, Switzerland

**Background:** The combined influence of a healthy lifestyle on heart rate variability (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 deviation (SD) of 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, a BMI <25kg/m², consuming >5 servings of fruits or vegetables per day, performing physical activity >150 minutes per week, having a systolic and diastolic blood pressure <120 and <80mmHg without using antihypertensive 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 cardiovascular 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 individuals 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 (−8.55; 8.42), 6.90 (0.20; 13.79), 14.99 (8.18; 21.79), 20.39 (13.28; 27.50) and 24.60 (15.39; 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 relationship was attenuated but remained significant after additional adjustment for conventional HR (β-estimate (95% CI) 3.48 (2.30; 4.66), p<0.001) and was even more 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 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.

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### 1844 | BEDSIDE

**Threshold of ambient particulate matter level for increasing heart failure incidence may be lower than national standard**

Q. Huyhn, 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 linearly associated with acute increase in ambient air pollution. However, it is unclear whether there is a threshold level of particulate matter <2.5μm (PM2.5) to the increase in HF incidence. We sought to answer this research question by performing a time-series analysis of the relationship between daily PM2.5 level and HF admission rates in Tasmania, which is one of the world’s cleanest air qualities.

**Methods:** This Tasmanian statewide data linkage included all patients with a first-ever HF hospitalization during 2009–2012. Daily temperature and PM2.5 level were also recorded during this period. Poisson regression was used, with adjustment for time-trend, public and school holidays, day of week, average temperature, flu infections and relative humidity.

**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 period. 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 predictive of HF incidences (RR=1.14 [0.53, 2.47]). The entire study period was divided into nine periods of approximately 100 days each, based on PM2.5 concentration (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 incidences, 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.

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### 1845 | SPOTLIGHT

**Dose and time dependent associations of smoking to incident subarachnoid hemorrhage in men and women**

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**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 using independent, random, and representative population samples from different geographical areas of Finland, provided the risk factor data recorded at enrollment 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, hypertension, cholesterol, study year and area, provided the hazard ratios (HRs). We used a likelihood ratio test (LRT) to evaluate the significance of the interaction 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 smoked. 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 3.8–17.6) and 3.6% (95% CI 2.0–6.3). The difference between HRs by sex was significant in all cigarette-per-day categories (LRT p<0.001). 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 (0–5), the risk of SAH increased in women with a HR of 3.8 (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 smoked 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.

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**YOUNG INVESTIGATORS AWARDS SESSION: CLINICAL SCIENCE**

### 1886 | 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**

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**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 receptor 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 identified all patients with AS from 1997 to 2012. Patients receiving ACEI or ARB treatment at baseline were matched on propensity score with controls not receiving
ing treatment. Risk of all-cause mortality, cardiovascular mortality or AVR was 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) were baseline-identified and matched with 11 560 patients non-treated (mean age 76.3 years [SD 11.5], 48.7% male). During follow-up, a total of 2592 (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).

**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.

1847 | BEDSIDE
**Low cardiorespiratory fitness predicts arrhythmia recurrence in patients with symptomatic atrial fibrillation**

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**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 (≤ 90%), MOD (90–110%) 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.

1848 | BEDSIDE
**Sudden death in sport: insights from a national pathology referral center**

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**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 ≥ 29 ± 11 years, males 92%, Caucasian 76%) of individuals who engaged in regular sport activities during their lives, 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 unexplained death syndrome [SADS]), with differences according to age: a normal heart was present in 56% of adolescents and children (<18 years), 44% of young adults (18–35 years) and 26% of older (>35 years) individuals (P < 0.001 between <18 and >35, P = 0.004 between 18–35 and >35). Patients characterized by left ventricular (LV) fibrosis were significantly older (32 ± 12 vs 25 ± 11 years, P < 0.001), more characterized by a family history of SD (12/7 vs 7%, P = 0.05) and by a higher heart weight (478 ± 103 vs 377 ± 105 g, P < 0.001). Death occurred during exertion in 219 cases (61%). Presence of LV fibrosis and arrhythmogenic right ventricular 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% CI 1.97 to 18.32, P = 0.001; HR 2.11 95% CI 1.15 to 3.86, P = 0.001 and HR 0.96 95% CI 0.95 to 0.97, P = 0.002 respectively).

**Conclusions:** SD in athletic population is caused by variable aetiologies according to different age and it occurs more frequently during exertion. ARVC and LV fibrosis are the most important correlates of death during exertion. A better understanding of the substrate underlying SD in athletic individuals and circumstances of death is needed in order to select patients that may be at higher risk with possible implications for sports participation.

1849 | BEDSIDE
**Subclinical left ventricular dysfunction is associated with reduced brain structure and function**

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**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 (CISD). Hippocampal volume was measured by MRI. Fasting bloods including NT-proBNP levels were measured.
Conclusions: PDGF-BB facilitates non-canonical Smo-dependent Shh signaling measured in Fluo-4-loaded ventricular myocytes isolated from cardiomyocytes-mediated by strongly enhanced activity of the protein kinase A (PKA) and could fixing of Smo to the plasma membrane of AoAF but not in SMC. This effect was (SMC). Importantly, proliferation and migration of AoAF were strongly augmented migration of human adventitial fibroblasts (AoAF) and human smooth muscle cells 3 weeks after injury compared to sham-operated controls. In vitro, Shh induced proliferation and smoothened (Smo) were robustly increased in adventitial cells after exclusion of Gli-dependent transcription pathways excluding Gli-1-dependent transcription.

Methods and results: We analysed the effects of Shh on vascular remodeling processes and described transdifferentiation 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 adventitial cells, whereas the expression of its membrane-bound downstream proteins patched-1 (Ptc-1) and smoothened (Smo) 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 Smo inhibitor GDC-0449 (Vis modegib) significantly prevented the proliferative and migratory response of AoAF but not in SMC. Mechano-chemically, we found that PDGF-BB selectively induced trafficking of Smo 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 PAK resulted in a down-regulation of target genes of the Shh dependent transcription factor Gli1, as assessed by initial microarray analysis and subsequent qPCR and immunoblotting. Following wire-injury induced in C57BL/6 mice, perivascular application of GDC-0449 via a self-degrading Pluronic®-127 Gel significantly reduced neointima formation and proliferation of adventitial and neovascular cells (luminal surface 63.47±10.35% vs. 18.09±5.44%, n=6, P<0.01).

Conclusions: PDGF-BB facilitates non-canonical Smo-dependent Shh signaling in AoAF but not in SMC and thereby promotes AoAF proliferation and migration. The specific Smo inhibitor GDC-0449 impedes these effects in vitro and prevents neointima formation. Therefore, these data highlight the importance of adventitial cells and Shh signaling in vascular proliferative diseases.

1851 | BENCH Platelet-derived growth factor-BB selectively augments non-canonical sonic hedgehog signaling in adventitial fibroblasts J.-M. Daniel, J. Dutzmann, 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 adventitia, however, the signaling pathway containing the transcription factors and non-canonical pathways excluding Gli-dependent transcription.

Purpose: We analysed the effects of Shh on vascular remodeling processes and described transdifferentiating 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 adventitial cells, whereas the expression of its membrane-bound downstream proteins patched-1 and smoothened (Smo) 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 Smo 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 Smo 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 PAK resulted in a down-regulation of target genes of the Shh dependent transcription factor Gli1, as assessed by initial microarray analysis and subsequent qPCR and immunoblotting. Following wire-injury induced in C57BL/6 mice, perivascular application of GDC-0449 via a self-degrading Pluronic®-127 Gel significantly reduced neointima formation and proliferation of adventitial and neovascular cells (luminal surface 63.47±10.35% vs. 18.09±5.44%, n=6, P<0.01).

Conclusions: PDGF-BB facilitates non-canonical Smo-dependent Shh signaling in AoAF but not in SMC and thereby promotes AoAF proliferation and migration. The specific Smo inhibitor GDC-0449 impedes these effects in vitro and prevents neointima formation. Therefore, these data highlight the importance of adventitial cells and Shh signaling in vascular proliferative diseases.

1851 | BENCH CASK is an important regulator of cardiac excitation-contraction coupling J. Mustroph1, S. Gupta1, A. Dietz1, F. Baberi1, T. Islam1, A. El-Armouche1, L.S. Maier3, S. Wagner1. 1Dept. Cardiology, University Medical Center, Goettingen, Germany; 2Technical University of Dresden, Department of Pharmacology and Toxicology, Dresden, Germany; 3University 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 control (NF). CASK was robustly expressed in the heart. Interestingly, CASK expression (relative to GAPDH) was significantly increased in DCM vs. NF (densitometric values: 0.89±0.05 vs. 0.7±0.05, n=6 each, P<0.05). Intracellular Ca was measured in Flu-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 vs. 3.84±1.5, 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, 4.83±1.8 vs. 6.1±1.6, n=21 vs n=26, P<0.05). KO myocytes also showed a delayed Ca transient decay, a functional measure of SR Ca ATPase. Ca transient decay RTB0 was 0.41±0.15 vs. 0.31±0.13 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, WT, 158.3±49.2 vs. 32.4±7.6, n=34 vs n=24, P<0.05). Late Na current, known to be enhanced by CaMKII, was also increased in KO vs WT (whole-cell patch clamp). Late iNA integrals were -98.3±35.1 vs. -55.1±33.7 A/mF at 10V (KO vs WT, n=10 vs n=10). ApoA-I (apoA-I apolipoprotein in vivo apoA-I) and its fragment apoA-I delta6, and 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. Costantin1, F. Paneni1, L. Berrino1, M. Volpe1, T.F. Luscher1, F. Cosentino1. 1Karolinska Institute, Cardiology Unit, Stockholm, Sweden; 2Second University of Naples, Pharmacology Naples, Italy; 3Sapienza University of Rome, Department of Clinical and Molecular Medicine, Rome, Italy; 4Cardiovascular Research, Physiolog...
Background:
The increasing survival of children with congenital heart disease (CHD) provides a challenge to health care systems about how to deal with the influence of childhood socioeconomic disadvantage in the incidence of myocardial response to stretch in both animals and humans. Titin phosphorylation increased significantly over the 15 minutes following myocardial stretch in both human (11±1% vs 41±8% in atrium and 27±8% vs 71±21% in ventricle muscles) and rabbit (13±2% vs 23±3%) muscles.

Discussion:
The progressive decrease in myocardial stiffness after acute haemodynamic overload seems to depend on PKG activity, which represents potential therapeutic target in patients with pathologically rigid myocardium. Moreover, a decrease in myocardial stiffness was attenuated by 40% after PKG inhibition. Isolated NO scavenging and NPr-A antagonism did not modify the adaptive diastolic response to stretch. However, a significant (29%) blunting of the effect was observed when the three interventions were exerted simultaneously. Titin phosphorylation increased significantly over the 15 minutes following myocardial stretch in both human (111±6% in atrium and 27±8% vs 71±21% in ventricle muscles) and rabbit (13±2% vs 23±3%) muscles.

Results:
The progressive decrease in myocardial stiffness after acute haemodynamic overload seems to depend on PKG activity, which represents potential therapeutic target in patients with pathologically rigid myocardium. Moreover, a decrease in myocardial stiffness was attenuated by 40% after PKG inhibition. Isolated NO scavenging and NPr-A antagonism did not modify the adaptive diastolic response to stretch. However, a significant (29%) blunting of the effect was observed when the three interventions were exerted simultaneously. Titin phosphorylation increased significantly over the 15 minutes following myocardial stretch in both human (111±6% in atrium and 27±8% vs 71±21% in ventricle muscles) and rabbit (13±2% vs 23±3%) muscles.

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 in the incidence of CVD in a Chilean cohort, and before and after adjustment for risk factors and other covariates.

Methods:
The longitudinal analysis of a representative sample of Chilean adult population use 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) and adulthood (years of education, 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 (PROC GENMOD, SAS, 9.1)-link functions, 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 44.5% 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%. Multivariate analysis showed age-adjusted RRs=1.08. CI 1.04 to 1.13 for low SEP in childhood. After adjusting for risk factors the effect of low SEP remains significantly (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: FONIS (governmental grant)
Results: Kappa statistics for the agreement of the hospital modified-HEART score were assessed using Cohen’s Kappa. The hospital HEART score was established using medical records. Both the ambulance- and hospital-based triage were assessed using the modified-HEART score agreement were assessed using Cohen’s Kappa. Ambulance nurses tend classify chest pain patients in a higher category than in hospital. No patients assessed as high risk in-hospital were assessed as low risk by ambulance nurses.

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>0</td>
</tr>
<tr>
<td>Ambulance modified-HEART score</td>
<td></td>
</tr>
<tr>
<td>Low risk (0–3)</td>
<td>27</td>
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<tr>
<td>Intermediate risk (4–6)</td>
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<td>High risk (7–10)</td>
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</tr>
<tr>
<td>Total</td>
<td>254</td>
</tr>
</tbody>
</table>

Conclusions: Pre-hospital triage of patients with acute onset chest pain by ambulance nurses, using the modified-HEART score 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

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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, both 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 vitro 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 regulation of neointima formation reduction. A central role for miR-126 in MPs in the regulation of vascular health. 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

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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 TF, the human TF gene, is complex and needs to be explored further.

Purpose: To investigate if miRNAs (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 was performed, and we 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 (Reliance of Biomarkers for future risk of thromboembolic events in Uh 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 TF, the human TF gene, is complex and needs to be explored further.

Conclusion: MiR-223-3p post-transcriptionally regulates the expression of F3, the human tissue factor gene, and TF expression in acute coronary syndrome.
bone marrow cells displayed a comparable phenotype to global miR-155 knockout data implicated that the defective phenotype of miR-155 deficient mice follows direct targeting of suppressor of cytokine signaling (SOCS-1) by miR-155. These controls. Consistent with these results, we also found an impaired pro-arteriogenic capacity of bone marrow derived macrophages (BMDM) compared to wildtype controls. It's direct target gene angiotensin II type 1 receptor.

Surprisingly, miR-155 deficient mice showed an unexpected phenotype in vivo its direct target angiotensin II type 1 receptor. MicroRNA-155 exerts cell-specific anti-angiogenic but pro-arteriogenic vessel stabilization properties of ECs.

Adaptive neovascularization after arterial occlusion is an important for the angiogenic potential of ECs–as targets of miR-143 and miR-145, also identified hexokinase II (HKII) and integrin beta 8 (ITGb8)–two genes essential for the angiogenic potential of ECs–as targets 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 from SMCs to ECs and another. We report here 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 (TGFb) pathway, since a specific TGFb inhibitor (SB431542) suppressed 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 1 (ITGb1)–two genes essential for the 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 TGFb and vessel stress transduction of miR-143/145 transfer from SMCs to ECs.

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.

3p which are associated with angiogenesis were significantly up-regulated and the significantly up-expressed and highly enriched miRNAs were certified both in splenic DCs of MI mice was analyzed by Affymetrix miRNA 4.0 chip assays, respectively (as necrosis or control group). Exosomes isolated from the supernatant of BMDCs (DEXs) then added to primary cultured rat cardiac microvascular endothelial cells (HUV-ECs) had a stimulatory effect on proliferation and angiogenic tube formation via de-repression of its direct target gene angiogenin II type 1 receptor.

inhibitors, of Umbilical vein endothelial cells (HUVECs) had a stimulatory effect on proliferation and angiogenic tube formation via de-repression of its direct target gene angiogenin 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). This was observed in the supernatant of infiltrating circulating cells as well as an arteriogenic potential of the pro-angiogenic cytokine TNF-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 (BMMs) 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 knockout mice but transplantation of wildtype cells was not sufficient to rescue phenotype of 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 AGTR1.

To determine whether SMCs control EC functions through passage of CMPCs exosomes that are different in molecular composition to other cell types, including smooth muscle cells (SMCs), bone marrow-derived macrophages (BMDM), microvesicles (SMVs) and cardiomyocytes (CMs).

Background: Exosomes are small nanosized vesicles carrying cell-specific content including miRNAs, mRNAs and proteins. They have been suggested to be involved in the intercellular communication.

Methods: Exosomes were isolated from CMPC-conditioned medium by differential centrifugation. The presence of EMMPRIN knockdown exosomes was assessed by NanoSight, sucrose-gradient separation and Western Blotting.

Conclusion: EMMPRIN knockdown exosomes was markedly reduced compared to migration and sprout formation in vitro. The functional involvement of EMMPRIN was assessed by using an EMMPRIN neutralizing antibody and by knockdown of EMMPRIN in the donor CMPCs and their secreted exosomes. EMMPRIN knockdown exosomes are characterized by a specific size (50–100 nm) and marker expression (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 inhibition of exosome-stimulated endothelial cell migration. Knockdown of EMMPRIN in CMPCs efficiently reduced the migration of endothelial cells (45.1% vs 61.8% scratch closure) in vivo. In vivo migraft plug assays, migration of endothelial cells with EMMPRIN knockdown exosomes was markedly reduced compared to 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 CMPC-derived exosomes, of which one is the extracellular matrix metalloproteinase inducer (EMMPRIN). EMMPRIN plays an important role in angiogenesis by inducing the expression of pro-angiogenic factors and promoting extracellular matrix modulations 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.

Methods: Exosomes were isolated from CMPC-conditioned medium by differential centrifugation. The presence of EMMPRIN knockdown exosomes was assessed by NanoSight, sucrose-gradient separation and Western Blotting.
highly enriched in DEXs from necrosis group compared to those from control group.

**Conclusions:** These results suggest that exosomal miRNA especially angiogenetic 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**

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**Objective:** Endothelial microparticles (EMP) are released from activated or apoptotic 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 in pathological hyperglycaemic conditions, EMP-mediated miR-222-dependent anti-inflammatory effects are reduced.

**Conclusions:** We show for the first time that Nigericin and ATP, two established inflammasome activators, lead to inflammation activation and release of microparticles by vascular cells. Furthermore, we could demonstrate that these microparticles, when given to other vascular cells, cause cell death accompanied with reduced cell migration and proliferation.

**1960 | BENCH**

**Infammasome-induced intercellular signalling mechanisms via microparticles**

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**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 1μg/mL LPS 4h and subsequently stimulated with either 5μM ATP or 20μM Nigerin, 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 Nigerin for 8h (Mean: 37107±6727 MMP/μl). Highest EMP-release by HCAEC was detected after stimulation with ATP for 8h (Mean: 7912±1074 EMP/μl) and Nigerin for 48h (Mean: 6586±6594 EMP/μl). Inflammasome activation in THP-1 cells using ATP and Nigerin was confirmed by the release of IL-1β into the cell supernatant (ATP: Mean: 80±2.6 pg/ml; Nigerin: 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 20μM Nigerin (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 Nigerin, 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 20μM Nigerin for 48h lead to significant cell death shown by Viability Assay (Mean: 72% ± 6.62% Cell Viability). Furthermore, treatment of HCAEC with EMP derived from HCAEC treated with 1μg/mL LPS for 4h and subsequent treatment with 20μM Nigerin for 48h lead to reduced cell migration and proliferation shown by Scratch Assay (73% cell free area after 24h).

**Conclusions:** These findings demonstrate that caveolin-1 play an important role in miR33 regulated lipid metabolism, and may identify a new target for enhanced cholesterol efflux and atherosclerosis treatment.

**1961 | BENCH**

**Mir-33 antagonism increase cholesterol efflux and atheroma regression by transeing caveolin-1 expression in hypercholesterolemia rabbits**

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**Introduction:** Mir-33 embedded within introns of the SREBP gene, inhibits the expression of ApoA1, 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 J744 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, J744 cells were loaded with 100 μg/mL cholesterol in DMEM, incubating the cells for 24–48 h at 37οC, than transfected with 60M miR33 antagonism.

**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 enhanced cholesterol efflux and atherosclerosis treatment.
BLED scheme offers useful predictive capacity over other published schemas, Of the contemporary bleeding risk stratification schemas, the HAS-BLED score performed best in multivariate analysis, with a stepwise increase in rates of major bleeding (HR 1.27, 95% CI 0.98–1.7, P=0.07). HEMORR2HAGES was also an independent predictor of GI bleeding as a continuous and categorical variable (P=0.01). HEMORR2HAGES and ATRIA scores were not independent predictors of ICH.

### Results

**Predicted probability of 66 years old men**

<table>
<thead>
<tr>
<th>Event</th>
<th>Dabigatran</th>
<th>Warfarin</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidences</td>
<td>220/453 (51%)</td>
<td>183/773 (24%)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Odds ratio and 95% confidence intervals</td>
<td>2.9 (2.3–3.8)</td>
<td>1.0 (ref)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Predicted probability of 66 years old men with hypertension</td>
<td>61.8%</td>
<td>27.3%</td>
<td></td>
</tr>
<tr>
<td>Predicted probability of 66 years old women with hypertension</td>
<td>69.7%</td>
<td>32.1%</td>
<td></td>
</tr>
</tbody>
</table>

**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.

#### Time to cardioversion and risk of complications with dabigatran versus warfarin A nationwide study

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**Background:** Dabigatran is an alternative to warfarin as anticoagulation therapy in cardioversion of patients with non-valvular atrial fibrillation. Patients on apixaban incurred lower costs overall ($3,581) compared to those on dabigatran ($4,236; P <0.0001) and rivaroxaban ($4,144; P <0.0001).**

**Conclusions:** In a real world nationwide population of US patients, treatment with dabigatran was associated with lower risk of bleeding and hospitalisation as well as lower healthcare costs compared to other NOACs in anticoagulant naïve NVAF patients.

**Acknowledgement/Funding:** Bristol-Myers Squibb

#### Major bleeding, hospitalisation rates and healthcare costs among non-valvular atrial fibrillation patients naïve to oral anticoagulation and newly treated with novel oral anticoagulants

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**Background:** There is little evidence documenting the effectiveness and safety of novel oral anticoagulants (NOACs) in a real-world setting. This real-world study provides an early assessment of bleeding, all-cause hospitalisation and economic outcomes among a US nationwide sample of non-valvular atrial fibrillation patients (NVAF) patients initiating oral anticoagulant treatment with a NOAC.

**Purpose:** Examine the time to cardioversion and risk of subsequent cardiovascular complications in patients treated with dabigatran or warfarin.

**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] 2.7–5.1) 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 dabigatran. The cumulative incidences of stroke, bleeding or death were 0.8% and 1.7% at 30 days. **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.

#### Predicting intracranial bleeding risk in patients with atrial fibrillation

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**Several clinical risk factors have been incorporated into clinical risk stratification schemes to identify a higher risk of ICH.** Of 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 87711052 days. We compared the predictive value of the HAS-BLED score with 2 other bleeding risk scores (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<0.02) with increasing HAS-BLED risk category. HEMORR2HAGES and ATRIA scores were not independent predictors of ICH neither as continuous nor as categorical variables. For GI bleeding, the HAS-BLED score also performed best in multivariate analysis with a stepwise increase in rates of major bleeding increasing risk in patients (HEMORR2HAGES: CI 1.28 95% CI 1.06–1.55, p<0.01). HEMORR2HAGES was also an independent predictor of GI bleeding as a continuous (but not as a categorical) variable and ATRIA scores was not an independent predictor of GI bleeding neither as continuous nor as categorical variable.

**Conclusions:** Of the contemporary bleeding risk stratification schemas, the HAS-BLED scheme offers useful predictive capacity over other published schemas, simultaneously for severe bleeding, ICH and GI bleeding and may be simpler to apply.
or surgical consultation was more common among patients with NM bleeding on apixaban vs. warfarin (78.8% vs. 70.1%; p < 0.0001); a change in antithrombotic therapy (58.6% vs. 50.0%; p < 0.0001) and permanent study drug discontinuation (5.1% vs. 3.6%; p = 0.102) were more common with warfarin than apixaban.

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

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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

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Background: Renal impairment confers an increased risk of stroke, death, and bleeding in anticoagulated 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, 18,071 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 (SEE), mortality, and major bleeding increased with reduced renal function and displayed the highest event rates with eGFR deterioration >20% with HR (95% CI) of 4.16 (2.91–5.94), 7.09 (5.75–8.74), and 5.80 (4.37–7.69), respectively, vs. patients with stable eGFR >80. Irrespective of renal function over time apixaban compared to warfarin reduced stroke or SEE, mortality and major bleeding (Figure).

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.

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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

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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 01/01/2013–31/10/2014 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), and any bleeding while dabigatran appears to decrease the risk of major, CRNM, and any bleeding while dabigatran compared to apixaban and dabigatran compared to rivaroxaban 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 CHA2DS2-VASc 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).

Conclusion: 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.

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Association between atrial fibrillation and risk of seizure disorder: the usefulness of CHADS2 Score for risk stratification

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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, on the risks of development of seizure disorder in a nationwide, population-based cohort database in Taiwan.

Methods: Our analyses were conducted using information from a random sample of 0.5 million people enrolled in the nationally representative Taiwan National Health Insurance Research Database. A total of 11,552 subjects aged 18 years or above, including 5,776 subjects diagnosed with AF during the study period and an age-sex-matched 5,776 subjects without AF were enrolled in our study.

Results: During a 10-year follow-up, new onset seizure events occurred in 235 patients. By comparison, the AF group had a higher incidence rate of seizure occurrence. Cox proportional hazard regression model analysis showed that development of AF was independently associated with higher risk of developing future epilepsy (HR: 2.29 [95% CI, 1.73–3.04; p < 0.001). In multivariate Cox regression analysis adjusted for potentially confounding variables, a higher CHADS2 score was associated with a higher risk of epilepsy occurrence in a dose dependent manner (figure 1).
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 concurrent AF, and the proportion of patients requiring NOAC cessation or dose reduction according to prescribing guidance.

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 investigators 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 GFR 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 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, a priori 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 progresses, and would frequently mandate dose reduction or cessation of NOACs. Baseline renal function, the method of estimating GFR, and intensity of monitoring should be considered when commencing oral anticoagulation. Just as warfarin required organized systems of care, so too must health systems adapt to the new challenges of NOACs.

1978 | BEDSIDE
A telemedicine-based coagulation service versus regular medical care for oral anticoagulation of patients with atrial fibrillation - results from the thrombEVAL study
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Background: Oral anticoagulation therapy (OAC) with vitamin K antagonists (VKA) in patients with atrial fibrillation requires challenging drug management to prevent major bleeding. The risk for adverse events in patients treated with a telemedicine-based coagulation service may be useful to achieve a better quality of treatment.

Purpose: To examine the clinical outcome between patients with atrial fibrillation treated in regular medical care (RMC) and patients treated in a telemedicine-based coagulation service (CS) from the thrombEVAL trial (NCT01890915).

Methods: Data were obtained from clinical visits, computer-assisted personal interviews, self-reported data and laboratory measurements according to standard operating procedures with detailed quality control. Study monitoring was carried out by an independent institution; information on study endpoints was validated by medical records and adjudicated by a review committee.

Results: The samples comprised 1,137 individuals in RMC and 483 individuals in CS. Median follow-up time was 12.0 (11.8/12.0) and 14.8 (7.9/19.7) months respectively. The primary study endpoint (composite of thromboembolic events, major and clinically-relevant non-major bleeding, and death) differed significantly between both cohorts with 16.4 in RMC vs. 7.4 events per 100 patient-years (py) in CS (risk ratio: 2.2, 95% CI 1.5/3.2; p<0.001). Analysis of safety outcome (i.e. major and clinically-relevant non-major bleeding) demonstrated a substantially higher rate of bleeding events in RMC (11.4 per 100 py) than in CS (3.9 per 100 py; risk ratio 3.0, 95% CI 1.8/5.0; p<0.001). Thromboembolic events were approximately 30% more frequent in the RMC cohort, although they did not differ significantly (risk ratio 1.3, 95% CI 0.6/2.8; p=0.6). Hospitalization was 2.7 times more frequent in RMC (95% CI 2.3/3.2; p<0.001) and all-cause mortality 4.7 times more frequent for RMC vs. CS (95% CI 2.7/8.8; p<0.001). In Cox regression analysis with adjustment for age, sex, traditional cardiovascular risk factors and comorbidities, a significantly-increased risk for major and clinically-relevant non-major bleeding as the index outcome: the hazard ratio for the primary study endpoint was 2.7 (95% CI 1.6/4.6), for hospitalization 2.4 (95% CI 1.9/3.1) and for all-cause mortality 7.0 (95% CI 3.0/16.0; for all p<0.001).

Conclusions: Patients with atrial fibrillation, management of oral anticoagulation therapy with VKA in a telemedicine-based coagulation service substantially improved the clinical outcome. This specialized care model inherits great potential to improve outcome and should be evaluated for a translation to new drugs for oral anticoagulation.

Acknowledgement/Funding: Ministries of Health and Economics, Rheinland-Palatinate, Germany; Federal Ministry of Education and Research, Germany

1979 | BEDSIDE
Risk vs. benefit of anticoagulation therapy in elderly patients with atrial fibrillation and documented ground-level falls

Introduction: Patients with atrial fibrillation have a five-fold increased risk of stroke, which can be effectively reduced with oral anticoagulant therapy. However, elderly patients with atrial fibrillation and tendency to ground-level falls are often deprived of the treatment for 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 includes 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 Clopper-Pearson method was used for the exact two-sided confidence intervals for single proportion, and 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 VAF 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% (95% CI = 0.03% to 7.79%).

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
Impact of the environment on anticoagulation in non-valvular atrial fibrillation / What is new in aortic valve disease

1980 | BEDSIDE
Outcome of TAVI in Patients with Paradoxical Low-Gradient Aortic Stenosis: Results from a Multicenter Registry

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Objective: Patients with severe aortic stenosis (AS) may present with a mean transvalvular aortic gradient (MPG) >40 mmHg due to a reduced stroke volume despite preserved ejection fraction (paradoxic) low-flow, low-gradient, PLF-LGAS.

Here we analysed the procedural and clinical outcome of patients undergoing transcatheter aortic valve implantation (TAVI) for PLF-LGAS (stroke volume index [SVI] <35ml/m2, MPG >40 mmHg) versus high-gradient AS (HGAS; MPG >40 mmHg) based on data from 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 (14.8%); MPG: 27.1±8.3 mmHg; SVI: 26.9±5.4ml/m2 and n=776 (55.7%); MPG: 54.8±20.9mmHg; SVI: 37.5±11.3mm2/m2 patients, respectively. EuroScoreI (27.6±1.57 vs. 24.09±13.5; p<0.001) and postoperative 30-day mortality was 13.1±5.9 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%).

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 exception worse for the PLF-LGAS group (1-year mortality 42.2% vs. 30.7%, p<0.001). The reduction in left ventricular (LV) afterload associated with a significant reduction of MPG from 47.6±13.8mmHg to 37.9±11.8mmHg (p<0.001) and a decrease in LV mass index from 110.4±11.8g/m2 to 97.7±10.9g/m2 (p<0.001) were noted.

Conclusion: Paradoxical low gradient AS (PLF-LGAS) is associated with a significant functional benefit with improvement of NYHA-class and increased 9-month walking distance.

1981 | BEDSIDE
Aortic valve gradient and clinical outcome in patients undergoing transcatheter aortic valve implantation for severe aortic stenosis

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Background: Patients and low-flow gradient severe aortic stenosis (LEF-LGAS Severe AS) have increased Cardiovascular mortality following transcatheter aortic valve implantation (TAVI) as compared with patients with high aortic valve gradient. However, data on the relation between aortic valve gradient (AVG) as a continuous variable and clinical outcome after TAVI are limited.

Methods: We analyzed data on 319 consecutive patients with severe AS that underwent TAVI at our institution from 2008 through 2014. We investigated the relation between AVG as a continuous variable and outcome among all patients and in subgroups of patients without LEF-LGAS severe AS, using the Cox proportional hazard model adjusting for multiple prognostic variables.

Results: Patients had a peak AVG of (mean ± SD) 80±23 mmHg, mean AVG of 50.2±15.9 mmHg, and aortic valve area of 0.64±0.16 cm2. During a mean follow up of 1.9 years, baseline AVG was inversely associated with mortality and with cardiac hospitalization or death after TAVI. Every 10 mmHg increase in baseline mean AVG was associated with 20% reduction in mortality (Hazard ratio [HR] 0.80, 95% confidence interval [CI] 0.67-0.92, p=0.021), and 22% reduction in cardiac hospitalization or death (OR 0.78, 95% CI 0.67-0.92, p=0.003). Consistently, every 10 mmHg increase in peak AVG was associated with 15% (p=0.014) and 17% (p=0.002) reduction in mortality and cardiac hospitalization or death, respectively. By subgroup analysis of patients with left ventricular ejection fraction (LVEF) <40%, mean AVG -35 mmHg and peak AVG -60 mmHg yielded similar results (HR 0.778 p value 0.0173, HR 0.758 p value 0.0327 and HR 0.757 p value 0.0253 for patients with EF <40%, Mean AV gradient <35 mmHg and Max AV gradient <60mmHg, respectively). Aortic valve area as a continuous variable was not correlated with clinical outcome.

Effect of AVG gradient on survival

<table>
<thead>
<tr>
<th>Outcome</th>
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<th>Estimate</th>
<th>CI</th>
<th>p value</th>
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<tbody>
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<td>Death</td>
<td>AVG mean</td>
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<td>0.670–0.968</td>
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<td></td>
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<td>0.581</td>
<td>0.135–2.509</td>
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</tbody>
</table>

Conclusions: Both mean and peak baseline AVGs are directly associated with improved survival post TAVI, independent of EF or the presence of LEF-LGAS Severe AS, suggesting that AVG can be used to select patients most likely to benefit from TAVI.

1982 | BEDSIDE
Impact of transcatheter aortic valve replacement (TAVI) on severity of concomitant mitral regurgitation, pulmonary artery pressure and tricuspid regurgitation

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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 midterm 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 grade II. Patients with severe AS (LVEF ≤ 40%, mean AV gradient ≥ 40%, Mean AV gradient ≥ 35 mmHg, or peak AV gradient ≥ 60 mmHg yielded similar results) were included in this analysis. In this subgroup, the mean transvalvular gradient was decreased during TAVI from 40.7±16.8mmHg to 10.2±4.7mmHg (p<0.001).

Conclusion: 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.
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


**Background:** Usefulness and prognostic value of natriuretic peptides in aortic stenosis is still debated.

**Methods:** Patients with AS enrolled between 2006 and 2013 in 2 ongoing prospective studies constituted our cohort. Clinical, biological measurements including 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 (sudden 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-

**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


**Background:** Atrial fibrillation (AF) and new-onset atrial fibrillation (NOAF) predict 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 undergoing 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-

**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-

**1986 | BEDSIDE**

Predictors of mortality in patients with aortic stenosis: the role of myocardial fibrosis

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**Purpose:** Myocardial tissue characterization with cardiovascular magnetic reso-

**Conclusion:** 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-

Conclusion: Echocardiography overestimates aortic stenosis severity in patients with bicuspid aortic stenosis due to inaccuracies in the measurement of LVO extra and stroke volume consequently, theAVA.

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


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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 cTnI 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 502 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 an MI based on hs-cTnI with 90% 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: 0.5% vs. 8.1% based on CK-MB; TA-AVI: 22.2% vs. 99.5% p<0.001). In TF-AVI patients, every 1000 ngL hs-cTnI rise after TAVI increased the risk of in-hospital mortality by 6.5% (CI 95% 0.3–13%, P=0.03), and every 10 g/L rise in CK-MB increased the risk by 2.9% (95% 0.2–5.5%, P=0.02). These biomarkers were without long-term predictive value, however, in TA-AVI patients. In TA-AVI patients, no other hs-cTnI nor CK-MB were of predictive value.

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)

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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 antplatelet therapy in patients with atrial fibrillation and TAVI. Therefore the compatability, 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 ASSs, 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 compared to patients with VKA. Also a single therapy with DOAC after TAVI in patients with atrial fibrillation is safe and does not lead to an increasing degree of thrombotic complications. Taken together, a DOAC single therapy after TAVI for patients with atrial fibrillation seems to have advantages for the outcome but this presumption should be verified by larger prospective trials.

PREMATURE CARDIOVASCULAR AGING

2013 | BEDSIDE
Glycemic excursions trigger senescence-associated pathways and vascular ageing features in patients with type 2 diabetes

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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 investigated whether 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 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 (MAGE) and post-prandial incremental area under the curve (AUCpp). Pulse pressure (PP), a well-established marker of vascular ageing, 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 mononuclear cells, and expressed as fold change (FC).

Results: Patients with and without GE did not differ for age (62±8 vs. 61±14 years, p=N.S, respectively), gender (F:M, 7:5 vs. 6:6, p=N.S, respectively), BMI (27±3 vs. 29±5 kg/m², p=N.S, respectively), diabetes duration (13±11 vs. 15±10 years, p=N.S, respectively), CV risk factors and glucose-lowering medications. PP was significantly higher in patients with GE than in patients without GE (PP 81±13 vs. 74±12 mmHg, p=0.05). Profiling of senescent-associated genes showed that Telomerase Reverse Transcriptase (TERT), responsible for telomere ends maintenance, was markedly downregulated in T2D patients with GE (FC= −15.2, p<0.05) and increased cardiovascular disease (CVD) risk, even after intensive glycemic control targeting glycated haemoglobin (HbA1c) levels.

Results: Patients with and without GE did not differ for age (62±8 vs. 61±14 years, p=N.S, respectively), gender (F:M, 7:5 vs. 6:6, p=N.S, respectively), BMI (27±3 vs. 29±5 kg/m², p=N.S, respectively), diabetes duration (13±11 vs. 15±10 years, p=N.S, respectively), CV risk factors and glucose-lowering medications. PP was significantly higher in patients with GE than in patients without GE (PP 81±13 vs. 74±12 mmHg, p=0.05). Profiling of senescent-associated genes showed that Telomerase Reverse Transcriptase (TERT), responsible for telomere ends maintenance, was markedly downregulated in T2D patients with GE (FC= −15.2, p<0.05) and increased cardiovascular disease (CVD) risk, even after intensive glycemic control targeting glycated haemoglobin (HbA1c) levels.

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.

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Premature cardiovascular ageing / Hypertension population science

2022 | SPOTLIGHT
Risk of hypertension and chronic low grade inflammation among healthy young subjects living in the cities with different ambient air pollution

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Purpose of the study: We aimed to determine if there is any relationship between long term exposure to ambient air pollution and the blood pressure and inflammatory status in healthy young subjects.

Methods: We recruited permanent residents of two Polish major cities, Lublin and Krakow, with very similar urban structure characteristics, which significantly differ in mean 10-year ambient air pollution levels: PM2.5 (22.4 vs. 41.7 μg/m³) and PM10 (35.2 vs. 61.6 μg/m³) respectively. Data regarding BMI, lifestyle, ethnic and family history was collected. Measurements of blood pressure (BP) and heart rate (HR) were performed and blood tests, including inflammatory markers were studied.

Results: 826 subjects (558 females, 268 males) aged 18.02±1.12 were randomly recruited, 382 in Lublin, 444 in Krakow. There were no differences between groups in BMI (20.8±2.0 kg/m²), age, ethnic. We found no significant differences in BP parameters, pulse pressure (PP) between subjects differing in exposure to air pollution. Lublin vs. Krakow: DBP: 70.3 vs. 69.7; IQR 9.3 mmHg, SBP: 122.3 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 frequently than several times a week. We found significantly higher inflammatory parameters in inhabitants of highly polluted city. Lublin vs. Krakow: CRP (0.4; IQR 0.5 vs. 0.77; 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). Rheinlus was more frequent in subjects living in Lublin (16.12% vs. 13.0% Hcy, vs 0.035). Hs-CRP fibrinogen, hs-CRP, Hcy levels were in overweight subjects living in Cracow.

Conclusions: This study shows that, young adults living 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


Background: Could occupational determinants impact on changes in blood pressure over a five-year follow-up period.

Methods: 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.

Results: No physical factor (awkward postures, carrying heavy objects, and intense noise exposure) was significantly associated with changes in BP. Among organizational factors, only particular working hour schedule acted as a protective factor. The OR of BP changes was 0.35 (95% CI 0.19-0.66) for leisure 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.

2023 | BEDSIDE
Hypertension prevalence, awareness, treatment and control in four states in India: the DISHA study baseline results


Background: Hypertension: a global 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, 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. 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 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 | BESIDE

Rivaroxaban vs. warfarin with concomitant aspirin use in patients with atrial fibrillation: findings from the ROCKET AF trial


Purpose: In the double-blind ROCKET AF study, 14,264 patients with nonvalvular AF, apixaban 2.5 mg was used in pts with 2 or more dose reduction (DR) criteria and standard dose apixaban for stroke prevention in atrial fibrillation.

Methods: 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 apixaban vs. warfarin (n=17,370).

Results: Among pts assigned 5.0 mg of apixaban or warfarin, 40.6% (70 vs. 70) had one DR criteria. These pts were older (77 vs. 68 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=0.69). 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.

2032 | BESIDE

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


Purpose: To determine the risk of stroke and bleeding according to level of kidney function in non-anticoagulated patients with atrial fibrillation (AF).

Outcome | Subgroup | Apixaban | Warfarin | HR (95% CI)
--- | --- | --- | --- | ---
Stroke/SE | 5.0 mg BID with 0 DR criteria | 6675 | 137 (1.10) | 6681 | 176 (1.42) | 0.77 (0.62–0.97)
5.0 mg BID with 1 DR criteria | 2032 | 64 (1.79) | 2014 | 69 (1.95) | 0.92 (0.65–1.33)
5.0 mg BID with age DR criteria | 452 | 14 (1.73) | 453 | 13 (1.60) | 1.08 (0.51–2.30)
5.0 mg BID with weight DR criteria | 733 | 27 (2.20) | 706 | 32 (2.65) | 0.82 (0.49–1.37)
5.0 mg BID with creatinine DR criteria | 847 | 23 (1.50) | 855 | 24 (1.58) | 0.95 (0.54–1.69)
Major bleeding | 5.0 mg BID with 0 DR criteria | 6658 | 204 (1.77) | 6658 | 279 (2.46) | 0.72 (0.60–0.86)
5.0 mg BID with 1 DR criteria | 2052 | 108 (3.91) | 2059 | 152 (4.94) | 0.67 (0.52–0.86)
5.0 mg BID with age DR criteria | 448 | 30 (4.18) | 451 | 40 (5.75) | 0.73 (0.46–1.18)
5.0 mg BID with weight DR criteria | 731 | 26 (2.28) | 704 | 44 (4.00) | 0.57 (0.35–0.93)
5.0 mg BID with creatinine DR criteria | 841 | 50 (3.70) | 854 | 68 (5.29) | 0.70 (0.49–1.01)
ADVANCES IN BASIC SCIENCE: STATE OF THE ART ON PLAQUE VULNERABILITY

2058 | BEDSIDE
High-risk plaque features can be detected in non-stenotic carotid plaques of patients with ischemic stroke classified as cryptogenic using combined FDG-PET/MR imaging

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Introduction: High-resolution magnetic resonance imaging (MRI) can assess atherosclerotic plaque composition in carotid arteries with good correlation to histopathology. 18Fluoro-deoxyglucose (FDG) is a positron emission tomography (PET) radiotracer that accumulates in inflammatory cells present in atherosclerotic plaques.

Purpose: The aim of this study was to investigate in 18 patients with ischemic stroke classified as cryptogenic and presenting non-stenotic carotid atherosclerotic plaques.

Methods: Carotid arteries were imaged 150 minutes after injection of FDG with a combined PET/MRI system. American Heart Association (AHA) lesion type and plaque composition were determined on consecutive MRI axial sections (n=460) in both carotid arteries. FDG uptake in carotid arteries was quantified using tissue-to-background ratio (TBR) on corresponding PET sections.

Results: Prevalence of complicated atherosclerotic plaques (AHA type VI lesions) detected with high-resolution MRI was significantly higher in the carotid artery ipsilateral to ischemic stroke as compared to the contralateral side (39% vs. 0%; p<0.001). For all other AHA lesion types, no significant differences were found between ipsilateral and contralateral sides. Plaques containing a lipid-rich/necrotic core, intraplaque hemorrhage, or fibrous cap rupture accumulated significantly more FDG than did plaques lacking these features (TBR=3.55±1.21 vs. 2.38±0.83, 1.14±1.14 vs. 2.36±0.80, 3.48±1.1 vs. 2.40±0.84, respectively; p<0.05 for all). In addition, significantly higher FDG uptake was detected in advanced atherosclerotic plaques (AHA lesions ≥ type IV with high-resolution MRI) in the carotid artery ipsilateral to the stroke as compared with the contralateral artery (3.14±1.13 vs. 2.44±0.78, respectively; p<0.001).

Conclusions: Morphological and biological features of high-risk plaques can be detected with high-resolution MRI and FDG-PET in non-stenotic atherosclerotic plaques ipsilateral to the stroke, supporting a causal role for these plaques in stroke etiology. Combined PET/MRI systems provide unique diagnostic means to non-invasively co-register morphological and molecular signals for the more specific identification of high-risk plaques.

2059 | BEDSIDE
Impact of anti-oxidative capacity of high-density lipoprotein on vulnerability of coronary plaques in patients with type 2 diabetes mellitus

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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 and plaque composition and lesion characteristics using integrated high-definition intravascular ultrasound (IB-IVUS) in patients with type 2 diabetes mellitus (T2DM).

Methods: Thirty-three consecutive T2DM patients with CAD who underwent percutaneous coronary intervention (PCI) under IB-IVUS guidance were included. IB-IVUS 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 using as reference.

Results: HII was not related with plaque burden, but was significantly related with plaque composition. HII was positively correlated with percent lipid area and percent lipid volume (r=0.448, p=0.009 and r=0.356, p=0.042, respectively) and was negatively correlated with percent fibrous area and percent lipid volume (r=-0.432, p=0.012 and r=-0.346, p=0.048, respectively). The significant association between HII and percent lipid area (odds ratio 3.3, 95% confidence interval 1.4 to 8.1, p=0.008) was independent of HDL cholesterol, low-density lipoprotein cholesterol (LDL) control, or other conventional risk factors of CAD including age, gender, body mass index and smoking.

Conclusions: The anti-oxidative capacity of HDL was inversely related with lipid-rich plaques and may be a useful biomarker for predicting vulnerability of coronary plaques in patients with T2DM.

2060 | BEDSIDE
Pathological substrate for STEMI assessed by optical coherence tomography during primary PCI

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Background: The pathological mechanisms leading to coronary occlusion in STEMI, including plaque rupture, erosion or calcium nodule, have been largely investigated in acute phase, but before balloon or stent PCI. Plaque was categorized as fibroatheroma (thin cap [TCFA] if minimum cap thickness <70μm), fibrous or fibrocalcific.

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. Plaques were categorized as fibroatheroma (thin cap [TCFA] if minimum cap thickness <70μm), 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. This could be caused by plaque erosion or other feature not detected by this technique. Plaque microchannels (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) (wall spherical void suggestive of 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. Overall, 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.
2099 | BESIDE
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
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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 International 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 0.87, p<0.00001, light blue curve), the Morise score (c-index 0.61, p<0.00001, red curve) and the NCEP ATP III score (c-index 0.68, p<0.00001, 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 | BESIDE
Characterization of coronary plaques in patients with acute coronary syndrome by multidetector computed tomography
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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 (Aquilon, 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 and 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. 54.3%, p<0.03) and uneven contour (91.7% vs. 68.7%, p<0.002) was significantly higher. The minimum plaque density was significantly lower and length of plaque was significantly higher in the culprit coronary segments (40.1±25.3 HU vs 74.1±116.8 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 was in non-culprit (31.67% vs 17.91%, p=0.04) and CT score 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 and soft plaque type and presence of uneven contour, as well as a combination of the last three features.

2101 | BESIDE
Cardiac CT versus functional testing in suspected coronary artery disease - a randomised multicentre study
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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 as a first step. With that we want to establish the place of cardiac CT in routine practice.
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 April 2011 and July 2013. Patients were randomly assigned to the control group (n=175, standard of care based on functional testing) and the intervention group (n=175, cardiac CT). The cumulative radiation exposure was higher in the cardiac CT group (6.6±8.7 mSv vs. 6.1±3.3 mSv; p<0.0001) and the overall number of invasive angiographic procedures was less (2%, p<0.0001 and 12%, p=0.843). As 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 ($36 840 vs $44 040; p<0.0001). The cumulative radiation exposure was higher in the cardiac CT group (6.6±8.7 mSv vs. 6.1±3.3 mSv; p<0.0001) and the total diagnostic costs were lower ($36 840 vs $44 040; p<0.0001). The cumulative radiation exposure was higher in the cardiac CT group (6.6±8.7 mSv vs. 6.1±3.3 mSv; p<0.0001). The cumulative radiation exposure was higher in the cardiac CT group (6.6±8.7 mSv vs. 6.1±3.3 mSv; p<0.0001).
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 | BESIDE
Coronary atherosclerosis features for the prediction of ischemic events (CAFE-PIE study): a CT scan integrated score from a bi-center registry
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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 377 consecutive symptomatic intermediate-risk patients without history of known CAD undergoing CCTA 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<0.01).
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.

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2103 | BEDSIDE
Cardiac spectral CT scan to diagnose acute myocarditis

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Methods and materials: 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 acquisitions were 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 dyspepsia (12%), and 71% of patients had a recent history of viral infection. Mean CRP was 69±73 mg/l and troponin levels were 6.5±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 concordance Kappa tests.

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

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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 and materials: 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 acquisitions were 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).

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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 concordance Kappa tests.
Effects of heart imaging radiation on dna double-strand break levels in blood lymphocytes: the Heart-Break study

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Background: Potential genotoxic effects from ionizing radiation have raised safety concerns with increasing utilization of cardiac imaging.

Purpose: We aimed to compare double-strand break (DSB) levels in human blood lymphocytes before and after coronary computed tomographic angiography (CTA) and diagnostically 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 [11.9–12.5]) 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.

ANTBRADYCARDIA PACING

P2109 | BEDSIDE

Temporary transvenous cardiac pacing: risk-benefit ratio

Background: Severe symptomatic bradycardias have risk of asystole or bradycardia-dependent ventricular arrhythmias in the period between diagnosis and permanent pacemaker implantation. Previous data suggest that, with pharmacological therapy alone, 32% of these patients (pts) will develop severe arrhythmic events, fatal in 1.2% of cases. The temporary transvenous pacing effectively prevents these events, but is often under-utilized because of complications.

Purpose: To evaluate the indications, technical considerations and complications associated with the temporary transvenous cardiac pacemaker placement.

Methods: Observational, retrospective, single-center study of consecutive pts underwent placement of temporary transvenous cardiac pacemaker for a period of two years. We evaluated the occurrence of complications and compared the risk of serious life-threatening arrhythmic events extrapolated by modulation of our Hospital group study.

Results: Between January 2013 and December 2014, 249 temporary transvenous pacemakers were implanted to a total of 230 pts (54.8% male, 78±11 years). The indications for the procedure were complete atrioventricular (AV) block in 73.5% (n=183), high-grade AV block in 2.4% (n=6), 2nd degree AV block Mobitz II in 8.4% (n=21), polymorphic ventricular tachycardia in 3.6% (n=9), brady atrial fibrillation in 6.8% (n=17) and brady atrial flutter in 1.2% (n=3). The implantation was guided by fluoroscopy in 100% of cases, 84.7% of which by the right femoral vein. The mean stay of eletrocatheter was 4.2±2.9 days. In 33 pts (13.3%) complications related to the procedure occurred, including pericardial effusion in six pts (2.4%) - 2 of which required drainage; femoral hematoma in 2 cases (0.8%) and in 15 cases (5.6%) repositioning of eletrocatheter was required. In 3.6% (n=10) of the pts, a device-related infection was suspected, with microbiological isolation in 2 cases. 9 deaths occurred, none of which related to the procedure. By extrapolation our Hospital data, in the absence of implantation of a temporary pacemaker, expected mortality would be of 1% (2 deaths) and 26.4% life-threatening arrhythmic events (n=67), which were thus avoided.

Conclusions: The placement of transvenous temporary cardiac pacemaker is a safe and very effective technique in the prevention of serious arrhythmias. The threshold for temporary pacemaker implantation should be low given the very favorable risk-benefit ratio.

P2110 | BEDSIDE

Bachmann’s bundle pacing prevents left atrial dyssynchrony and improves left ventricle filling
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Background: Patients with sick sinus syndrome express certain interatrial conduction disorders. Some of them have atrioventricular conduction delay which worsens over time. Both pathologies can lead to atrial and atrioventricular dyssynchrony and diminish mitral diastolic flow especially in patients with broad P waves. Implantation of atrial lead in right atrium appendage (RAA) furthermore prolongs the left atrium electrical activation leading to hemodynamic impairment known as atrial dysynchrony syndrome.

Purpose: The aim of this study was to assess influence of different atrial pacing lead location on left ventricle diastolic filling and atrioventricular conduction and the percentage of ventricular pacing in population with SSS implanted with DDD pacemaker.

Methods: The study group consisted of 66 patients (42 F, 24 M) aged 71.8±15.8 years. Patients were divided in two groups: group I (n=28) with RAA pacing, group II (n=38) with Bachmann’s bundle pacing. Differences in interatrial and atrioventricular conduction in sinus rhythm and AAI 60 pacing were assessed. Also P wave width at sinus rhythm and during atrial pacing as well as percentage of ventricular conduction in sinus rhythm and AAI 60 stimulation were assessed. AVD was set at 220/200 ms (pacing/sensing). Two-dimensional and Doppler echocardiography was performed. Total LV filling time was determined as the time interval from the onset of early diastolic flow - E wave at the mitral annulus to the offset of A wave. Mitrall velocity flow integral (VTI MR) was assessed.

Results: There were no differences in baseline P wave duration in sinus rhythm between the groups (105.1±16 ms vs 101.3±19 ms, p=n.s.). Atrial pacing 60 bpm revealed longer P wave duration with atrial lead location in RAA compared to Bachmann’s bundle region (141.6±24.3 vs 102.2±18 ms, p<0.01). The percentage of ventricular pacing was higher in group I (28.6±5.3%, p<0.01). Total LV filling time was shorter in RAA lead location (47±3±51 vs 54±2±52 ms, p<0.05) which reflected smaller smaller VTI MR (17±3±31 vs 21.3±4±2 cm, p<0.001).

Conclusions: 1. Bachmann’s bundle pacing results in better left ventricle filling pattern preventing the left atrial dysssynchrony. 2. RAA pacing impairs mitral diastolic flow increasing the diastolic dysfunction of the left ventricle. 3. In patients...
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

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**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 fluoroscopic and pacing 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 confirmed placement of the lead in 177 patients (17.4%), 65 mid-septum (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 <140 ms with 38% and 63%, the absence of notching in the inferior leads with 59% and 44%, an early preordial QRS transition with 22% and 81%, respectively. The combined verification of absence of notching in the inferior leads and early preordial QRS transition allowed to identify septal positioning with a sensitivity of 17% and specificity of 91%.

**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

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**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.

**Methods:** Electromagnetic simulations of lead placement were done in 170 patients (17 high-, 65 mid- and 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 <140 ms with 38% and 63%, the absence of notching in the inferior leads with 59% and 44%, an early preordial QRS transition with 22% and 81%, respectively. The combined verification of absence of notching in the inferior leads and early preordial QRS transition allowed to identify septal positioning with a sensitivity of 17% and specificity of 91%.

**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.
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
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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 for long durations (trend for declining HR from tertile 1 to 3: <0.001) and less mortality (28.6% vs. 32.4%, 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]=2.14 [1.26–3.63], 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.

P2117 | BEDSIDE
Advanced age and high-residual platelet reactivity in patients receiving dual antiplatelet therapy with clopidogrel or ticagrelor
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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 Multisite 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 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 HRPR (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]=2.14 [1.26–3.63], p=0.003). Similar results were obtained among 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.

P2119 | BEDSIDE
Impact of intravenous lysine acetylsalicylate versus oral aspirin on a prasugrel inhibited platelets: results of a prospective, randomized, crossover study
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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 was lacking about the effects of achieving faster and stronger cytochromea 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
administration of oral prasugrel and intravenous LA versus prasugrel and aspirin orally on platelet aggregation.

Methods: This was a prospective, randomised, 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 and vasodilator-stimulated phosphoprotein phosphorylation.

Results: The primary endpoint of the study, inhibition of platelet aggregation after ter arachidonic acid (AA) 1.5mg at 30 min, was significantly higher in subjects treated with LA compared with aspirin: 85.3% vs. 44.3% respectively, p=0.003. This differential effect was observed at 1 hour (p=0.002) and 4 hours (p=0.048), but not after 24 hours (figure 1).

Conclusions: The administration of intravenous LA resulted in a significantly reduction of platelet reactivity compared to oral aspirin on prasugrel inhibited platelets. Loading dose of intravenous LA achieves cyclooxygenase platelet inhibition faster and greater than oral aspirin.

P2120 | BEDSIDE
Temporal trends in incidence of acute myocardial infarction and the effect of baseline cardioprotective therapy on initial clinical presentation: a nationwide study
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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: Using individual-level linkage of data from Danish nationwide registries, we identified all patients aged ≥30 years admitted with a first-time MI in the period 2003–2012, and their use of cardioprotective medication during the initial 3 months prior to the index date. For each year, incidence rates per 100,000 person-years (IRs) of STEMI and NSTEMI and percentages of patients receiving cardioprotective medication were calculated. Logistic regression models adjusted for gender, age, calendar year, and medication were used to calculate the likelihood for patients using individual cardioprotective drugs to present with NSTEMI compared to STEMI.

Results: During the study period, IRs for NSTEMI decreased by 36% from 225 in 2003 to 143 in 2012, whereas IRs for STEMI peaked in 2007 and subsequently declined each year from 81 to 73 (10% reduction). Prior cardioprotective medication use increased in both groups, i.e. for statins from 9.8 to 23.7%, amino-pteridines from 1.4 to 4.8%, and thienopyridines from 1.4 to 4.7% in patients with NSTEMI (all p<0.001). In the STEMI group, an increase was observed in use of statins (from 7.0 to 13.7%, p<0.001), ACEIs/ARBs (from 15.2 to 20.9%, p<0.001), and thienopyridines (from 0.6 to 1.5%, p=0.003), but no change in use of beta-blockers (from 11.3 to 10.9%, p=0.66), and a decline in the use of aspirin (from 13.3 to 10.8%, p=0.01). Use of all these drugs was associated with higher likelihood of presenting with NSTEMI than with STEMI, i.e. odds ratio (OR) 1.72 (CI 1.62–1.84) with aspirin, OR 1.33 (CI 1.25–1.42) with statins, OR 1.27 (CI 1.19–1.36) with beta-blockers, OR 1.16 (CI 1.10–1.22) with ACEIs/ARBs, and OR 2.14 (CI 1.77–2.59) with thienopyridines.

Conclusion: In an unselected Danish population, incidence of first-time MI declined considerably after 2003 for NSTEMI and after 2007 for STEMI. Increased use of cardioprotective medication is likely to have contributed to this development and use of these drugs was associated with higher likelihood of initial presentation with NSTEMI than with STEMI.

P2121 | BENCH
Rac-1 as a new target to modulate endothelial function and platelet aggregation in diabetes mellitus
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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 arterioles (n=4 for each group) from C57BL/6 mice were exposed to low (5mM) and high (25mM) glucose concentrations. At high glucose levels arterioles 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 abolishment 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 pre-incubated with glucose (25mM) 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 haemoglobin, 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 platelets 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.
P2124 | BENCH
Rapid endovascular moderate hypothermia before reperfusion provides more cardioprotection than mild hypothermia in a porcine model of myocardial infarction
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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 salavage and depth of rapid therapeutic hypothermia.

Methods: Swine (n=24, 46±3 kg) were randomly assigned to 3 groups: normothermia (38°C), mild hypothermia (35°C) and moderate hypothermia (32°C). AMI was induced by 1-hour ischemia-reperfusion of mid LAD. Then an endovascular balloon catheter controlled temperature to either 32°C or 35°C. Cooling started 30 minutes before reperfusion, target temperature was reached in 9±5 (35°C) and 29±8 (32°C) 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 35°C and 32°C groups showed significant IS reduction (62% and 91%) per AAR compared to 38°C (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, 32°C group showed significant IS per AAR reduction compared to 35°C (p=0.013) suggesting further tissue salvage from deeper cooling. Delayed-enhancement CMR of IS per LV also showed significant reduction at 32°C (10±4*, 8±3*, 3±2*, p<0.001). Cardiac output (CO) change at follow up related to baseline was less affected in the 32°C group only (−30%±16*, −24%±7, −17%±18*, p<0.041).

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
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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 thienopyridines-class antiplatelet 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-ligand-induced binding sites of the activated platelet GPIb/IIa (LIBS-MPIO). In comparison, a control antibody was applied (control-MPIO). Necrosis was depicted via late gadolinium enhancement magnetic resonance imaging (MRI). 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−/− animals (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 towards 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. 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 | BENCH
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
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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 >35% as assessed using magnetic resonance imaging (MRI) were treated with intramyocardial bone marrow 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
Ultrasmall 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. Ultrasmall superparamagnetic particles of iron oxide (USPIO) are engulfed by resident macrophages in inflamed 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 were performed immediately before and 24 h after USPIO (ferumoxsil, 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 magnetic resonance imaging. We assessed the amount of 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...
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 in the first two weeks following acute MI. Increased USPIO enhancement in the ‘reparative’ phase following MI is associated with functional improvement at 3 months. This imaging tool holds promise to non-invasively assess and monitor myocardial cellular inflammation after MI and in other inflammatory cardiac conditions.

### P2128 | BEDSIDE

**Non-invasive estimation of pulmonary vascular resistance by cardiovascular magnetic resonance in systolic heart failure:**

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**Background:** Pulmonary hypertension is associated with poor prognosis in heart failure. However, non-invasive diagnosis is still challenging in clinical practice.

**Purpose:** We sought to assess the prognostic utility of non-invasive estimation of pulmonary vascular resistances (PVR) by cardiovascular magnetic resonance to predict adverse cardiovascular outcomes in heart failure with reduced ejection fraction (HFrEF).

**Methods:** Prospective registry of patients with left ventricular ejection fraction (LVEF) <40% and recently admitted for decompensated heart failure during three years. PVR were calculated based on right ventricular ejection fraction and average velocity of the pulmonary artery estimated during cardiac magnetic resonance. Readmission for heart failure and all-cause mortality were considered as adverse events at follow-up.

**Results:** 105 patients (average LVEF 26.0±7.7%, ischemic etiology 43%) were included. Patients with adverse events at long-term follow-up had higher values of PVR (6.92±1.9 vs. 4.6±1.7 estimated Wood Units (eWu), p<0.001). Kaplan-Meier curves according to tertiles of PVR showed an increased risk for upper tertiles to reach outcomes at follow-up (Log-rank: p<0.03 between 1st and 2nd tertile, p<0.001 between 1st and 3rd tertile) (Figure). In multivariate Cox regression analysis, PVR ≥5 eWu (cutoff value according to ROC curve) was independently associated with increased risk of adverse events at 9 months follow-up (HR 2.98, 95% CI 1.12–7.88; p=0.03).

**Conclusion:** In patients with HFrEF, the presence of PVR ≥5.0 Wu is associated with significantly worse clinical outcome at follow-up. Non-invasive estimation of PVR by cardiac magnetic resonance might be useful for risk stratification in HFrEF, irrespective of etiology, presence of left gadolinium enhancement or LVEF.

### P2129 | BEDSIDE

**T1 mapping by cardiac magnetic resonance imaging: from histological validation to clinical implication**

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**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 diagnostic and prognostic 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 (28 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 Tissue-FAXS analysis (TissueFAXS-ECV) and correlated with ECV by CMR T1 mapping (MOLLI-ECV).

For the assessment of the prognostic value of MOLLI-ECV, 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-ECV (r=0.915, p<0.001). MOLLI-ECV was 29±7% on average. When patients were divided into quartiles according to ECV (quartiles 1-3: 18%; 25-27.1%, 27.2-29.7% and ≥29.8%), those with higher MOLLI-ECV had a reduced event-free survival (log-rank: p<0.001). By univariable Cox-regression, patients with higher MOLLI-ECV 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-ECV 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-ECV allows accurate non-invasive quantification of extracellular matrix expansion and is independently associated with event-free survival.

### DIET, LIPIDS AND THE VASCULATURE

**P2130 | BENCH**

**Dyslipidemia impairs high-density lipoprotein cardioprotective effects leading to larger infarcts. HDL-characterization by lipid analysis and differential proteomics**

G. Vilahur1, J. Cubedo1, M. Guiterez2, L. Casani2, A. Capdevila3, G. Pons-Llado1, F. Carreras3, A. Hidalgo1, L. Badimon1, 1Barcelona 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

**Background:** Prospective epidemiological studies have reported an inverse association between HDL-cholesterol levels and cardiovascular disease. However, HDL-cholesterol value has shown limited value for predicting cardiovascular risk in patients with coronary heart disease patients underscoring the need of understanding the extent to which the presence of cardiovascular risk factors modify HDL functionality.

**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 (NC-HDL; cholesterol: 76±4 mg/dL) or fed a Western-type hypercholesterolemic (Hyper-C-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 Hyper-C-HDL were performed prior infusion. NC-HDL and Hyper-C-HDL antioxidant potential was assessed.

**Results:** Despite similar extent of myocardium-at-risk in all animals after MI those having received infusion of Hyper-C-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. Hyper-C-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 Hyper-C-HDL recipient pigs (p<0.001 vs NC-HDL). HDL characterization revealed that neutral lipids were increased in Hyper-C-HDL vs NC-HDL (P<0.05). Proteomic analysis indicated that Hyper-C-HDL had significantly reduced content of lipid- (ApoE and aysulfatase-G)isoform1), lipocalins- and vitamin A-transporters and metabolic compounds. No changes were observed in ApoA-I profile. Antioxidant activity of Hyper-C-HDL was 18% lower than that of NC-HDL (P<0.05).

**Conclusions:** We demonstrate, for the first time, that the presence of hyper-
Methods and results: ATF3 regulates high-fat diet–induced adipocytes hypertrophy and lipid metabolism in mice via ChREBP repression.

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.

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 relationship 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(+)KDR(-), CD34(+)KDR(+) and CD34(+)KDR(+)CD133(+) in peripheral blood samples) was used to assess circulating EPC numbers. The adhesive function, and 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 (31.23 vs 24.69, p=0.009).

EPC levels in CAD patients

<table>
<thead>
<tr>
<th>EPC levels (%)</th>
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<tr>
<td>CD34</td>
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EFT, epicardial fat thickness; EPC, endothelial progenitor cells.

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 phenotype by repression of ChREBP signaling pathway
C.-F. Cheng1, H.-C. Ku1, T.-L. Tseng1, H. Lin2. 1Tzu Chi General Hospital, Hualien; 2Taipei Medical University, Institute of Physiology, Taipei, Taiwan, ROC

Background: Obesity is a severe and complicated health issue related to lifestyle body weights significantly increased as compared to B6 wild-type (WT) littermate. Several studies revealed that such enlargement of adipocytes can be reversed by AAV8-ATF3 therapy in which such enlargement of adipocytes can be reversed by AAV8-ATF3 therapy in obese ATF3−/− mice receiving AAV8-GFP as control group (AAV8-ATF3: 36.5±0.7 gm, p<0.05, n=6). Further signaling of adipocytes and circulating EPCs was performed.

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(+)KDR(-), CD34(+)KDR(+) and CD34(+)KDR(+)CD133(+) in peripheral blood samples) was used to assess circulating EPC numbers. The adhesive function, and 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 (31.23 vs 24.69, p=0.009).

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EFT, epicardial fat thickness; EPC, endothelial progenitor cells.

Conclusions: Patients with CAD and thicker EFT have decreased circulating EPC numbers and functions and higher syntax score than those with thinner EFT.

P2133 | BEDSIDE
Arginase inhibition improves endothelial function in patients with familial hypercholesterolemia
O. Kovamees, 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 of 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 (age 32±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 Nω-hydroxy-nor-L-arginine (L-NH2-NO) (50 mg i.a.). FH patients were examined both while on lipid-lowering medication and 4 weeks after medication withdrawal.

Results: In FH patients LDL-C increased from 4.3±0.4 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 2.4±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.

Conclusion: Arginase inhibition results in greater improvement in endothelial function in patients with FH with elevated LDL-C 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
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Background: Patients with end-stage renal disease (ESRD) are characterized by increased cardiovascular morbidity and mortality. Hemodialysis per se entails vascular dysfunction in ESRD patients. 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.

Objective: To investigate the effects of a flavanol-rich dietary supplement on endothelial function in patients with ESRD.

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 flavanols on endothelial function and hemodynamics. In a subsequent study following a 30-day ingestion period, we studied the effects of flavanols 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: Patients with ESRD were included (mean±SD, 42% male, age 65±13 years, BMI 29±5 kg/m², dialysis vintage 41±32 months). Flavanol ingestion was safe and well-tolerated. Acute ingestion was associated with an increase in circulating catechine metabolites and increased FMD by 53% (p<0.0001) with no effects on blood pressure or heart rate. A 30-day ingestion of flavanols led to an increase of baseline FMD by 18% (p<0.001) with increased heart rate (70±2 bpm to 74±3 bpm; p=0.007) and reduced diastolic blood pressure (74±2 mmHg to 70±3 mmHg;p=0.004). No effects were observed for placebo. Acute ingestion of flavanols during hemodialysis alleviated hemodialysis-induced vascular dysfunction (Delta FMD flavanols 0.71±0.1 vs. placebo 1.48±0.1, p=0.001).
**P2135 | BENCH**

Occurrence of coronary lipid deposits and myocardial fatty dystrophy in dabigatran etexilate-treated diabetic rats

A. Scroidon1, D. Gheban2, A. Marginean2, M. Perian1, R.C. Serban3, D. Dobresan1, 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, Nopca, 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 the D group, 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 glucose, total cholesterol, and triglycerides were significantly higher in D 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). In the D group, myocardial lipid deposits were found in G and D rats, while 4 CD rats (50%) and 7 DD rats (85.7%) presented myocardial fatty dystrophy. None of the C rats presented aortic lipid deposits, while 6 CD rats (75%), 4 DD rats (80%), and 6 DD rats (75%) presented mild aortic lipid deposits. Coronary lipid deposits were only present in DD 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 animals. 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. Socchett2, F. Mahmud1, J. Deanfield1, 1. University College London, Institute of Cardiovascular Sciences, London, United Kingdom; 2. Hospital for Sick Children, Department of Paediatrics, Toronto, Canada

**Background:** The prognosis for childhood-onset type 1 diabetes (T1D) remains poor. Apart from poor glycemic 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 −12.7 to −1.8), p: 0.01) and the low ACR group (beta +0.71 (95% CI −12.6 to −1.7), p: 0.012). Similar trends but no significance were also seen in endothelial superoxide release and serum PON-1 levels in T1D with high ACR compared to controls. No difference was seen in HDL 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 both with low and high ACR. Findings suggest 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. Melboom3, M.C. Post3, 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

**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 multicenter study included TOF patients from a prospective nationwide registry. Notches in the QRS complex in ≥2 contiguous leads on standard 12-lead electrocardiograms (ECCG), not related to right bundle branch block (RBBB), were defined as fQRS. The extend 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 in inclusion was classified as none in 52% of patients, moderate in 32% and severe in 16%. During long-term (median 10.4 yrs) 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 multivariate analysis, the extend of fQRS (HR: 2.38/class, 95% CI: 1.50–3.79, p: 0.001, and age (HR: 1.00/class, 95% CI: 1.05–1.09, p: 0.001) were independently predictive for mortality. QRS duration was no longer predictive for mortality (HR: 1.00/class, p: 0.79) in multivariate analysis. The extend of fQRS was also predictive for sustained VT (HR: 1.41/class, 95% CI: 1.38–4.20, p: 0.002) and the combined endpoint (death or VT) (HR: 2.30/class, 95% CI: 1.59–3.31, p: 0.001) in multivariable models.

**Conclusion:** Fragmented QRS complexes are present in about half of adult TOF patients. The extend of fQRS fragmentation is superior to QRS duration in predicting death or VT.
Relation between exercise capacity and skeletal muscle metabolism during exercise in patients with repaired tetralogy of Fallot

A. Frigiol1, K. Bull1, M. Papademetriou2, A. Hoskote1, G. Derrick1, S. Cullen2, F. Walker2, A. Giardini1, 1Great Ormond Street Hospital for Children, London, United Kingdom; 2University College London, London, United Kingdom; 3The Heart Hospital, London, United Kingdom

Background: Peak oxygen uptake (VO2) is affected by central haemodynamics and by peripheral factors although the relative contribution is still debated. The coronary flow augmentation is the main factor limiting peak VO2 in patients with congenital heart disease (CHD). Investigations into the effect of peripheral factors on peak VO2 in patients with CHD are very scarce. Peripheral factors, which affect oxygen extraction, including reduced physical activity and fitness in patients with CHD, may rather be a marker of intrinsic LV pathology, highlighting the important role of the LV in determining late outcome after repair of ToF.

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 oxygen tension (TOI), from the right vastus lateralis muscle. Patients also underwent cardiac magnetic resonance imaging (MRI). Patients had lower peak VO2 than controls (27±5 vs 35±9 mL/kg.min, p =0.001), lower peak HR (93±8 vs 100±5% of predicted, p =0.001) and similar VE/VO2 slope (p=0.825). Right ventricular end diastolic diameter in the ToF population was 100±22 mm, ejection fraction was 59±7%, and pulmonary regurgitant fraction was 18±14%. Resting peak exercise changes (Δ) in 2-OH-hemoglobin, total-haemoglobin and TOI were not significantly different between the two groups (p between 0.444 and 0.520). On simple linear regression analysis, peak VO2 correlated with ΔTOI (r=0.004 and p=0.001), Δ total-haemoglobin (p=0.203 and p=0.013), and peak HR (p=0.029 and p=0.001) both in ToF patients and in healthy controls and with Δ2-OH-hemoglobin (r=0.004 and p=0.014) in ToF patients only. No MRI variable was associated with peak VO2. On multiple linear logistic regression analysis only ΔTOI was predictive of peak VO2 in patients and 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) changes in peak TOI and HR. One SD increase in peak TOI and HR 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 interindividual differences in muscle oxygen extraction than on HR response to exercise augmentation of the oxygen uptake. These findings 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.I. Jones2, F. Walker2, S. Cullen2, P. Bonhoeffer2, V. Tsang2, T.Y. Hsia2, B. Pandya2, 1University Hospital Santariskiu Klinikos, Vilnius, Lithuania; 2The Heart Hospital, Great Up Congenital Heart Unit, London, United Kingdom

Background: Percutaneous pulmonary valve implantation (PPVI) avoids the need for repeat cardiopulmonary bypass and sternotomy and reduces perioperative morbidity. Infective endocarditis (IE) has been described following both pulmonary homografts and percutaneous valves.

Purpose: To quantify the incidence and define the clinical course of CHD patients experiencing either PVR or PPVI.

Methods: Retrospective analysis of patients undergoing either PVR or PPVI at our centre for adults with CHD between 2005 and 2013 to identify and compare confirmed 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 PPVI. 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 =0.044). Freedom from IE at 1 year was 92±8% compared with 94.1±8% in the PPVI group (p =0.707). The incidence of IE after valve function failure was higher 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 cardiological remodelling post-pulmonary valve replacement in patients with repaired tetralogy of Fallot

E.L. Heng1, M.A. Gatouzi1, C.C. Smith1, D.F. Shore1, B. Sethia2, H. Uemura2, G.P. Diller2, S.Y. Ho4, D.J. Pennell5, 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, London, United Kingdom; 3University Hospital of Muenster, Division of Adult Congenital and Valvular Heart Disease, Muenster, Germany; 4University of Toronto, St. Michael’s Hospital, Toronto, Canada; 5Royal Brompton Hospital, Cardiovascular Magnetic Resonance Unit & NIHR Cardiovascular Biomedical Research Unit, London, United Kingdom

Background: Although early post-PVR volumes or function have been studied, the emerging role of the right ventricle (RV) volumes or function in adult patients with repaired ToF. 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 of ToF.

Results: The overall cohort mean age was 30±9 years, 55% were males, with a mean Ps of 116±11.3 mmHg, SV 58±16.4 mL and a left ventricle (LV) ejection fraction of 64.3±6.8%. The ToF group (mean age 30±8 years; mean follow-up time since rToF 23±7 years) had a smaller body surface area (1.70±0.18 vs 1.79±0.21 m2, P=0.01) but bigger aortic diameters (30±3.6 vs 28±3.2 mm, STJ 32±4.2 vs 30±3.7 mm, AoA 33±4.1 vs 35±3.4 mm, p ≤0.001), with effacement of the STJ in 43% of cases. The prevalence of aortic dilatation (AoZ ≥2) in this cohort was 28%. The global peak CAAS was lower in ToF patients (5.7±4.2 vs 7.4±4.6, P=0.036) with a higher aortic stiffness index (17.7±23.7 vs 11.7±19.5, P=0.045). By multivariate analysis the AoZ and dilatation was predicted by gender (β=0.28, P=0.009) and LV end diastolic volume index (β=0.44, P=0.024).

Conclusion: The prevalence of dilated and stiffer ascending aorta is significant in tetralogy of Fallot patients late after repair. This may reflect an intrinsic aortopathy and highlights the importance of a careful aortic follow-up in this population.

P2137 | BEDSIDE

Relation between exercise capacity and skeletal muscle metabolism during exercise in patients with repaired tetralogy of Fallot

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Background: During exercise in patients with repaired tetralogy of Fallot (ToF), the overall cardiac output augmentation is the main factor limiting peak VO2. 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 of ToF. 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 of ToF.
156.1±11.9mm² vs ePVR 104.9±28.4mm², RVEF 74.9±26.2mm² vs ePVR 57.4±22.7mm², indexed RV mass gPVR 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 reverted to pre-PVR baseline at midterm follow-up. PVR produced a continued improvement in corrected RVEF despite the non-linear volume competency, in addition to RV remodel but significant improvement of LVEF. Right atrial remodelling was also evident.

Conclusions: Cardiac remodelling is generally regarded as a gradual process. Post-PVR RVEF demonstrates for the first time that the major improvement in RV volumes seen at midterm 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 midterm.

P2143 | BEDSIDE
Age at intervention is the main risk factor for prosthetic pulmonary valve failure in patients with congenital heart disease
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Background: 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. Receiver operating characteristic (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 re-interventions 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 0.88; 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 0.95; 95% CI 0.92–0.98; 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
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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% in 1997 to 30.7% in 2007. The overall CHD event rate for age <65 was 1.35 per 100 patient-years of follow up in the pre-statin cohort compared with the pre-statin cohort (140 mg/dL at 132 mg/dL, p=0.001). Despite 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=0.89]. The population attributable risk of CHD due to elevated LDL-C was also numerically lower in the post- versus pre-statin era (13.2%, 10.8%–15.6%, 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 mostly 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
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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 causes related to 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. Death-related 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, >30mg/dL) according to the Lp(a) level at baseline.
Results: The incidence of each death 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], 4.25 [2.62, 7.14]) compared with those in the lowest Lp(a) tertile, whereas there was no significant difference of the risk between the above two groups in terms of mortality from all causes, coronary artery heart 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-
dioviscous disease (2.34 [1.09, 5.01]) and a trend toward increased RR of death from cerebrovascular disease (2.70 [0.95, 7.64]); 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 hypercholesterolemia in the EUROASPIRE IV project

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**Background:** The prevalence of Familial Hypercholesterolemia (FH) is estimated in the community at 1/200–500 persons. In patients with established coronary heart disease (CHD) the prevalence is less well documented.

**Purpose:** The aim of this substudy of EUROASPIRE IV 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-completion questionnaires. FH was estimated using the adapted version of the Dutch Lipid Clinic Network Criteria.

**Results:** Of 3,670 patients included, 2,342 had a lipid profile assessed at admission (with a 48-hour delay) and 17 did not consent. FH was diagnosed in 8.3% of patients. FH+ patients were younger than FH- patients (98% vs 85%, p < 0.01).

**Conclusion:** The prevalence of 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 acute myocardial infarction. The FAST-MI 2005 registry


**Methods:** The FAST-MI is a nationwide French registry including consecutive patients with AMI, treated during a one-month period (with a one-month extension for diabetic patients) in 213 institutions of 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 modulating therapies was used to define probable or definite FH (FH+).

**Results:** From 3,670 patients included, 2,342 had a lipid profile assessed at admission, among whom FH could be estimated from the algorithm in 2,286. The prevalence of FH was 2.5% (n=57) (probable FH 1.7%, definite FH 0.7%). FH+ patients were younger (54±12 vs 67±14 years, p < 0.001), with a lower GRACE risk score (120 ± 147, p < 0.001), and more family history of premature coronary artery disease (67% ± 23%, p < 0.001). LDL at admission was 216±56 vs 110±53 mg/dl, p < 0.001. LDL at admission was 216±56 vs 110±53 mg/dl, p < 0.001. LDL at admission was 216±56 vs 110±53 mg/dl, p < 0.001.

**Conclusion:** In this well-characterised cohort of patients admitted for AMI, patients with FH were 13 years younger on average than non FH patients, but had a similar long-term mortality. After multivariate adjustment, however, 5-year mortality was two-fold 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

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**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 and without (n=1,371) 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 body weight between Phase 1 and Phase 2 were significantly greater in the Rel subgroup 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 glycohemoglobin 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.
CAD risk (Odds Ratio) was increased 5.5-fold in patients with \( \text{Lp(a)} = 110 \text{ mg/dl} \).

**Conclusion:** \( \text{Lp(a)} \) is an independent strong predictor for manifestation and severity of coronary artery disease and should be included in the standard risk factor assessment.

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**P2150 | BEDSIDE**

**Whole exome sequencing combined with integrated variant annotation prediction identifies asymptomatic Tangier disease with compound heterozygous mutations in ABCA1 gene**

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**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 results for diagnosing, and there is 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 after the standard variant quality controls. We have filtered out the variants 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% in Asian population (1000 Genome Project) 3) Segregation unmatched under the assumption of recessive form of inheritance 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 (\text{c.7117C}→A or p.P2077H/c.6223G→A or p.S2066N, c.1134C→G or p.G948R/c.1130C→T or p.P337L).

**Conclusion:** WES combined with integrated variant annotation prediction successfully identified asymptomatic Tangier disease with novel ABCA1 mutations for the first time ever 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.

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**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-matched analysis**

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**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 transmyocardial 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 endpoints were cardiovascular death, cardiac death, stroke and repeated target vessel revascularization.

**Methods:** Among 533 consecutive patients undergoing myocardial revascularisation techniques between 2002 and 2012, a propensity-score analysis was performed based on the technique 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.

**Results:** The use of total arterial myocardial revascularisation was 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 was associated with a significantly higher incidence of both myocardial infarction and repeat revascularisation, thereby underlying the need for a careful patients’ selection.

**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 events.

**Purpose:** To evaluate the impact of hybrid revascularization on clinical outcomes after coronary artery bypass grafting.

**Methods:** From January 2003 to May 2009, 3,071 patients underwent CABG in our center. Preoperative brain MRI/MDA criteria were 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 asymptomatic patients (group B). The primary end point was major adverse cardiac and cerebrovascular event (MACCE), defined as the composite of death, myocardial infarction, and stroke.

**Results:** The non-CABG/MI/MDA group had a significantly lower mortality rate, lower incidence of MACCE and lower incidence of stroke compared with the non-CABG/MI/MDA group. The use of CABG was associated with a lower rate of stroke after discharge compared with the non-CABG/MI/MDA group.

**Discussion and conclusion:** These results suggest that CABG is associated with a lower rate of stroke after discharge compared with the non-CABG/MI/MDA group. The use of CABG was associated with a lower rate of stroke after discharge compared with the non-CABG/MI/MDA group.
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

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Objective: The objective of the present study was to test whether a perioperative course of colchicine, in patients undergoing standard coronary artery by-pass grafting (CABG), would result in reduced postoperative rise 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 [30.6–68.8] ng/ml and 93.0 [48.0–182.3] ng/ml, respectively (p=0.002). The median AUC of 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 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 [30.6–68.8] ng/ml and 93.0 [48.0–182.3] ng/ml, respectively (p=0.002). The median AUC of 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 93.0 [48.0–182.3] ng/ml, respectively (p=0.002). The median AUC of hsTnT was 20.363 [13,891–31,661] pg.h/ml in controls versus 40,755 [20,868–79,176] pg.h/ml in the colchicine group (p=0.002). AUCs for CK-MB were 2552 ng.h/ml [1564–4791] in controls and 93.0 [48.0–182.3] ng/ml, respectively (p=0.002). The median AUC of hsTnT was 20.363 [13,891–31,661] pg.h/ml in controls versus 40,755 [20,868–79,176] pg.h/ml in the colchicine group (p=0.002). AUCs for CK-MB were 2552 ng.h/ml [1564–4791] in controls and 93.0 [48.0–182.3] ng/ml, respectively (p=0.002).

Conclusion: A short perioperative 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 11,981 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 10 years (interquartile range: 4.8 to 11.8 years; maximum 17.3 years). Both groups were similar in terms of baseline characteristics and intraoperative factors. EuroScore (3.7 (0.03) vs 3.8 (0.03), SMD=0.038) was similar between OPCAB and ONCAB and groups and median 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 (χ2 (1) = 2.93; Pr: χ2=0.0870); 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

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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). The group A was older and had higher incidences of diabetes, chronic kidney disease, 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 and are at higher risk than others. The fear of postoperative dialysis rates after CABG appears overestimated since only about 5% of patients needed dialysis shortly after operation. The current study provided evidence that OPCAB could be associated with better survival and freedom from cardiovascular events than PCI.

P2157 | BEDSIDE
4-year mortality in 22,737 patients surviving 30 days after a first isolated coronary artery bypass graft procedure in 2002-2006, compared to the general population

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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 CABG with mortality rates to those of 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 by using standardised mortality rates.
ratios (SMR) with 95% CI. In addition the absolute excess risk (AER) was estimated.

Results: Men and women (<55 years) had higher mortality compared to the general population, with a SMR 1.76 (95% CI 1.35–2.22) in men and 4.49 (95% CI 2.74–6.68) in women. In contrast, patients >55 years and over had better survival compared to those of the general population with SMR 0.74 (95% CI 0.70–0.78) in men and 0.82 (95% CI 0.74–0.91) in women aged >55.

Conclusions: Men and women <55 years, surviving 30 days after CABG surgery had a higher mortality risk than the general population, which was much more marked for women than for men, with a more than 6-fold increase in risk, compared to women of the same age. In contrast to this, men and women >55 years of age, had a lower risk for mortality after CABG when compared to the general population.

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

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Background: Cardiac angiogenesis is an important determinant of heart failure, and spontaneous microvascular collapse may contribute to the progression from hypertrophy 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 hypertrophic mass [P <0.01] and heart-to-body weight ratio [P <0.05] and left ventricular dilation (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 the cardiac and systemic fibrosis. The cardiac QTLs linked to collagen accumulation were screened for potential candidates by expression QTL analyses, allowing of transcriptional data of CC14-treated BXDs (Affy 1.0 ST arrays). Raf Kinase Inhibitor Protein (RKIP), Phosphatidylethanolamine-Binding Protein-I (PEBP-I) was identified as genetic marker of individual fibrosis progression.

Conclusions: End.PTP1B-KO mice presented improved cardiac function during chronic pressure overload and hypertrophy.

P2159 | BENCH
Ca-homeostasis in human cardiac hypertrophy and end stage heart failure is directly impacted by modulations of protein phosphatase 1 and -2a activity

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Disruption of Ca-homeostasis is a key pathomechanism in heart failure. While the role of respective kinases has been extensively studied, the contribution of con- versely acting serine/threonine phosphatases to arrhythmias in structural heart disease remains unknown. We studied the two major cardiac protein phosphatases PP1 and PP2A in three types of human tissue: 1) healthy human myocardium from organ donors (NF), 2) hypertrophied heart to the observed alterations in End.PTP1B-KO mice, and 3) end stage failing myocardium (HF). Western blot experiments revealed no upregulation of PP1 expression in HF but increased expression in HF compared to NF (n=7 and 23 vs. 8; all parameters). The expression of its endogenous inhibitor (II) was decreased in Hy and HF compared to NF (P <0.05) suggesting increased PP1 activity. The expression of PP2A was decreased in Hy and HF compared to NF (P <0.05).

Diastolic SR Ca leak (confocal microscopy, Fluor-3-AM) and systolic Ca release/SR Ca load (fluorescence microscopy, Fura 2) were analyzed in freshly isolated human ventricular cardiomyocytes (CM). In HF, Ca spark frequency (CaSpF) was increased by 99±25% compared to Hy (n=148/13 vs. 45/5, P <0.05). An inhibition of PP1 and PP2A in Hy using ouabain acid (OA, 100μM) resulted in increased CaSpF (by 163±49%, n=36/4 vs. 28/4) and Ca spark density leading to a 6.5-fold increase of the calculated SR Ca leak (p <0.05 each, n=36/4 vs. 28/4). Conclusively, the frequency of arrhythmic events (Ca-waves, -clouds) was also increased (p <0.05). Interestingly, phosphatase inhibi- tion increased SR Ca load and amplitude of systolic Ca transients in Hy (P <0.05).

In Hy, when phosphatase inhibition (OA) was further increased by the addition of basal CaSpF 87±37% leading to a 4.5 fold increase of the calculated SR Ca leak (n=70/7 vs. 54/7, P <0.05 each) and a higher frequency of arrhythmic events by 47±10% vs. control (n=65/3 vs. 137/5, P <0.05) in human end stage failing CM.

P2160 | BENCH
Raf kinase inhibitor protein regulates interstitial and replacement cardiac fibrosis

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Background: Genetic determinants of cardiac fibrogenesis are not completely understood. QuantiTec (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 CC14 (0.7 mg/kg, 12 ip 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, allowing of transcriptional data of CC14-treated BXDs (Affy 1.0 ST arrays). Raf Kinase Inhibitor Protein (RKIP, Phosphatidylethanolamine-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 C57Bl/6 wild-type and C57Bl/6-RKIP-deficient mice (RKIP−/−) were subjected to transverse aortic constriction (TAC, 360 μm) or sham-operation or treatment with CC14 for 6 weeks, untreated mice served as controls (n=9–10 per group). RKIP-deficiency reduced both CC14-induced interstitial- and TAC-induced replacement fibrosis in C57Bl/6-RKIP−/− compared to TAC-operated C57Bl/6-WT mice (P <0.05) and reduced the frequency of arrhythmic events (P <0.05). SR Ca leak was not changed upon phosphatase inhibition in Hy (P <0.05). Importantly, a selective activation of PKC by a novel phosphatase disrupting peptide (PDP, 100μM) yielded a prominent reduction of the SR Ca leak by 73±8% (n=37/5 vs. 44/5, P <0.05) and reduced the frequency of arrhythmic events by 47±10% vs. control (n=65/3 vs. 137/5, P <0.05) in human end stage failing CM.

Conclusions: These data identify Raf Kinase Inhibitor Protein as an important regulator of interstitial and replacement cardiac fibrosis.

P2161 | BENCH
Contrasting effects of exercise training after myocardial infarction versus aortic stenosis depend critically on endothelial nitric oxide synthase

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Purpose: The cardiovascular benefits of exercise training (EX) are widely pre- dicted. Previously, we found that cardiac effects of EX critically depend on
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 echocardiography. 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 luminal-enhanced chemiluminescence. eNOS uncoupling was measured by western blot. eNOS Glutathionylation was measured by coimmunoprecipitation. Results: Phactr1 suppressed 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- and glutathionylation of eNOS by EX in MI and TAC, respectively.

Effects of exercise

<table>
<thead>
<tr>
<th>SEDHEX</th>
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<tr>
<td>Fractional shortening (%)</td>
<td>37±2</td>
<td>39±1</td>
<td>61±1</td>
<td>121±5</td>
<td>185±2</td>
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<td>Collagen content (%)</td>
<td>1.3±0.1</td>
<td>1.9±0.3</td>
<td>6.9±0.7</td>
<td>3.0±0.8</td>
<td>11.4±2.5</td>
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<tr>
<td>LV O2- production (RLU/sec/mg)</td>
<td>198±1</td>
<td>249±2</td>
<td>412±2</td>
<td>281±15</td>
<td>453±15</td>
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<tr>
<td>eNOS uncoupling (IAU)</td>
<td>1.0±0.1</td>
<td>1.0±0.2</td>
<td>2.1±0.1</td>
<td>1.5±0.1</td>
<td>3.0±0.4</td>
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<tr>
<td>Peroxynitrite formation (IU/mL)</td>
<td>0.0±0.0 ± 0.0</td>
<td>0.02±0.03</td>
<td>0.22±0.05± 0.12±0.02</td>
<td>0.27±0.01± 0.64±0.01± 0.34±0.03</td>
<td></td>
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<tr>
<td>eNOS Glutathionylation (AU)</td>
<td>1.0±0.1</td>
<td>1.0±0.1</td>
<td>4.1±1.1</td>
<td>1.1±1.1</td>
<td>5.1±2.1</td>
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</table>

Data are mean ± SEM. eNOS, endothelial nitric oxide synthase; RLU, relative light unit; AU, arbitrary unit; n=6–20/group. *p<0.05 vs SH; #p<0.05 vs EX.

Conclusion: The contrasting effects of EX in MI vs TAC appear mediated by divergent effects of EX on eNOS Glutathionylation, eNOS uncoupling and ONOO-forming, 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

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Background: Phasphatase 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: Phactr1 gene delivery into the anterior wall of the left ventricle was used to induce Phactr1 overexpression both in normal and infarcted rats. Neonatal rat ventricular myocytes (NRVMs) were used for the cell culture studies. Results:

Phactr1 mRNA and protein levels were markedly reduced (60%, P<0.01) 2 weeks after adenovirus-mediated Phactr1 gene delivery. Likewise, skeletal α-actin to cardiac α-actin ratio was lower at 2 weeks in infarcted hearts overexpressing Phactr1. In NRVMs, adenovirus-mediated Phactr1 overexpression for 48 hours markedly increased skeletal α-actin to cardiac α-actin isoform ratio associated with enhanced DNA binding activity of serum response factor. Phactr1 overexpression had no major effects on expression of other cardiac genes or LV structure and function in normal and infarcted hearts during 2 weeks follow-up period. In human subjects, MI associated PHACTR1 allele was not associated significantly with levels of galectin-3 and other cardiovascular risk factors.

Conclusion: Phactr1 regulates reprogramming of cardiac gene expression, particularly skeletal to cardiac α-actin isoform ratio.

P2163 | BEDSIDE

Impaired cardiac function in MMP13 knock out mice after myocardial infarction due to impaired remodeling

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Background: During myocardial infarction (MI) an extensive cardiac remodelling 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 these cardiac remodelling processes. The MMP-13 is considered to be the major interstitial collagenase in the heart.

Methods and results: In this study, we induced MI in wild type and MMP13 knockout mice. Five days after MI mice deficient for MMP13 showed an aggravaion 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 detected. More collagen was detected in MMP13 deficient animals. During MI, the gene expression of MMP13 is increased in scar tissue of wild type animals but not in the non-MI zone compared to control mice. Fibroblasts are those cells within the myocardium which are important for the remodelling processes. In these cells isolated primary murine 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 mechanical properties of MMP13 deficient fibroblasts.

Conclusion: 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

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Background and introduction: Central blood pressure (cBP) shows actual pressure load 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. However, arterial blood pressure monitoring implemented with this analysis program, such as ARC Solver algorithm, is now put into practical use. But 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.

Objectives: To determine whether cBP dysfunction was associated with indirect cBP indices attained by ARC solver algorithm, we validated and compared the measured data according to cardiac function and calibration mode.

Methods: We enrolled 210 patients undergoing elective coronary angiography in

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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 ejection fraction (EF) on left ventriculography. cBP indices were calculated through two available calibration modes: calibration with systolic/diastolic BP (cSBP, cDBP) and mean arterial BP (cMAP). We defined central pulse pressure (cPP) as aortic systolic BP minus aortic diastolic BP and fractional pulse pressure (FPF) as pulse pressure per mean BP.

Results: In Cal2, Central systolic BP (cSBP), cPP and FPP values did not significantly differ between low and normal EF group (cSBP: low EF 154±29 mmHg, normal EF 145±21 mmHg, p = 0.11; cPP: low EF 63±17mmHg, normal EF 59±18mmHg, p = 0.47; FPP: low EF 0.54±0.16, normal EF 0.55±0.14, p = 0.64). Noninvasive data showed comparable linear correlation with invasive values in both groups, whereas mean difference in cSBP was markedly better in normal EF group (cSBP: low EF r = 0.76, difference 7.1±5.19,normal EF r = 0.71, difference 0.15±1.68; cPP: low EF r = 0.69, difference 10.1±18.0mmHg,normal EF r = 0.70, difference 14.7±14.4mmHg; FPP: low EF r = 0.56, difference 0.09±0.15,normal EF r = 0.56, difference 0.14±0.14). Cal1 consistently showed inferior accuracy than Cal2 regardless of cardiac function.

Conclusion(s): Cardiac function does not significantly affect the indirect cBP parameters attained by ARC solver algorithm. Furthermore, calibration with mean/diastolic BP consistently shows better data accuracy.

P2169 | BEDSIDE
Aortic pulsatility assessed by a brachial cuff-based oscillographic method is a strong predictor for the presence of coronary artery disease
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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 Mobi1-O-Graph system provided an indirect estimate of brachial/aortic 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/aortic 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/aortic PP and FPF (PP: brachial 48±15.2 versus 55±16.2 mmHg, aortic 51.7±19.3 vs 62±31.9 mmHg; 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±2.3 mmHg; p = 0.05), Pb (21.7±7.8 vs 26.7±6.5 mmHg; p < 0.05) and lower value of PPA (0.80±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, aortic FPF, PPA, and Pb were associated with the presence of CAD. Among them, when aortic FPF was entered into the multivariate logistic regression model along with each hemodynamic index, only aortic FPF remained an independent predictor for the presence of CAD. When brachial FPF was entered into the model instead of aortic FPF, brachial FPF remained a significant predictor independent of PPA 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 PPA.

P2168 | BEDSIDE
Association between resting heart rate and organ damage in high risk Japanese patients
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Introduction: Resting pulse rate is associated with cardiovascular events and mortality. Clinicians should be aware of the potential for various asymptomatic organ damages that include but are not limited to cardiac and arterial damage.

Hypothesis: To investigate whether resting pulse rate is associated with organ damage.

Methods: In 4310 patients recruited for the J-HOP study with one or more cardiovascular risk factors, we analyzed 2756 patient with no use of beta blocker and less than 400 pg/ml of N-terminal pro-brain-type natriuretic peptide (NT-proBNP).

In addition, we measured resting pulse rate (PR) in clinic and urinary albumin creatinine ratio (UACR), the indices of echocardiography, and pulse wave velocity (PWV) as organ damage.

Results: Using analysis of covariance, UACR in the top quintile of clinic PR (more than 85bpm) were significantly higher than in the lowest quintile (less than 63bpm) after adjusted by age, sex, body mass index, clinic mean blood pressure and pulse pressure (19.6% [95% confidence interval: 17.7–21.6%] vs. 15.1% [13.7–16.6%] mg/gcr; p < 0.001). PWV in the top quintile (1747 ±1804 cm/s) was significantly higher than in the lowest (1572 ±1600 cm/s; p < 0.001) and second quintile (vs. 1654 [1605–1683] cm/s, p < 0.001). On the other hand, left ventricular diastolic dimension assessed by echocardiography divided by body surface area (29.2 ±28.9±27.9 mm/m² vs. 28.2 ±27.7±26.6 mm/m²; p = 0.014) and NTproBNP (48.6 ±45.3±52.0 pg/ml vs. 42.0 ±39.2–45.1 pg/ml, p = 0.044) in the lowest quintile of clinic PR was significantly higher in the highest quintile.

Conclusion: Increased resting pulse rate is associated with organ damage, but is negatively associated with cardiac volume overload.
Abdominal obesity is a major risk factor for hypertension. However, a recent study conducted at Copenhagen University Hospital, Department of Medicine, Copenhagen, Denmark, evaluated the relationship between abdominal adiposity distribution quantified by ultrasound and incident hypertension in a general population. The study included a sample of Danish adults. Thus, ultrasonic VAT measurements provide insights into the physiological and metabolically inactive. Visceral adipose tissue (VAT) is located around the internal organs and is metabolically active.

**Results:**

The study found that 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 Health2006 cohort. Normotensive participants were studied on isolated murine cardiac fibroblasts stimulated with TGF-β. The effects of LOXL2 inhibition by knockdown of the LOXL2 gene were study after 10 weeks. Administration of an anti-LOXL2 antibody decreased the degree of cardiac fibrosis and significantly improved hemodynamic function.

**Conclusion:**

Myocardial LOXL2 is increased in clinical and experimental HFpEF. Inhibition of LOXL2 ameliorated myocardial fibrosis and LV stiffness by decreasing total collagen amount, collagen cross-linking and LOXL2 amount, as well as progressive diastolic and systolic dysfunction 10 weeks after TAC. Administration of an anti-LOXL2 antibody decreases the degree of cardiac fibrosis and significantly improved hemodynamic function.
volume loops (PV) and LV morphometry were performed. LV cardiomyocytes were isolated and contractile function and Ca2+ 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 Ca2+ 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+/Ca2+ exchanger with SEA0400 significantly attenuated cardiomyocyte remodeling and diastolic dysfunction in this model of HFpEF.

2207 | BEDSIDE
Prophylactic epicardial left ventricular lead implantation in patients undergoing open heart surgery.

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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 lead implantation during open-heart surgery, identifying patients who subse- quently 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 (8.8%) 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 127.26±104.09 days (range: 2–299 days, median interval: 157 days). No major adverse event were reported to the procedure. At a one-year follow-up, LV lead performance parameters (paced threshold, sensing, 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 improve 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.

Conclusion: Prophylactic epicardial LV lead implantation may have a role in patients with LV function impairment undergoing open-heart surgery.

2209 | BEDSIDE
Primary graft failure after cardiac transplantation: prevalence, prognostic and risk factors.


Introduction: Primary graft failure (PGF) is a common and devastating complica- tion after cardiac transplantation. The increased use of “marginal donors” has leverage his prevalence, despite the advances in perioperative treatment.

Purpose: To evaluate the prevalence of PGF in a single institution, its impact on survival. To explore associated risk factors.

Methods: From November 2003 through December 2013, 258 patients were submitted to cardiac transplantation and were classified into a PGF group: 35 (14%) (defined as use of high-dose inotropic or mechanical support during the first 24 hours); and a non-PGF group: 223 (86%). Recipients’ characteristics were similar between groups (p=0.801 for age (53±13 vs. 55±10; P=0.40), sex (78% vs. 74%; p=0.62) and comorbidities such as diabetes, arterial hypertension or vascular arteriopa- thy. Patients in the PGF group had marginally higher transmural gradient (10.4±5.1 vs. 9.4±4.5; P=0.24) and pulmonary artery systolic pressure (51±15 vs. 48±15; P=0.21). Those in the non-PGF, ischemic (39% vs. 26%; p=0.13) and dilated (31% vs. 23%; P=0.30) aetiology prevailed (also not statistically signifi- cant). Donors to the PGF group were older (37±10 vs. 34±11 years; P=0.05) and predominantly female (40% vs. 22%; P=0.02).

Results: Mean total ischemic (108±35 vs. 87±38; P<0.01) and cardiopulmon- ary bypass (135±71 vs. 95±38; P<0.01) times were longer in PGF group. Total hospital mortality was 23% for PGF and 2% for non-PGF (P<0.01). Sur- vival at 1, 5 and 8 years was 45±9% vs. 94±2%, 42±9% vs. 83±3% and 42±5% vs. 74±4%, respectively for PGF and non-PGF groups (P<0.01). By multivari- ate analysis, risk factors for PGF were donor age (OR: 1.07; 95% CI: 1.02–1.11; P=0.002), ischemic (OR: 1.02; 95% CI: 1.01–1.03; P=0.01) and diastolic myocardial bypass time (OR: 1.01; 95% CI: 1.01–1.02; P=0.01) and non-ischemic (OR: 0.21; 95% CI: 0.08–0.58; P<0.01) or dilated aetiology (OR: 0.27; 95% CI: 0.05–0.12; P<0.01).

Conclusions: This data confirms PGF as a frequent early complication of cardiac transplantation with dismal prognosis. Risk factors were identified and, if not avoidable, should be viewed as alarm flags to closely monitor the patients.

2210 | BEDSIDE
Combination of preoperative left and right ventricular echo parameters can predict right ventricular failure following left ventricular assist device implantation.

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Background: Right ventricular failure (RVF) after left ventricular assist device (LVAD) placement is associated with increased morbidity and mortality. Echocardiogra- phy is a primary imaging modality in the assessment of cardiac function; therefore, we aimed to find echo parameters predicting RVF following LVAD implantation across centers.

Methods: The mean age of the echocardiograms was obtained from 80 patients undergoing elective LVAD implantation at one university in USA and one university in Japan. RVF was defined as right ventricular assist device and/or dependency on inotropic agents or pulmonary vasodilators at 14 days after surgery. Patients were classified into groups: Patient Group RVF, Group Non-RVF. Conventional and tissue Doppler echo parameters of both left and right ventricle were investigated.

Results: A total of 25 patients (31.3%) met the criteria for RVF. The RVF group showed lower TAPSE (2.0±2.2 vs. 4.3±2.0 cm, p=0.038), lower RV S’ (1.5±0.9 vs. 2.4±0.3, p=0.035), lower RV free wall strain (27±19 vs. 52±7±8.0, p=0.028) and higher mitral E/E’ (24.9±6.5 vs. 20.9±8.0, p=0.034) than the non-RVF group. An echo-based RVF score (Echo-RVF score) was created according to the uni-variante analysis using clinically relevant cut-off values.
2211 | BEDSIDE
Diastolic dysfunction is prognostic of long-term mortality in liver transplant recipients


Purpose: To evaluate the association between diastolic dysfunction and mortality after LT.

Methods: Consecutive cirrhotic patients undergoing LT at a tertiary medical center between 2003 and 2013 were identified. Patients with combined heart and liver transplant, amyloidosis, hemochromatosis, sarcoidosis or carcinoid liver disease 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±7.1 vs 51.1±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 (PH-HFpEF) in elderly patients


Purpose: The clinical significance and predictive value of PH remains to be elucidated in this specific disease entity.

Methods: Patients with PH-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 21–24mmHg, and manifest PH was diagnosed when mPAP ≥25mmHg. DPG was calculated as difference between systolic arterial pressure and mean pulmonary arterial 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±117.1 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 ventricle (42.1±8.9 mm versus 37.4±7.1 mm, p<0.010) and a larger capillary oxygen partial pressure (63.4±9.8 mmHg versus 73.3±7.1 mmHg; p<0.021) 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 0.023).

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?


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 (HFpEF). 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 HFpEF and HF with preserved ejection fraction (HFpEF). 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.

Results: Patients with a Cpc-PH had a shorter six-minute walk distance (253.5±128.7 m versus 318.4±117.1 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 ventricle (42.1±8.9 mm versus 37.4±7.1 mm, p<0.010) and a larger capillary oxygen partial pressure (63.4±9.8 mmHg versus 73.3±7.1 mmHg; p<0.021) 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 0.023).

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.
astolic dysfunction with preserved systolic function resulting from ongoing cardiomypocyte loss and cardiac fibrosis. The protease activated receptor (PAR) 2 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 examined the role of PAR2 in the aged heart regarding fibrosis and hemodynamic function.

Methods: 8 weeks (wks) and 1 year (yr) old wild-type (wt) and PAR2 knockout (ko) mice underwent hemodynamic measurements with a 1.2F microcathode catheter and hearts were collected for histological and biochemical analysis. Collagen release and Smad2 phosphorylation were determined with western blots and the ROS activity was analysed with a DCF dependent immunfluorescence assay on adult cardiac fibroblasts. The PAR2 gene expression was determined in myocardial biopsies from HFPEF patients.

Results: 1 year old 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 deposition in the heart and the collagen I/Ili 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: 4.2±1.78 vs. 6.4±2.53, p<0.05). The GSH/GSSG ratio in hearts of 1 yr hearts pointed also to an increased oxidative stress in PAR2ko mice compared to wt mice (wt vs PAR2ko: 8.3±1.29 vs. 4.8±2.13, 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

The effects of excessive body mass on cardiac geometric remodeling, diastology and myocardial contractile mechanics in asymptomatic population

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Purpose: Excessive body size in terms of greater body mass index (BMI), traditionally defined as obesity, had been shown to cause detrimental effects on cardiac function. The aim of this study is to evaluate the potential impacts of BMI on cardiac structural remodeling, diastolic dysfunction and contractile disturbances.

Methods: We consecutively assessed 4049 asymptomatic participants (age: 50.7±10.63) from cardiovascular health survey. Mitrail inflow, tissue Doppler parameters and 2D-based speckle-tracking of global longitudinal (GLS), circumferential (GCS) strains and twist/torsion were all analyzed and correlated with BMI.

Results: With graded increases in BMI, there was a trend toward larger LV mass index, LV wall thickness, diastolic interventricular septal thickness, diastolic annular anterior motion and elevated E'/E ratio (all trend p<0.001), whereas LVEF (mean: 62.0±4.9%) only had borderline reductions (WMD: 0.085 mg/L, 95% CI: −0.225–0.395, p=0.592) (figure). This effect of supplementation with green tea catechins on plasma CRP concentrations.

RCTs investigating the impact of green tea supplementation on plasma CRP concentrations.

Conclusion: Increased %VAT is independently associated with the incidence of MACE, indicating that adipose tissue composition is a useful predictor of cardiovascular outcome.

2229 | BEDSIDE

Effects of supplementation with green tea catechins on plasma C-reactive protein concentrations: a systematic review and meta-analysis of randomized controlled trials

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Introduction: Promising experimental and clinical trials suggest that green tea decreases the inflammatory process in cardiometabolic diseases, but evidence about the effects on plasma CRP levels seems inconsistent.

Purpose: To evaluate the impact of green tea supplementation on plasma CRP concentrations.

Methods: We searched selected database up to October 26, 2014 to identify RCTs investigating the impact of green tea supplementation on plasma CRP concentrations.

Conclusion: Meta-analysis of data from 11 RCTs arms did not indicate a significant effect of supplementation with green tea catechins on plasma CRP concentrations (WMD: 0.085 mg/L, 95% CI: −0.225–0.395, p=0.592) (figure). This effect size was robust in sensitivity analysis and omission of each individual study did not have a significant effect. The non-significant effects of green tea catechins on plasma CRP concentrations were also observed in subgroups of studies with...
green tea supplementation duration of ≥8 weeks (WMD: 0.029 mg/L, 95% CI: −0.239–0.288, p=0.828) and ≥8 weeks (WMD: 0.009 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: −0.251–0.388, 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 recruiting healthy subjects (WMD: −0.028 mg/L, 95% CI: −0.216–0.160, p=0.699), and those recruiting subjects with cardiometabolic diseases (WMD: 0.260 mg/L, 95% CI: −0.815–1.334, p=0.636).

Conclusion: 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?

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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 that a changes of period of low-calorie diet and physical training intervention in a cohort of patients with obesity (2230) 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±2 kg/m²) participating in a multimodal weight reduction program and in 45 healthy lean controls (BMI 22±2 kg/m²). The HR 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, p=0.130). As expected obese had a significantly higher HR than lean subjects (72±15 vs. 65±12 bpm, p=0.001). Obese had a higher HR corrected QT when using Bazett’s and Ashman’s formula, and Karajalainen’s nomogram methods, but 5 alternative correction methods, including Friderica, Sages-Framingham, Hodges, Rautaharju and Pfreufer, revealed comparable QTc in obese and lean subjects. Analogous results were obtained when comparing obese with and without the metabolic syndrome (MetS), whereby subjects with the MetS presented with higher HR than subjects without the MetS. After marked weight loss (15, 11±11.9 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 nomogram methods 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 when 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 partly relevant changes to QT interval. The BMI should be considered when using Bazett’s HR correction.

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2231 | BEDSIDE

Nutritional state predicts long-term survival in heart failure

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Introduction: NICE recommends screening for malnutrition. We hypothesize that the following NUTRIC Status index (CONUT) score predicts all-cause mortality with patients in 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 women. 1568 (31%) were in NHYA classes III/IV, and 2517 (49%) had a history of hypertension. 2230 had dyslipidemia, 996 (49%) had type 2 diabetes, BMI was 28 (25.32) kg/m², 1872 (37%) were obese (≥30kg/m²). Cholesterol was 4.4 (3.7, 5.4) mmol/L, lymphocyte count was 1630 mm³ (1230, 2080). Albumin was 38 (35.45, 40) g/L. CONUT score was recorded in 3818 patients with a median value of 2 (1.3).

Results: 2453 died (all-cause mortality); 961 had a hospital admission due to HF (position 1). Median survival time was 40 months (21, 166). 1660 (45%) were completely malnourished (CONUT 0-2) (289 died); 1645 (45%) were lightly 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 and is also predicted all-cause mortality and HR 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

2232 | BEDSIDE

Waist circumference versus other obesity indices as prognosticators of coronary artery disease in essential hypertension

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Background and introduction: There is still controversy over which obesity parameter has the strongest cardiovascular predictive value.

Purpose: The aim of this study was to assess the predictive role of body mass index (BMI), waist circumference and waist to hip ratio for the incidence of coronary artery disease (CAD) in a cohort of essential hypertensive patients (2232).

Methods: We followed up 2361 essential hypertensives (mean age 57.8 years, 1131 males, office blood pressure (BP)=143/89 mmHg) free of cardiovascular disease for a mean period of 6 years. All subjects had at least one annual visit and had baseline underwent complete echocardiographic study for determination of left ventricular mass index (LVMI) and blood sampling for assessment of metabolic profile. Moreover, weight and height were measured by standard techniques and waist circumference was estimated at the midpoint between the low rib margin and the iliac crest. LV hypertrophy (LVMH) was defined as LVMI ≥125 mg/m² in males and LVMI ≥110 mg/m² in females, while CAD was defined as the history of myocardial infarction or significant coronary artery stenosis revealed by angiography or coronary revascularization procedure.

Results: The incidence of CAD over the follow-up period was 2.37%. Hypertensives who developed CAD (n=56) compared to those without CAD at follow-up (n=2305) had at baseline greater waist circumference (100.7±11.3 vs 96.5±11.9 cm, p=0.007), LVMH (117±26.8 vs 103.3±27 g/m², p=0.0001) and prevalence of LVMH (43% vs 26%, p=0.014). No difference was observed between hypertensives with CAD and those without CAD with respect to baseline office BP BMI and waist to hip ratio values (p=NS for all). In successive multivariate Cox regression models waist circumference (HR 1.027, p=0.014) and LVMH (HR 1.012, p=0.003) were independent predictors of CAD.

Conclusions: In essential hypertensive patients baseline waist circumference predicts future development of CAD, whereas BMI and waist to hip ratio have no independent prognostic value. These findings suggest that among obesity indices waist circumference constitutes an easy clinical tool to assess risk in hypertension.

2233 | BEDSIDE

Adherence to Mediterranean diet has an incremental protective effect over statin therapy against cardiovascular disease 10-year incidence: results of the ATTICA study

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Background and aims: The protective role of Mediterranean diet on Cardiovascular Disease (CVD) risk has been extensively discussed in literature, but its incremental effect over the use of CVD risk reducing agents (such as hypolipidemic treatment) has rarely been evaluated.

Methods: The ATTICA study was carried out in the Athens area during 2001–2003 and involved 3042 participants free of CVD at baseline (48.8%, men, aged 18–89). Adherence to Mediterranean diet was assessed using the MedDietScore (range 0–55) and statin use was recorded for all subjects. During 2011–2012, 2583 out of the 3042 baseline participants attended the 10-year follow-up of the ATTICA study (15% lost-to-follow-up) and the development of CVD was recorded.

Results: Adherence to Mediterranean diet (highest tertile) decreased the CVD risk by 29.3% (Hazard Ratio (HR):0.707, 95% Confidence Intervals (CI): 0.537–0.831) whereas subjects with hyperlipidemia under statin therapy that had unhealthily dietary habit (lowest tertile) had 75% increased CVD risk than normallipidemic subject with healthy dietary habits (HR=1.75, 95% CI: 1.33–2.29). The addition of Mediterranean diet tertiles in multivariable model correctly reclassified 46.7% of subjects to the CVD classes.
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

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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 of whom 63 were 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 with a 256-slice CT-scanner. For each twin subject epicardial fat volume (EFV), waist circumference (WC) and body mass index (BMI) were assessed. To quantify phenotypic similarity, in-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 was 27.8±5.5 kg/m² (means SD). The intra-pair correlation between EFV WC and BMI values were stronger in MZ twins as compared to DZ twins (MzEFVr=0.75, rDZEFV=0.27; MzWCr=0.70, rDZWCr=0.40; rDFCr=0.67, rDZCr=0.16; all p<0.05), which implies a strong genetic dependence of these parameters. The structural equation models revealed four main findings: \( A^{EFV}=75\% \), \( A^{WC}=71\% \), \( A^{BMI}=66\% \); \( E^{EFV}=25\% \), \( E^{WC}=29\% \), \( E^{BMI}=34\% \). 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

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Background: Adolescence is critical stage for obesity, which is associated with incorrect eating habits developed in the family. Parenting styles is 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 neglective parents. When parents are very responsive and undemanding, they are indulgentes, demand and responsiveness 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. The aim of this study is to determine about 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 the socio-demo-graphic questionnaire, scales of demandingness and responsiveness, Comprehensive Feeding Practices Questionnaire - CFPQ 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 neglective 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 when associated with negligent and authoritarian 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 increased time spent eating, higher frequency of eating and obesity. "Pressure to eat" reduces the overeating 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 as important as what we eat: eating behaviours and heart rate variability

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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 DietScore), 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: ~39.3–1.6 P: 0.033).

Table 1

<table>
<thead>
<tr>
<th>Variable</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 (29.3%)</td>
<td>28 (27.7%)</td>
<td>0.020</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>146.1±72.8</td>
<td>158.4±68.7</td>
<td>0.041</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>68.2±30.3</td>
<td>69.3±29.3</td>
<td>0.681</td>
</tr>
<tr>
<td>SDNN</td>
<td>141.1±68.8</td>
<td>122.2±66.6</td>
<td>0.036</td>
</tr>
<tr>
<td>RMSSD</td>
<td>58.8±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±18.9</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

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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 in single 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 injected ARVMs with adenoviral constructs carrying CUTe chimera generated by fusion of the cAMP reporter to Tnpl (part of the tropinin complex at the sarcomere), AKAP18 (part of the SERCA2/PLB complex at the sarcoplasmic reticulum) and AKAP79 (part of the adenyly cyclase/Adrenergic Receptor complex at the plasmalemma) and we measured cAMP changes by FRET imaging at these sites. We found that on treatment with iso the cAMP response is significantly smaller at the level of Tnpl compared to AKAP79 and AKAP18. In contrast, the CAMP increase generated on application of the non-selective phosphodiesterases (PDEs) inhibitor, IBMX 100 m)U was identical in the three subcompartments, indicating a key role of PDEs in the local regulation of cAMP Myocytes treated with...
ISO 0.3mm or IBMX 100μM to generate the same amount of global cAMP, an increase in contractility with both treatments but interestingly the increase was significantly higher than ISOAR stimulation than on PDEs inhibition. Such difference is calcium independent as both treatments elicited an identical increase in the calcium transient. These findings demonstrate for the first time that CAMP is differentially and tightly regulated at individual macromolecular complexes that are involved in the regulation of ECC. Such regulation is mediated by the PDEs activity and is required to maximise the positive inotropic effect of catecholamines.

Acknowledgement/Funding: British Heart Foundation grants PG/10/75/28537, RG/12/3/29423 and PG/15/3/1110

2243 | BENCH
RyR2 stabilization by inhibiting aberrant Ca2+ release mediated by CaMKII signaling and Ca2+ buffering function suppresses arrhythmogenesis in Tropinin T-related familial hypertrophic cardiomyopathy
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Background: Cardiac Tropinin T (TnT) mutation-linked Familial Hypertrophic Cardiomyopathy (FHC) which increases myofilament Ca2+ sensitivity leads to sudden death in young age. However, the underlying mechanisms leading to lethal arrhythmias remain elusive. Here, we investigated the pathogenic role of aberrant cardiac RyR2-mediated CaMKII activation and RyR2-related local Ca2+ release events. Moreover, dantrolene, which stabilises RyR2 structurally in transgenic mouse (TG) model with FHC-related TnT mutation (delta160E).

Methods and results: In 6-months-old's TG, there was no appreciable difference in the structural or functional features of hearts, compared with non-TG. In response to isoproterenol (ISO; 10nmol/L), the Ca2+ spark frequency (Spf; s−1 100μm−2 by fluo4) was much higher in TG cardiomyocytes (ISO-TG: 7.8±0.6; p<0.01) than in non-TG cardiomyocytes (3.4±0.4). It was largely reversed by CaMKII inhibitor (KN-93; 1μM; 5.2±0.5; p<0.05), but not by PKA inhibitor (H-89; 1μM; 7.3±0.4; n.s.). ISO-TG showed the significant increase of spontaneous Ca2+ transient (scAT) after 5Hz pacing (42%; vs ISO-treated non-TG 14%), whereas it was again attenuated by KN-93 (15.8%), but not significantly by H-89 (33%). The events of aberrant Ca2+ release through RyR2 in ISO-TG were reproduced by adding EGTA-AM into ISO-treated non-TG, suggesting that increased Ca2+ buffering capacity, causing an increase in diastolic [Ca2+], predisposes to aberrant Ca2+ release events. Moreover, dantrolene (1μM) attenuated ISO-induced Spf (5.4±0.3; p<0.05 vs ISO-TG) and scAT (25.9%) in TG.

Conclusions: In FHC-related TnT mutated hearts, aberrant local Ca2+ release through defective RyR2 was induced by beta-adrenergic stimulation, presumably due to mutation-linked, increased Ca2+ buffering capacity, and subsequent CaMKII activation. RyR2 stabilization by inhibiting CaMKII-mediated aberrant Ca2+ release could be a new therapeutic approach to prevent the development of arrhythmias in FHC.

2244 | BENCH
Exenatide exerts a PKA-dependent positive inotropic effect in human atrial myocardium
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Background: Glucagon-like peptide-1 receptor (GLP-1R) agonists are a rapidly advancing class of drugs developed for treating type-2 diabetes mellitus. Although beneficial cardiovascular effects have been reported, exact mechanisms of GLP-1R-agonist action in the heart, especially in human myocardium, are poorly understood.

Methods and results: The effects of GLP-1R-agonists (exenatide, GLP-1 (7–36)NH2; PF-06464009, PF-06466667) on cardiac contractility were tested in non-failing atrial and ventricular trabeculae from 72 patients. The GLP-1 (7–36)NH2 metabolite, GLP-1 (9–36)NH2, was also examined. In electrically stimulated trabeculae, the effects of compounds on isometric force were measured in the absence and presence of pharmacological inhibitors of signal transduction pathways. The role of β-arrestin signalling was examined using a β-arrestin partial agonist, PF-06466667. Expression levels were tested by immunoblots. Translocation of GLP-1R downstream molecular targets, Epac2, GLUT-1 and GLUT-4, were assessed by fluorescence microscopy.

All tested GLP-1R-agonists significantly increased developed force in human atrial trabeculae, whereas GLP-1 (9–36)NH2 had no effect. Exendin (9–39)NH2, a GLP-1R-agonist, and H89 blunted the positive effect of exenatide. In addition, exenatide increased PKA-dependent phosphorylation of phospholamban (PLB), GLUT-1 and Epac2 translocation, but not GLUT-4 translocation. Surprisingly, exenatide failed to enhance contractility in ventricular myocardium.

Conclusions: Exenatide increased contractility via GLP-1R-cAMP/PKA pathway and decreased GLUT-1 and Epac2 translocation in human atrial myocardium, but had no effect in ventricular myocardium. Therapeutic use of GLP-1R-agonists may therefore impart beneficial effects on myocardial function and remodeling.

RESISTANT HYPERTENSION

2264 | BEDSIDE
Prevalence and comorbidity of resistant hypertension in community population
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The purpose of this study was to investigate the prevalence and clinical and metabolic risk factors of resistant hypertension (RH) in Korean hypertensive patients treated by primary care physicians. A total of 3109 hypertensive patients were analyzed. The mean age was 62.3±11.3 years, and 1502 (43.6%) of them had RH.

All hypertensive patients with <2 recorded BP measurement during a minimum period of 6 months was identified. Patients were considered uncontrolled if their most recent BP during the study period were systolic BP>140mmHg or diastolic BP>90mmHg. Uncontrolled patients taking-3 therapy classes including diuretics or controlled patients taking-4 therapy classes were regarded as RH.

Uncontrolled BP was found 30.9% (SBP alone 25.7%, DBP alone 11.4%, both SBP and DBP 6.3%). Overall, 26.3% of uncontrolled patients were RH. The prevalence of RH were 41%. Patients with RH were characterized by a significantly higher number of male (54.8%, p<0.033), and showed significantly higher body weight, waist circumference (65.9% vs 34.1%, p=0.002), and smoker (p=0.01) compared with non-RH hypertension. Patients with RH also showed significantly higher multimorbidity (including dyslipidemia, LVH, impaired renal function, and cardiovascular disease) compared with patients with non-RH hypertension.

In conclusions the results of this community based study indicate considerable number of hypertensive patients treated by primary care physician are maintained as uncontrolled or resistant status. Therefore, more aggressive interventions and referral to hypertension specialist are needed to patients with uncontrolled or RH treated in community.

2265 | BEDSIDE
Cardiovascular morbidity of severe resistant hypertension among treated uncontrolled hypertensives: a 4-year follow-up study
A. Kasiakogias, C. Tsoufis, I. Bafakis, A. Kordalis, K. Dimitriadis, T. Tsachiras, E. Andrikou, K. Kintis, I. Kalikazaros, D. Tousoulis. First Cardiology Clinic, University of Athens, Hippokration Hospital, Athens, Greece

Background: Data regarding the prognosis of resistant hypertension (RHT) with respect to its severity is limited.

Purpose: We investigated the cardiovascular risk of severe RHT among patients with treated uncontrolled hypertension.

Methods: In a prospective observational study, 1700 hypertensive patients (aged 57±12 years, 50% males) with office blood pressure (BP) ≥140 and 90mmHg despite antihypertensive treatment, were followed for a mean period of 3.6±1.8 years. At baseline, clinical data were collected and patients underwent echocardiographic measurements, routine blood testing and additional workup for exclusion of secondary causes of RHT. Three groups were identified depending on the presence of RHT (office-based uncontrolled hypertension under at least 3 drugs including a diuretic) and levels of office systolic BP: 1,187 patients (70%) without RHT, 313 (18%) with not-severe RHT (systolic BP>160mmHg) and 200 (12%) with severe RHT (systolic BP>160mmHg). Endpoint of interest was cardiovascular disease compared with patients with non–RH hypertension.

Results: During follow-up, 58 events were recorded (9.5 cases per 1,000 person-years). Incidence rates of cardiovascular events were 7.1 cases per 1,000 person-years in the group without RHT, 12.4 cases per 1,000 person-years in the group with not-severe RHT and 18 cases per 1,000 person-years in the severe RHT group. Unadjusted analysis showed that compared to uncontrolled patients without RHT, patients with not-severe RHT exhibited a similar risk but patients with severe RHT had a significantly higher risk by 2.5 times (C1: 1.28–4.73, p=0.007) for the composite cardiovascular outcome. Multivariate Cox regression revealed that even after adjusting for a series of established risk factors, severe RHT remained as an independent predictor of the cardiovascular outcome, (OR: 2.57, CI: 1.27–5.19, p=0.008).
Purpose: 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. Plewka, J.D.K. Kasprzak. Medical University of Lodz, Cardiology, Lodz, Poland

Introduction: With emerging new therapeutic concepts including renal denervation (RDN), there is a renewed interest in resistant hypertension (ResH). Among patients suspected of having ResH, the diagnostic process now 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 modification and reassessment.

Methods: All pts referred to our center for RDN underwent a standardized stepwise screening. Candidates were recruited from pts hospitalized in wards of cardiology, 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 exclusion of secondary hypertension. If ResH was persistent, pts were hospitalized with repeated ABPM on day 4. Further, renal angiography was performed and a multidisciplinary team analyzed 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 (angiotensin 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 diagnosis of secondary hypertension was made in 21 (25.6%) pts (7 primary aldosteronism, 2 active adrenal gland tumor, 12 renal artery stenosis). However, in 59 pts (67,8%) BP control was achieved after optimization of medical therapy, with mean ABPM 134/84 mmHg. The final treatment included ACEI –100%, β-blockers 92%, Indapamide 94%, amlopidine 76%, spironolactone 61%. Medication in most of these pts (52/59, 88%) included single-pill triple combination (38-64,4%) or double combination (21-35,6%). A subset of 23 pts (33,7%) became controlled only when medicated under in-hospital surveillance, with possible compliance 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 separate from myocardial scar improves response to cardiac resynchronization therapy (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 echocardiographic speckle-tracking radial strain and single-photon emission computed tomography (SPEC/T) to define 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 (measured 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 following: follow-up 1) death or heart failure hospitalization; 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). Compared with controls, the Imaging group had more LV leads placed in the optimal CS branch (83% versus 65%, p<0.01). The QLV interval was comparable between groups (Imaging vs. control, 136±36 ms vs. 133±21 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.

Conclusion: Multimodality imaging-guided LV lead placement towards the optimal 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

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Purpose: Among treated yet uncontrolled hypertensive patients, severe RHT exhibits a significantly higher cardiovascular risk indicating the need for prompt management.

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.

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). Compared with controls, the Imaging group had more LV leads placed in the optimal CS branch (83% versus 65%, p<0.01). The QLV interval was comparable between groups (Imaging vs. control, 136±36 ms vs. 133±21 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.

Conclusion: Multimodality imaging-guided LV lead placement towards the optimal 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

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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 quartiles).

**Results:** Among patients with non-LBBB, the 7-year cumulative probability of HF or death was 32% in the ICD-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 > 150 msec (lower quartile) experienced a significant 2.4-fold (p=0.015) increased risk for HF or death with CRT-D vs. ICD only therapy, whereas the effect of CRT-D in patients with QRS ≥135 msec was neutral (HR=0.97, 95% CI: 0.69–1.36, p=0.86; p-value for QRS duration by treatment interaction=0.024), and remained neutral with QRS > 150 msec cutoff (HR=0.88, 95% CI: 0.50–1.52, p=0.637). There was no clinical benefit with CRT-D vs. ICD regardless of QRS morphology in RBBB (HR=1.01, 95% CI: 0.61–1.66, p=0.975), or in IVC 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, there appears to be a significant increase in HF or death in those with non LBBB and QRS duration > 135 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**

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**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 afterload 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 cm LV chamber). The PreS-S slope was constructed from 18 segmental strain curves obtained by Speckle tracking and correlated to the end-systolic PV relation (ESPVR) and the pre-load recruitable stroke work (PRSW).

**Results:** Systolic blood pressure increased (103±18.3 vs. 136±30.1, p=0.01), LV stroke volume (p=0.01) and ejection fraction (p=0.01) decreased during balloon inflation. Conversely, the PreS-S slope was not influenced by loading (p=0.68). When comparing absolute values of the PreS-S slope with ESPVR and PRSW we found no correlation while comparing the rate of change in contractility, PreS-S slope correlated with PRSW (p=0.01) and ESPVR (p=0.05) (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**

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**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 tetrylogy of Fallot was surgically reproduced in 2-month-old piglets (n=8). 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 calcium transients were recorded in RV isolated myocytes (IonOptix). Contractile reserve was assessed by in-vivo (dobutamine 5 μg/kg) and ex-vivo (isoprorenaline 100 nM)-adrenergic stimulation. The integrity of T-tubules was controlled after Di-4-ANEPS labeling.

**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 cardiac 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.
### 2318 | BEDSIDE

**Development and validation of a risk score for cardiac surgery in infective endocarditis**

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**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 ongoing 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, periannular complications, Staphylococcus aureus infection, acute renal failure before surgery, septic shock before surgery, acute heart failure or cardiogenic shock, and platelet count <150 000. 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, periannular complications, sepsis manifestations) besides the universal ones (age, hemodynamic conditions), independently predicted mortality in IE surgery. Our model had a superior predictive accuracy than Euroscore I.

### 2319 | BEDSIDE

**Incidence, pathogenesis and outcome of patients developing infective endocarditis after transfemoral transcatheater aortic valve implantation**

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**Purpose:** Infective endocarditis (IE), e.g., prosthetic valve endocarditis (PVE), is a severe complication following valve replacement. In patients after surgical valve replacement, PVE occurs in 1–6% of patients. There is a paucity of data on the incidence, pathogenesis, and clinical phenotypes of patients with IE after 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%. 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 septicemic event occurred in 24%. Blood cultures (positive in all cases) included staphylococci 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 multiocular 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 33%. However, there was no difference in mortality between patients with and without echocardiographic evidence of PVE compared to those without, underlining the necessity of aggressive therapy in all TAVI patients with bacteremia.

### 2320 | BEDSIDE

**Acute-onset infective endocarditis: the potentiality of early surgery**

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**Purpose:** Acute-onset infective endocarditis (A-IE) is a medical urgency which requires promptness and accuracy in decision making. However, there are no formal recommendations for treatment of A-IE. Our aim was to analyze the clinical features, in-hospital evolution and prognosis of patients with A-IE, and the potentiality of early surgery.

**Methods:** From 1996 to 2014, 1053 patients with left-sided IE were prospectively and consecutively recruited at 3 referral hospitals. They were classified in 2 groups: G-I (n=491), patients with A-IE; G-II (n=562), patients with non-acute IE. IE was considered acute when the time from the beginning of symptoms to diagnosis was less than 15 days.

**Results:** There were no differences in age, gender distribution and comorbidities between both groups. At admission, those patients with A-IE showed more renal failure (22.8% vs 13.5%, p<0.001), stroke (p=0.022) and septic shock (11% vs 2%, p<0.001), whereas patients from G-II had more heart failure (46.3% vs 35.6%, p<0.001). S.aureus was more frequently isolated in G-I (27.7% vs 7.8%, p<0.001), while S.bovis (5.9% vs 2.6%, p=0.01), S.viridans (17.3% vs 7.3%, p<0.001) and enterococcus sp (15.9% vs 7.1%, p=0.001), were more frequent in G-II. Periannular complications were found similarly in both groups. During hospitalization, patients in A-IE group evolved to septic shock more frequently (11.8% vs 6.8%, p=0.005). Patients from G-II underwent surgery in a higher proportion (64.2% vs 51.1%, p<0.001), without differences in the time-delay to surgery. Mortality was higher in A-IE group (42.7% vs 30.1%, p<0.001). The impact of surgery was also analyzed (Table). In the cohort of patients with A-IE and septic shock, surgery was still associated with lower mortality (66% vs 89%, p=0.002).

**Impact of surgery on mortality**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Mortality % (n)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute onset (Group I)</td>
<td>Surgery</td>
<td>35.3% (88)</td>
</tr>
<tr>
<td>Non-acute onset (Group II)</td>
<td>Surgery</td>
<td>26.5% (95)</td>
</tr>
<tr>
<td>No surgery</td>
<td></td>
<td>36.7% (73)</td>
</tr>
</tbody>
</table>

**Conclusions:** Patients with A-IE show a worse prognosis. Surgical treatment reduces the mortality of this group even in high-risk patients who develop septic shock. Early surgery might prevent the development of complications which make the surgical risk unaffordable.

### VASCULAR BIOLOGY – NEW MOLECULAR AND GENETIC FINDINGS

**2334 | BENCH**

**Inhibition of FGF2 signaling with PD173074 ameliorates monocrotaline-induced pulmonary arterial hypertension and rescues BMPR-II expression**

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**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)
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 FGF-R1 was upregulated in lung tissue after monocrotaline injection, and it was accompanied by hemodynamic changes and pulmonary vascular remodeling. PD173074 treatment significantly alleviated 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 a useful option for PAH. Our data also suggest a role of FGF-2/2BMP signaling interaction in PAH.

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**2335 | BENCH**

**PI3Kalpha induced SMC migration and cell cycle progression is crucial for neointima formation following vascular injury.**

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**Background:** Endothelium-derived C-type natriuretic peptide (CNP) possesses vascular remodeling in vivo.

**Results:** This data demonstrates that CNP-53 is specifically generated through the PI3Kb specific generation of cGMP. Furthermore, infusion of CNP-53 in SHRs generated significant plasma and urinary cGMP and lowered MAP without renal enhancing actions. Such findings advance the concept that CNP-53 is a vasoactive peptide and may represent a potential innovative therapeutic targeting the diseased blood vessel.

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**2337 | BENCH**

**The role of macrophage STAT3 signaling in pathogenesis of aortic dissection.**


**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, Akt activation in the cell cycle has been described in a human aorta tissue. However, it is unclear exactly how IL-6 and STAT3 participate in pathogenesis of AD, or how they 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, K67 staining showed that cell cycle was activated in these 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 periaortic 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 revealed 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. K67 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. Decluttering such molecular events during the development of AD will be essential to develop a new diagnostic and therapeutic strategies for this lethal disease.
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-protein (BAPN), an inhibitor of collagen/alanin cross-linking enzyme lysyl oxidase, and angiotensin II (AngII) using osmotic pumps. BAPN-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 before and during the BAPN-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 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 IL-17 knockout mice. Deletion of IL-17 gene dramatically abolished the exacerbating effect of NaCl on the severity of AD by BAPN-AngII. Transcription analysis of aortas before the onset of AD showed that strong induction of proinflammatory cytokines 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 and IL-17 may represent important therapeutic targets for AD. 

We aimed to use genetically engineered mice to determine whether endothelial mesenchymal transition contributes to the development of pulmonary arterial hypertension caused by a VEGF receptor inhibitor in mice R. Okamoto1, I. Goto1, Y. Ogihara1, N. Yamada1, H. Okada2, M. Ito1.

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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 endothelial mesenchymal transition contributes to the development of IPAH.

Methods: To generate reporter mice, tdTomato and Tie2-Cre double transgenic mice were crossed with Tie2-Cre double transgenic mice, all conditioned in our experiments. Because ECM is essential to maintain the tensile strength of arterial 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.

Results: We found that Nrf2 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 premature Nrf2 KO hearts showed an impaired response to beta adrenergic stimulation by isoproterenol, as shown by lower developed pressure and dP/dtmax as compared to WT mice, while systolic left ventricular function was preserved. Administration of the cardiac glycoside ouabain in vivo increased dP/dtmax and developed pressure in WT mice, but did not increase diastolic or systolic left ventricular function in the KO mice as assessed by Millar catheter. Surprisingly, blood pressure in Nrf2 KO mice was significantly decreased, and endothelial function of arterial conductance and coronary resistive vessels was preserved. This is consistent with increased expression of an eNOS in the aorta and in the heart of KO mice as compared to WT mice.

Conclusion: Nrf2 KO results in significantly impaired cardiac diastolic function, which is associated with a decreased myocardial relaxation, a reduced response to pharmacological regulation of Ca2+ homeostasis within the myocardium, while systemic and coronary endothelial function are preserved. This indicates that Nrf2-dependent pathways play a central role in preserving cardiac diastolic function in mice.

376 Vascular biology – New molecular and genetic findings

Casein kinase 2 beta is a critical player in platelet activation, arterial thrombosis and ischemic stroke O. Borst1, P. Muenzer1, B. Walker2, M. Chatterjee1, F. Langhauser3, R. Zehedi4, A. Fotinos5, C. Kleinschmit1, F. Lang2, M. Gawaz1, 1Department of Cardiology and Cardiovascular Medicine, University Hospital Tubingen, Tuebingen, Germany; 2Department of Physiology, University of Tubingen, Tubingen, Germany; 3Department of Neurology, University Hospital Wuerzburg, Wuerzburg, Germany; 4Leibniz-Institut für Analytische Wissenschaften, ISAS, Dortmund, Germany; 5Department of Neuroscience, University of Basel, Basel, Switzerland.

Background: Platelet adhesion to subendothelial collagen results in platelet activation, aggregation and thrombus formation with consecutive development of acute arterial thrombotic occlusions. Casein kinase 2 is an ubiquitous expressed tetramer which is composed of two α and two regulatory β subunits. CK2 is expressed in platelets and becomes activated upon platelet stimulation, but the impact of CK2-dependent signaling on platelet activation and arterial thrombosis is unclear. The present study aimed to elucidate the impact of the serine/threonine kinase CK2 on platelet activation and arterial thrombosis.

Methods and results: CK2β-deficient mice were crossed with PF4-Cre mice to generate platelet-specific CK2β-deficient mice (ck2βcre/+) and wildtype littermates (ck2βcre/cre/+). According to FACS analysis, luminescence measurements and aggregometry activation-dependent platelet alpha and dense granule secretion as well as integrin αIIbβ3 activation and platelet aggregation were severely impaired in ck2βcre/cre/+ platelets in response to activation with collagen-related peptide (CRP) or thrombin. Fura-2-AM-storm photoluminescent Ca2+ measurements pointed to a significant reduction in activation-dependent cytosolic Ca2+ increase due to a defective Ca2+ influx in ck2βcre/cre/+ platelets upon stimulation with CRP or thrombin in a consequential, in vitro thrombin formation vitro thrombin formation via collagen-coated surface under high arterial shear rates (1700 s-1) and thrombotic vascular occlusion in vivo following FeCl3-induced vascular injury of mesenteric arteries were significantly diminished in ck2βcre/cre/+ mice compared to ck2βcre/cre/+ mice. Furthermore we could show that ck2βcre/cre/+ mice are protected against aortic constriction and are subjected to occlusion of the middle cerebral artery (MCAO). ck2βcre/cre/+ mice displayed drasticaly reduced cerebral infarct volumes and developed significantly fewer neurological deficits (grip test, Bederson score) following MCAO compared to ck2βcre/cre/+ mice while tail bleeding time was only mild prolonged in ck2βcre/cre/+ mice. Finally, we identified potent antiplatelet targets of CK2 in platelet activation by phospho-proteomic approaches.

Conclusions: The present observations unravel CK2β as a novel powerful regulator of platelet activation, arterial thrombosis and ischemic brain infarction.
RNA editing is essential for vascular homeostasis in vivo and controls gene expression in patients with cardiovascular disease.

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 ischemia. To evaluate the clinical importance of our bench findings, we sequenced the transcriptome of peripheral blood mononuclear cells from 4 age-matched control subjects, 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. Increased CTSS editing correlated 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 in hypoxia 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.
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 per ms), a longer corrected QT-time (1.02, 1.00–1.03 per degree) 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, 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
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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 safe, effective and reasonable alternative to warfarin for patients undergoing ECV.

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, CHA2DS2-VASC score was 3.6±1.9, 1234 had one or two ECV procedures (Mean of 1.67±1.06 per pts), a longer corrected QT-time (1.02, 0.61–1.03 ms), a longer atrial refractory period (579±50 ms), a longer atrial conduction block (252±50 ms), a longer LA contraction (130±13 ms) and higher heart rate (90±13 bpm) vs NOAC. NOAC pts had significantly lower clinical relevant bleeding (0.3%, p<0.01). Stroke and systemic embolism rates at 90 days were lower in NOAC group (0.1%) vs warfarin (0.3%). There was no significant difference in the age of patients on warfarin compared to NOAC (Mean of 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=0.19). 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 compared to that in 2012.

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
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Purpose: Chronic renal failure (CRF) is known to increase myocardial susceptibility to ischemia/reperfusion (I/R) injury. The aim of this study is to examine if epoetin beta pegol (continuous erythropoietin receptor activator, CERA) can restore 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 was commenced at a week after the operation. At 5 weeks after the operation, rats underwent blood sampling and 20-min coronary artery occlusion/reperfusion. Level of serum creatinine was higher in SNx than in Sham (0.82±0.06 vs. 0.34±0.02 mg/dl), confirming development of CRF in SNx. Hemoglobin level was lower in SNx than those in Sham (14.2±0.2 vs. 17.5±0.2 mg/dl). Blood pressure was similar between Sham and SNx regardless of treatment with CERA. However, the hemoglobin level was preserved in SNx by CERA (16.4±0.7 mg/dl). Infarct size was larger in SNx than in Sham (69.4±0.4 vs. 43.9±2.2% of risk area, p<0.05). CERA significantly reduced infarct size in SNx (36.8±3.9%), though the effect of CERA in Sham was modest (31±4.6%). There was no improvement in serum creatinine level by CERA in SNx, but infarct size was negatively correlated with hemoglobin level (r=−0.55, p<0.01), indicating that activated erythropoietin receptors play a role in CERAreduced infarct size reduction. Hemoglobin level was positively correlated with expression level of Akt (r=0.61, p<0.001). CERA significantly increased expression of Akt in SNx. However, expression level of PHPP-1, a phosphatase specifically regulating phosphorylation of Akt-Ser-473, was higher in SNx than in Sham. CERA restored Akt-Ser-473 phosphorylation in SNx.

Conclusions: Continuous erythropoietin receptor activation reverses increased myocardial susceptibility to I/R injury in CRF presumably by attenuation of myocardial susceptibility to ischemia/reperfusion injury in chronic renal failure.

P2348 | BEDSIDE
Use of novel oral anticoagulants results in shorter waiting times for elective DC cardioversion
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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 INRs in the therapeutic range for this timeframe. This can result in long waiting times 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) prescription reduces waiting times for elective DC cardioversion.

Methods: A view of an electronic database of elective DCCV admissions at our institution was performed. Data recorded included, 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. 577 of these admissions were elective. Of these (82%) were successfully cardioverted to sinus rhythm. Age at admission ranged from 27–86 years (mean of 65 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 of 66.22 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=0.19). The average 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 compared to that in 2012.

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

P2351 | BENCH
High sensitivity cardiac troponin T significantly increases after a diagnostic stress test
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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 for other cardiac and extracardiac conditions and even in normal subjects.

Aim of the study: To evaluate changes in plasma concentrations of hs-cTnT and T in response to diagnostic stress tests (echo-stress test, echo-dipyridamole test, echo-dobutamine test), in comparison with CK-MB.

Methods: Plasma concentrations of hs-cTnT were evaluated before and 6 hours after a stress test in 100 consecutive patients. A total of 125 tests were performed.
Department of Pathology, Tokyo, Japan

via enhanced glucose utilization in mice. Contributing to cardiac energy metabolism during ischemia-reperfusion injury (IRI)

role of SGLTs in the heart remains to be fully elucidated. We herein investigated the role of SGLTs 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 ischemia and its mechanism 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 is highly expressed in both human autopsied hearts and murineperfused 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±3.5 vs 89±7.6%, n=5 each, P=0.05) and rate pressure product, associated with an increased infarct size, as demonstrated by TTC staining (%MII; 22±12.7 vs 11±1.1%, P<0.01) and CPK activity released into the perfusate (19±0.54 vs 0.9±0.3 U/L, 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 lenticular mass volume ratio by CMR: association with heart failure in thalassaemia major patients

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Introduction: Recently two novel 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 (LVMVR). 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 LVMVR is indicative of concentric remodelling. A LVGFI <37% and a LVMVR >1 were shown to be associated with the occurrence of cardiovascular events in non-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 LVMVR 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 LVMVR were quantitatively evaluated by SSFP cine images. The T2* value in all the 16 cardiac segments was evaluated and a global heart T2* value ≤20 ms was considered indicative of myocardial iron overload (MIO).

Results: Eighty (9.9%) patients had a LVGFI <37% and, compared to the patients with a normal LVGFI, they showed a significant higher frequency of heart failure (43.8% vs 4.2%, P<0.0001). Patients with a LVGFI <37% had a significant higher risk of heart failure (odds-ratio OR=17.59, 95% CI: 9.95–21.09; P<0.001). The risk remained significant also adjusting for the presence of MIO (OR=15.54, 95% CI: 8.05–26.27; P<0.001).

Conclusions: Thirty (3.7%) patients had a LVMVR >1 and, compared to the patients with a normal LVMRI, they showed a significant higher frequency of heart failure (20.0% vs 7.7%; P<0.015). Patients with a LVMVR >1 had a significant higher risk of heart failure (OR=3.01, 95% CI: 1.18–7.64; P=0.021). The risk remained significant also adjusting for the presence of MIO (OR=3.44, 95% CI: 1.31–9.01; P<0.012).

In a multivariate model including LVGFI, LVMVR and heart, the significant predictors of heart failure were a LVGFI <37% (OR=14.05, 95% CI: 7.66–25.77; P<0.001) and a global heart T2* ≤20 ms (OR=1.94, 95% CI: 1.08–3.47; P=0.026).

Conclusions: In TM patients a LVGFI <37% was associated with an higher risk of heart failure, independent by the presence of MIO. A widespread program using CMR exploiting its multi-parametric potential can have considerable power for the early identification and treatment of patients at risk for heart failure.

BEST POSTERS IN MYOCARDIAL ISCHAEMIA / BEST POSTERS IN CARDIOVASCULAR MAGNETIC RESONANCE

P2352 | BEDSIDE

Long term outcome following remote ischemic postconditioning during percutaneous coronary interventions

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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 (RP-Post) 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 RP-Post (induced by ischemia to arm or thigh) and a third, a control. RP-Post was applied during PCI immediately following stent deployment, by three 5 minute cycles of blood flow interruption 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 flow interruption to arm or thigh (20 mmHg to the arm in control) with 5 minute breaks between each cycle.

Results: There were no differences in baseline characteristics. Periprocedural myocardial injury (troponin T levels >3 x ULN) occurred in 33%, with no difference between groups (p=0.64). Outcomes at 1 year (Table) and during 3 years of follow-up (Figure) were not different between groups.

Conclusions: Remote ischemic postconditioning during PCI did not affect long-term cardiovascular outcome. Similar effect was obtained when remote ischemia was induced to the upper or lower limb.

P2353 | BENCH

Expression of SGLT1 in human hearts and impairment of cardiac energy metabolism by phlorizin during ischemia-reperfusion injury in mice

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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 ischemia and its mechanism 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.
P2356 | BEDSIDE
Troponin positive patients with unobstructed coronaries: incremental value of cardiovascular magnetic resonance
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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 diagnosis of troponin utility 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 indeterminate.
Results: Median troponin value was 500ng/L (IQR 183,840). Consensus panel diagnosis of CMR and CMR were concordant in only 67/125 (53%) patients. There was only moderate level of agreement between the three cardiologists (κ=0.466, p<0.01) and a poor level of agreement between the consensus panel and CMR (κ=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 provided diagnoses 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 demonstrating a high association with subclinical coronary artery calcification
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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 volume was 12,1 ml in men and 7,4 ml in women. Most lesions were found periventricular and in the parietal and frontal lobe. 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) (1.165 (0.91–1.4), p<0.001), which persisted after adjustment for risk factors (0.598 (0.3–0.99), 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
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Aim: Numerous studies showed that CMRI with adenosine stress and delayed enhancement are highly sensitive and specific for myocardium perfusion evaluation. Aim of our study to determine the dynamics of myocardial viability using stress-CMRI in patients with chronic total occlusion before and after PCI.
Methods and results: We present the results of prospective randomized trial of stress-CMRI 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-CMRI before coronary recanalization. Clinical coronary recanalization was performed 6 months after stress-CMRI, the minimal time period with coronary patency was 6 months. CMRI was performed with 3 Tesla magnets. Before and after冠状动脉再血管化，所有的患者均进行了CMRI检查。结果:在第一组中，39例患者接受了冠状动脉再血管化治疗，33例患者则接受标准药物治疗。所有患者均进行了心脏磁共振成像(CMRI)检查。我们随机将患者分为两组。在第一组中，冠状动脉再血管化治疗后，患者的心肌灌注情况得到了改善。结论:CMRI在冠状动脉再血管化治疗前和后能够检测到 myocardial perfusion in chronic total occlusion patients.

P2360 | BENCH
P21 deficiency is protective against high fat diet-induced metabolic disturbances and myocardial dysfunction
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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 models. However this is of limited clinical interest because of p53's eminent tumor-suppressive role, p21 is a p53 downstream target without any tumorigenic 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: We used Wild-type (WT, C57BL/6J, n=8) and p21-deficient 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 adverse diabetic states and therapeutic approaches to manipulate p21 expression as a means to confer protection against HFD-induced metabolic disturbances and myocardial dysfunction. doi:10.1136/eurheartj.2013.347695

BEST POSTERS IN CARDIOVASCULAR MAGNETIC RESONANCE / BEST POSTERS IN METABOLISM AND THE HEART

Table 1. Linear regression for the association of WML with traditional cardiovascular risk factors

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Beta-estimate (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>age</td>
<td>0.073 (0.061–0.084)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>gender male</td>
<td>0.35 (0.174–0.525)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>cholesterol</td>
<td>0.002 (0.000–0.005)</td>
<td>0.049</td>
</tr>
<tr>
<td>blood pressure (syst)</td>
<td>0.01 (0.011–0.022)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>0.041 (0.02–0.062)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.342 (0.173–0.512)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>smoking</td>
<td>-0.096 (-0.22–0.028)</td>
<td>0.128</td>
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</table>
P2361 | BENCH

Identification of a glucose sensor in the heart
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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). SGLT isoforms in heart must therefore be able to transport glucose. The underlying molecular mechanism is still awaited.

Methods: SGLT3 and SGLT2 expression was evaluated, based on their substrate affinity (galactose transported 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 SMT1 were expressed in mice and rat hearts as well as isolated cardiomyocytes. SGLTsb corresponding to the human SGLT3 was marginal. SGLT2, SGLT5 and SMT2 were not detected. SGLT4 was only expressed in rat heart. The human heart expressed SGLT1 and SMT1. Under SGLT4 glucose background, incubation of rat ventricular cardiomyocytes with 16 mM galactose or 1 DOG did not activate NOX2. By contrast, addition of 16 mM myo-inositol completely reproduced toxic effects of HG (21 mM 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. Finally, adenoviral SMT1 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 10 mM glucose, being nearly maximal (which was normally observed at 21 mM glucose).

Conclusion: Adult cardiomyocytes express SGLT1 and SMT1. SMT1 but not SGLT1 senses an increase in glyceric, inducing NOX2 activation. This work strongly supports that SMT1 acts as a glucose sensor in the heart.

BEST POSTERS IN PULMONARY HYPERTENSION TREATMENT STRATEGIES

P2362 | BENCH

TIMP3 acts through apelin to maintain cardiac metabolic flexibility
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Background: TIMP3 acts through apelin to maintain metabolic flexibility of the heart through regulation of PPARα/AMPK signaling, especially in the fasted state.

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 IP3IR antagonist 2-APB as well as in functional IP3 i/k o mice. Following mitochondrial Ca uptake, the mitochondrial membrane potential depolarized by 51±4% (20 min, n=9). Interestingly an effect on ROS production could not be seen within the first 20 min (+1±5%, 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 isoprenaline (iso) resulted in a faster and smaller mitochondrial Ca uptake which reached its maximum of 15±4% at 15 min (n=10). Furthermore, iso stimulation did not alter the mitochondrial ATP concentration.

This implies two different underlying mechanisms. To explore the underlying molecular mechanism we blocked the mitochondrial Ca uniporter (mCU) using Ru360. This did not influence mitochondrial Ca uptake following cellular stimulation with ET-1 (+3±17% after 20 min, n=11) but prevented iso induced mitochondrial Ca release (−52±6%, n=8). In contrast, when blocking the mitochondrial ryanodine 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 (+18±5%, 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.
P2366 | BEDSIDE
Efficacy and safety of first-line oral triple upfront combination therapy in severe pulmonary arterial hypertension
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Background: Selexipag is an orally available, selective IP receptor agonist target ing arterial remodeling. In the Phase III STRIKE II/PHRONIX 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.

Purpose: To compare the efficacy, safety and tolerability of selexipag according to background PAH therapy.

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, 376 (32.4%) were receiving PDE5i monotherapy and 375 (32.5%) were receiving ERA and PDE5i combination therapy at baseline. The baseline characteristics were balanced across 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, 1.41); 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 (headache, dizziness, nausea and jaw pain) were less frequent in the subgroups of patients receiving one or no PAH therapy at baseline compared with those receiving two. No new AEs were observed with selexipag on top of an ERA and/or PDE5i.

Conclusions: The effect of selexipag on morbidity/mortality in patients with no PAH therapy at baseline as well as those receiving PAH therapy as monotherapy or as combination therapy was similar to that of the overall study population with an acceptable safety profile. For the first time, a clinically relevant benefit on long-term outcomes has been shown when adding a third PAH drug on top of dual combination therapy.

P2367 | BEDSIDE
Treating pulmonary hypertension in patients with heart failure and preserved ejection fraction: safety and efficacy in comparison to IPAH in COMPERA
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Background: While targeted therapies are available for idiopathic pulmonary arterial hypertension (IPAH), evidence based treatment recommendations for pulmonary hypertension (PH) associated with heart failure and preserved ejection fraction (HFpEF) are lacking. However, individual patients with severe PH and HFpEF reported to respond to targeted therapy, tolerability and efficacy of PAH drugs were reduced in patients with PH and HFpEF while survival was not different.

Methods and results: Out of 5,568 patients in the prospective COMPERA registry, we analyzed clinical characteristics, hemodynamics and treatment responses of patients with IPAH (n=1,101) or PH-HFpEF (n=217) who received targeted PH therapies. Patients with PH-HFpEF were significantly older (74 vs. 70 years), had a higher body mass index (30.4 vs. 26.7 kg/m^2), and a higher rate of co-morbidities (98.3 vs. 79.9%, all p < 0.001). Mean pulmonary artery pressure (46.3±9.8 vs. 45.2±12.5 mmHg), cardiac index (2.2±0.8 in min in both groups), and mixed venous oxygen saturation (61.6±7.6 vs. 62.5±8.8%, all n.s.) were almost identical in both groups. As compared to IPAH, PH-HFpEF patients had a higher PAWP by definition (20±4.3 vs. 9.5±3.4 mmHg). This was a result of lower body surface area (1.70±0.13 vs. 1.73±0.13 m^2), and lower body mass index (26.7 vs. 27.9 kg/m^2, both n.s.). PH-HFpEF patients had a lower ejection fraction (56.5±17% vs. 58±15%, all n.s.), and a higher rate of co-morbidities (98.3 vs. 79.9%, all p < 0.001).

Conclusions: Despite almost identical alterations of pulmonary artery pressure and cardiac output patients with PH-HFpEF differed with respect to age, co-morbidities and certain hemodynamic features when compared to IPAH. Although both groups responded to targeted therapy, tolerability and efficacy of PH drugs were reduced in patients with PH and HFpEF while survival was not different.
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±4 vs. 25±5 mmHg) or right-sided heart failure (HF) (brain natriuretic peptide, 37±24 vs. 45±60 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 senescent marker expression in circulating mononuclear cells

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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 randomized to a control group (no change of inactive life-style) or to one of three training interventions: 1) aerobic endurance training (AET, continuous running); 2) high-intensive interval training (IT, 4x4 method) or 3) strength endurance training (SET; circuit training on 8 devices).

Results: Telomerase activity and mRNA expression (real-time PCR) of telomere repeat-binding factor 2 (TRF2) and senescent marker p16 were measured.

Conclusion: The training induced an increase of both, submaximal fitness parameters such as running speed on the treadmill at a pulse of 150/min (control: 22.3±1.1; AET: 0.79±1.2; IT: 1.0±0.5; SET: 0.18±0.0 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 the training induced an increase of both, submaximal fitness parameters such as running speed on the treadmill at a pulse of 150/min (control: 22.3±1.1; AET: 0.79±1.2; IT: 1.0±0.5; SET: 0.18±0.0 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 greater results were observed in EarlyExT+MCT. In contrast to SET, ExT improved exercise tolerance and survival in all MCT-exercised groups. EarlyExT+MCT showed improved cardiac output despite the presence of elevated preload (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), reduced 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.

P2371 | BENCH
Screening for cardiac conditions predisposing to sudden cardiac death: the diagnostic yield and financial implications

1Faculty of Medicine University of Porto, Porto, Portugal; 2University of Aveiro, Department of Chemistry, Aveiro, Portugal; 3Faculty of Sport from University of Porto, CIAEF, Porto, Portugal

Introduction: Right ventricular failure (RVF) is the most common cause of death in patients with pulmonary arterial hypertension (PAH). Growing evidences suggests that exercise training (ExT) is safe and beneficial for this population but its impact on RVF 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

D. Gonçalves1, R. Ferreira2, H. Fonseca3, A.I. Padrao4, A.F. Silva1, F. Vasques-Nova1, N. Gonçalves1, J. Alberto Darte3, A. Leite-Moreira1, J. Camarim-Coelho1, Faculty of Medicine, University of Porto, Porto, Portugal; 2University of Aveiro, Department of Chemistry, Aveiro, Portugal; 3Faculty of Sport from University of Porto, CIAEF, Porto, Portugal

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 evaluation. 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, but late ExT+MCT showed improved cardiac output despite the presence of elevated preload (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), reduced 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.

Conclusion: Among fit sportsmen ≥45 years with a low ESC SCORE risk, lifelong exercisers with ideal cardiovascular health are most likely to have perfect coronary arteries (see table for crude prevalence and adjusted odds ratio’s).

Table 1. Prevalence (%) of coronary arterys and multivariable odds ratio’s (95% confidence intervals)

<table>
<thead>
<tr>
<th>Coronary arterys</th>
<th>Lifetime exercisers (n=112)</th>
<th>Irregular exercisers (n=171)</th>
</tr>
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<tbody>
<tr>
<td>Ideal CVH (n=130)</td>
<td>64% (5, 2.6–12.2)</td>
<td>23% (1, 1.0–4.3)</td>
</tr>
<tr>
<td>Non ideal CVH (n=153)</td>
<td>39% (2, 1.0–4.3)</td>
<td>23% (1, 1.0–4.3)</td>
</tr>
</tbody>
</table>

Note: pre/post: control 45±150; AET 287±150; IT 225±85; SET−15±52 HEK cell equivalents. Expression of the telomere capping factor (TRAP assay, compared to HEK cells as positive controls) in MNC revealed a significant 4–5-fold increase in both endurance exercise groups, but greater results were observed in EarlyExT+MCT. In contrast to SET, ExT improved exercise tolerance and survival in all MCT-exercised groups. EarlyExT+MCT showed improved cardiac output despite the presence of elevated preload (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), reduced 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 | BENCH
Screening for cardiac conditions predisposing to sudden cardiac death: the diagnostic yield and financial implications

H. Dhutia, 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 inherited cardiac diseases that can be detected during life. The ESC recommend preparticipation screening (PPS) with history and physical examination (H+P), ECG and early exercise echocardiography (EEG) 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 potentially life-saving cardiac conditions 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 EEG inter- preted in line with 2010 ESC recommendations. On site echocardiography (TEE)
was performed in those considered to have abnormalities on preliminary assessment at no extra cost. Individuals requiring further evaluation were referred to a specialist. Data of investigations performed and outcome was available in 78% of the referred individuals.

**Results:** 4,099 (13%) athletes undergoing PPS and 26,443 (87%) self-presenting and apparently healthy general population individuals were evaluated. 7.9% (n=319) athletes and 9% (n=2,387) general population individuals had abnormalities on preliminary assessment. On site TTE reduced referral for further evaluation by 53% (n=170) in athletes and 60% (n=1,446) in the general population. The predominant reason for referral in both groups was an ECG abnormality. Athletes were less likely to be referred for H+P abnormalities. The prevalence of sinister cardiac diseases was similar in both groups; however, the cost per diagnosis was higher in the general population (Table).

**Conclusion:** The cost of diagnosing a condition associated with SCD in the young ranges from €23,944 to €33,777.

**BEST POSTERS IN PCI: EXPOSING BASIC SCIENCE AND RADIATION… INTO CLINICS**

**P2373 | BENCH**

*Research Foundation, Department of Science, Rotterdam, Netherlands; B.J. Tefft1, S. Uthamaraj2, J.J. Harburn3, D. Dragomir-Daescu2, G.S. Sandhu1.*

**Background:** Our previous bench studies PLASMONICS and NANOM-FIM trial...**.

**Conclusions:** Plasmonic resonance-mediated therapy using noble-metal NP associated with significant regression of coronary atherosclerosis below a 40% PB and minimal nanotoxicity.

**P2377 | BEDSIDE**

*University, Modern Nanotechnologies, Yekaterinburg, Russian Federation; Institute of Cardiology, Yekaterinburg, Russian Federation; Ural Federal University, Modern Nanotechnologies, Yekaterinburg, Russian Federation.*

**Background:** Our previous bench studies PLASMONICS and NANOM-FIM trial documented 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 allogeneic stem cells carrying NP after MSCT-, IVUS- and OCT-guided mapping of the vessel), and plasmonic photothermal 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 craters on surface of erythrocytes (from 0.34 to 6.12 per cell, p<0.05) within 72 hours after exposure of NP (Fig 1).

**Abstract P2373 – Table 1. Yield and overall cost of screening**

<table>
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<th>General Population (N=26,443)</th>
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<tr>
<td>Total abnormal preliminary assessments (% of total screened)</td>
<td>319 (7.9%)</td>
<td>2,387 (9%)</td>
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<tr>
<td>Number referred for further evaluation after on site TTE (% of total screened)</td>
<td>149 (3.6%)</td>
<td>941 (3.6%)</td>
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<tr>
<td>Referral indication – H+P (% of total screened)</td>
<td>22 (0.5%)</td>
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<td>Referral indication – ECG (% of total screened)</td>
<td>95 (2.3%)</td>
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<tr>
<td>Potentially sinister cardiac condition diagnosed (% of total screened)</td>
<td>12 (0.3%)</td>
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<td>Minimum cost per potentially sinister condition diagnosed† (including subsidized screening costs)</td>
<td>€23,944</td>
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†Based on UK National Health Service tariffs.

A. Kharlamov1, J. Gabinsky2, V. Shur3 on behalf of NANOM-PCI.

**Conclusions:** Magnetic endothelialisation may enable the development of small caliber synthetic vascular conduits, thereby enabling additional therapeutic revascularisation options for smaller vessels.

**P2374 | BEDSIDE**

*Mayo Clinic, Cardiovascular Diseases, Rochester, United States of America; Mayo Clinic, Engineering, Rochester, United States of America; 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 3x15 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 neonintima (~200 μm thick) along with confluent endothelium. Fluorescence microscopy (Fig 1B) demonstrated the presence of delivered endothelial cells within the neonintima.

**Conclusions:** Magnetic endothelialisation may enable the development of small caliber synthetic vascular conduits, thereby enabling additional therapeutic revascularisation options for smaller vessels.

**Abstract P2374**

**Table 1. Yield and overall cost of screening**

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A. Kharlamov1, J. Gabinsky2, V. Shur3 on behalf of NANOM-PCI.

**Conclusions:** Magnetic endothelialisation may enable the development of small caliber synthetic vascular conduits, thereby enabling additional therapeutic revascularisation options for smaller vessels.
Private Practice collect 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 values of a single centre with the values of the whole registry from 2002 to 2013, but not fluoroscopy time. We found the same trend, a decrease in the whole centre (−10%), but higher ones for dye consumption (+13%). The decline of DAP in the centre data 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 interventionists 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 progression 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 comparing femoral to radial or radial right to radial left 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 comparing femoral to radial or radial right to 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 comparing femoral to radial or radial right to radial left access have previously been published, but no data comparing the three access sites are available to our knowledge. The adjusted operator radiation exposure was significantly lower in the RFA group (0.30±0.36 Gy cm²) compared to the RRA (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 | BEDSIDE

Hypothyroidism predicts the mortality of idiopathic dilated cardiomyopathy

J.R. Siles Rubio, C. Pera-Rojas, A. Ramirez Moreno, R. Bravo-Marques, M. Noureddine, L. Inigo-Garcia, J. Munoz-Belido, A. Milan-Pinilla, A. Val-Alberca, E. Zambrano-Medina, C. Cardiology Department, Hospital, Estepona, Spain; 2Hospital of Estepona, Anesthesiology, Estepona, Spain; 3Hospital Costa del Sol, Marbella, Spain; 4Servicio de Medicina Interna, Hospiten, Estepona, Spain

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 long-term mortality of patients with idiopathic dilated cardiomyopathy.

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 with wild-types vs NYHA I-II. During the follow-up (17±8) months, there were 111 cumulative deaths. 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 hyperthyroidism (HR=2.869, 95% CI: 1.817–4.532). Subclinical hyperthyroidism 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.

P2380 | BENCH

Deletion of osteoprotegerin gene exacerbates cardiac hypertrophy and systolic dysfunction in aged mice

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Background: Receptor activator of nuclear factor-kappab ligand (RANKL) and osteoprotegerin (OPG) are associated with the pathogenesis of osteoporosis 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. Here, we investigated whether OPG can be eluciated 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 (RANKL+/−/−). 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 eleva-
tion of peak left ventricular blood pressure (163±15 mmHg vs 138±17 mmHg, p<0.0012), and greater increase of heart weight/body weight (8.9±0.64 vs 7.4±0.12 mm/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 (250%, p<0.0032), angiotensin converting enzyme (79%, p=0.0344) and matrix metalloproteinase-2 (61%, p=0.0332), 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 (333±31 vs 301±16 ng/ml, p<0.0001) in the serum, along with decrease in trabecular bone volumen/site volume at the proximal metabolism of ibiza (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.

P2382 | BENCH

Myocardial gene expression of osteopontin is higher in idiopathic than ischemic end-stage dilated cardiomyopathy

M. Cabatá, B. Svezia, L. Botta, C. Caselli, A. Bucciat, V. Lionetti, S. Del Ry1, 1Institute of Clinical Physiology of CNR, Pisa, Italy; 2Sant’Anna School of Advanced Studies, Institute of Life Sciences, Scuola Superiore Sant’Anna, Pisa, Italy; 3Reguigards Ca’ Grand’s Hospital, Department of Cardiac Surgery, Milano, Italy; 4University Hospital of Pisa, Histopathology Department, Pisa, Italy

Purpose: The morphological and molecular features of cardiac remodelling are
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±110 ml) and ICM patients (n=8; age: ~50yrs; LVEF≈19.5±5.2; LVEDV≈270±57 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 out 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 ICM). A similarly trend was observed for OPN cardiac protein concentration (C: 1.12±0.26; DCM: 1.29±0.22; ICM: 1.0±0.077 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.

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. 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±107 pg/ml vs. post: 83±36 pg/ml, P=0.02). BP responders showed a greater reduction of the norepinephrine gradient compared to non-responders (~340±423 pg/ml vs. -18±122 pg/ml, P=0.01). Patients with reduction of norepinephrine gradient in both kidneys showed the most pronounced decrease of the systolic BP (~25±14 mmHg) compared to patients with reduction of norepinephrine gradient in only one kidney (~7±15 mmHg) or patients without norepinephrine reduction (~3±19 mmHg, P=0.03 vs. bilateral reduction).

Conclusions: 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. Doerr1, C. Liebertau2, H. Moellmann3, L. Gaede4, C. Troidl5, J. Wiebe6, S. Voss4, T. Bauer1, C. Hamm1, H. Neet1. Justus-Liebig University Giessen, Medical Clinic I, Cardiology, Giessen, Germany; 1:Kernhoff Clinic, Department of Cardiology, Bad Nauheim, Germany

Background: Renal sympathetic denervation (RDN) represents an effective method to gauge the extent of renal nerve ablation.

Objective: To examine the effect of RSD on collagen turnover by analyzing serum levels of the markers of cardiac extracellular matrix turnover and deposition.

Methods: Twenty-nine patients with heart failure with reduced ejection fraction were included in this study. A therapeutic response was defined as an office systolic blood pressure reduction of ≥10 mmHg 6 months after RSD. Various blood samples for measurement of serum PICP, PINP, and PIIINP were collected prior to and 6 months after RSD.

Results: A significant reduction in office systolic BP of 24.3 mmHg (SBP baseline: 166.9 [IQR: 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 levels and the extent of RSD-related serum level reduction 6 months after RSD (PICP: R=0.87, PINP: R=0.44, PIIINP: 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).
**Conclusion:** In addition to the effective blood pressure reduction in response to RSD, this study demonstrates an effect of RSD on biomarkers reflecting cardiovascular ECM turnover and deposition. These results provide information on a beneficial effect of RSD on cardiovascular fibrosis, ECM turnover and HHD in high-risk patients.

**Methods:**

Of RSD to at least partially reverse increased aortic stiffness.

To assess the impact of baseline arterial stiffness as assessed by aortic

**Purpose:**

thetic denervation (RSD) for resistant arterial hypertension as well as the potential

**Background:**

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 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 pac-

**Results:**

ing lead was positioned based on the criterion of the latest electrically activated site during intrinsic ventricular activation and the second lead as remote as possi-

**Conclusion:**

ble from the first lead. Acute hemodynamic response was evaluated as variation of LVP/dtmax by means of a RADI pressure wire within the LV. One-way analy-

sis 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±1±1.8 pacing sites were evaluated per patient. During standard BiV pacing LVP/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%).

**Fig. 1.** Baseline condition. RV, right ventricular pacing; BiV, conventional biventricular pacing; TRIV, triple site pacing.

**Conclusion:** In pts with HF and RV pacing TRIV pacing produces a small but significant further increase in acute hemodynamic response compared to con-

**P2389 | BEDSIDE**

**Conclusion:** Features of a novel CRT Toolkit: an accurate algorithm for the measurement of ventricular conduction delays

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**Introduction:** Studies have shown that pacing at the site of late electrical acti-

vation on the quadripolar lead increased dP/dtmax if the delay between the early and late site pacing is >10ms. The latest St. Jude Medical devices for cardiac resynchronization therapy (CRT) allows to automatically calculate the delays be-

 tween each electrode of the left ventricular quadripolar lead (LV) and the right ventricular (RV). The purpose of this survey is to evaluate the functionality of this algorithm in the real clinical practice.

**Methods:** Data were collected from 237 patients (pts) in 67 Italian Hospitals (QRS 161±25ms; EF 28±8). Pre-discharge the electrical delays from RV lead and LV lead (delay: distal, M2-M3, media; P4, proximal) were measured both RV-sense (in 237 pts) or RV-pace mode (in 229pts).

**Results:** In RV-sense mode the mean of the delay between the early and late site pacing (delta delay) was 27±30 msec and in 189 (80%) pts the delta delay was <10 ms; in RV-pace mode the mean of the delta delay was 32±29 msec and in 197 (86%) pts was >10ms. The table shows the average delay of each electrodes and the most delayed electrode. In 129 pts the activation pattern was distal-proximal with the earlier electrode as D1 or M2 and the latest P4, only in 15 patients we had an opposite activation pattern (earlier electrode P4 or M3 and latest D1). In 53 patients the activation pattern was distal-proximal and in 43 patients we had an opposite activation pattern.

**Conclusion:** In the real clinical practice using an automatic algorithm it was pos-

**P2387 | BEDSIDE**

**Aortic pulse wave velocity as a marker for arterial stiffness predicts outcome of renal sympathetic denervation and remains unaffected by the intervention**

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**Purpose:** To assess the impact of baseline arterial stiffness as assessed by aortic pulse wave velocity (PWV) on blood pressure (BP) changes after renal sympa-

thetic denervation (RSD) for resistant arterial hypertension as well as the potential of RSD to at least partially reverse increased aortic stiffness.

**Methods:** Fifty-eight patients with refractory hypertension (daytime systolic BP > 135 and/or diastolic BP > 90 mmHg on ambulatory BP measurement) under-

went RSD. All patients had a stable antihypertensive drug regimen of >3 agents including a diuretic. All RSD procedures were performed using the Simplicity Flex Catheter. Aortic PWV was assessed invasively by simultaneous pressure record-

ings 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 sig-

ificant reduction in mean systolystic ABPM from 154.3±11.4 to 146.2±13.0 mmHg (p<0.0001). Patients with baseline PWV below the median (14.4 mm/s) dis-

played a significantly greater reduction in mean systolic ABP from 154.3±11.4 to 146.2±13.0 mmHg (p<0.0001). When compared to patients with PWV above the median (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 asso-

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.

**P2388 | BENCH**

**The effectiveness of chemical renal denervation by vincristine depends on the flow rate of delivery**

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**Background:** Real artery denervation by vincristine has been proven to be promising regarding its safety and efficacy.

**Aim:** The aim of the study was to compare in an experimental model the efficacy of constant versus random flow rate delivery of vincristine on renal sympathetic denervation.

**Methods:** We used 10 juvenile Landrace swine. After the introduction of a 7 Fr sheath into the femoral artery, a guidewire was advanced into the distal part of the renal artery. Then the first delivery balloon catheter that delivers vincristine in random flow rate, was advanced at the proximal part of the artery and the balloon was inflated in order to locally deliver vincristine to the media of the renal artery. Similarly the process was repeated in the contralateral renal artery, with the use of the double balloon catheter that delivers vincristine with a constant flow rate. Sacrifice of the animals was performed at 28 days. All sections were processed for histological and immunohistochemical analysis.

**Results:** The delivery of vincristine with both catheters was successful and uncomplicated. Immunohistochemistry showed that the mean number of intact nerves in all sections was significantly lower in the group of vincristine delivered with constant flow catheter compared to the group that the delivery was performed in a random fashion (1.8±0.37 vs 1.76±0.41, p=0.04).

**Conclusion:** Chemical renal denervation with vincristine by a constant flow rate catheter is more effective compared to the denervation performed by a catheter that delivers vincristine in a random fashion.
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.

### P2391 | BEDSIDE
**Super-response to cardiac resynchronisation therapy in patients with congestive heart failure**

V.A. Kuznetsov, N.N. Melinik, D.V. Krouchnik, A.M. Soldatova, 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.

**Materials:** 59 CRT patients (mean age 52.9±9.0 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:** Both groups demonstrated significant improvement of NYHA functional class, reductions of left ventricular ejection fraction and LVESV. All parameters of mechanical dyssynchrony were significantly higher in super-responders group. Multiple logistic regression analysis showed that LVPEP was an independent mechanical dyssynchrony were significantly higher in super-responders group.

**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.

### P2392 | BEDSIDE
**The latest NICE guidelines on the use of cardiac resynchronisation therapy and implantable cardioverter defibrillator devices in heart failure may significantly increase implant rates**

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**Introduction:** Implantable cardiac electronic devices (ICEDs) have revolutionised the management of heart failure in patients with a reduced left ventricular ejection fraction (LVEF). In June 2014 the National Institute for Health and Care Excellence (NICE) released new guidelines (TA314) regarding such devices, updating the management of heart failure in patients with a reduced left ventricular ejection fraction. For 24 month follow-up there was significant reduction in the end-systolic volume was greater in Group I compared to Group II. For 24 month follow-up there was significant reduction in the QRSst width in Group I, \(p=0.042\). Final values of the QRSst and QRSn-st width were lower in Group I, \(p=0.016\) and \(p=0.044\) respectively. End-systolic and end-diastolic LV volumes significantly decreased in both groups; reduction in end-systolic volume was greater in Group I compared to Group II, \(p=0.039\). EF increased in both groups, the degree of EF increase was higher in Group I, \(p=0.048\). FC of HF decreased in both groups; the final FC value was lower in Group I, 2.12 versus 2.64 in Group II, \(p=0.022\).

**Conclusions:** VFD optimization improves hemodynamic parameters in the long-term period. The narrowest biventricular QRS can represent an optimal cardiac resynchronisation. ECG is reproducible method for CRT optimization.

### P2393 | BEDSIDE
**ECG for cardiac resynchronisation therapy optimization**

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**Background:** Atrioventricular (AVD) and interventricular delay (VVD) optimization is an important part of response in CRT devices. No optimization or incorrect performance may reduce the positive effect of CRT and enhance heart failure (HF) severity. Widely used AVD and VVD selection with different ways of echocardiography requires special skills and time-consuming.

**Aim:** To assess the impact of VVD optimization in CRT devices based on changes in the QRS complex width using standard ECG on hemodynamic parameters in the long-term period.

**Materials:** Randomized study involving 120 patients in sinus rhythm after CRT implantation according to the conventional guidelines. Study design: all patients were randomized into 2 groups – 1) VVD optimization, n=60, 2) conventional treatment (only AVD optimization), n=60. Standard follow-up protocol, echocardiographic parameters as optimization were repeated every 6 months. Observation period was 24 months. The optimal sensed/paced AV interval was assumed to the finished symmetrical intrinsic/stimulated P wave respectively. VFD optimization was implemented by gradual change of stimulation parameters following the response to CRT to the optimal QRS parameters. VFD optimization was implemented by gradual change of stimulation parameters following the response to CRT.

**Results:** There were no significant differences in cardiomyopathy etiology, baseline LVEF, QRS parameters QRS parameters QRS parameters between the groups. For 24 month follow-up there was significant improvement of NYHA functional class assessing was implemented by a six-minute walk test.

**Conclusions:** VFD optimization improves hemodynamic parameters in the long-term period. The narrowest biventricular QRS can represent an optimal cardiac resynchronisation. ECG is reproducible method for CRT optimization.
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 cardiac 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 | BEDSIDE
No association between cardiac resynchronization therapy response and left atrial size and function as assessed by computed tomography
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Background: Cardiac resynchronization therapy (CRT) is an established treatment for patients with chronic heart failure and wide QRS. However, 30–40% of patients are non-responders. The aim of this study was to determine whether baseline left atrial (LA) volume and function measured by computed tomography (CT) were associated with clinical or echocardiographic response to CRT.

Methods: We prospectively included 137 patients (all LBBB, 28 female, age 69±3, NYHA class III/IV 69/64, QRS duration 25±6) receiving a CRT system who underwent a dynamic cardiac CT with measurement of LA size and function (Table). Patients alive, not hospitalized for heart failure, and improving ≥ 1 NYHA class or ≥ 10% in a 6-minute walk test after six months follow-up were classified as clinical responders. Echocardiographic response was defined as ≥ 15% reduction in left ventricular end-systolic volume.

Results: Ninety-five patients (68.8%) were clinical responders whereas 113 (81.9%) were echocardiographic responders. We found no significant association between baseline measures of LA volume or function and clinical or echocardiographic response to CRT (Table).

Conclusions: Baseline LA volume and function as assessed by cardiac CT are not associated with clinical or echocardiographic response to CRT.

Acknowledgement/Funding: Department of clinical medicine, Aarhus university, The Central Denmark Region, Manufacturer Karl G Andersens Fund.

P2397 | BEDSIDE
Optimization of pacing parameters with 3D-echo increases response to CRT in patients with ventricular bigeminy
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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 patient population requiring cardiac pacing for complete atrioventricular block (CAVB), using 3D-echo (3DE) to optimize V-V 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 (2D), end-systolic volume (ESV), ejection fraction (EF), systolic dysynchrony 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 (25–75% quartiles), p < 0.05 is significant.

Results: 22 patients (7 F), aged at implantation 9 (1–28) years, with systemic LV and CAVB, 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), posterobasal lateral base (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 (1–2) (p = 0.0001). A linear regression model showed: increase of V-V intervals (coefficient 1.9, p = 0.01). Significant increase of EF (coefficient 3.4, p < 0.0001) and decreases of QRS duration (−7.2, p < 0.0001), 2 (−0.8, p < 0.0001), 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 1

<table>
<thead>
<tr>
<th>Year</th>
<th>Pre-CRT</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
<th>4–6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRS, ms</td>
<td>150 (120–160)</td>
<td>120 (90–140)</td>
<td>110 (80–120)</td>
<td>105 (80–120)</td>
<td>105 (80–120)</td>
</tr>
<tr>
<td>z</td>
<td>4.7 (3.1–5.4)</td>
<td>1.4 (0.7–2.7)</td>
<td>0.8 (0.7–1.8)</td>
<td>0.5 (0.4–0.8)</td>
<td>0.5 (0.2–1.0)</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>
<tr>
<td>SDI, %</td>
<td>–</td>
<td>6.3 (3.6–13.8)</td>
<td>3.5 (2.4–11.1)</td>
<td>4.0 (2.9–6.3)</td>
<td>2.9 (2.1–3.7)</td>
</tr>
</tbody>
</table>

Conclusions: In young patients with CAVB and CRT, 3DE/ECG individualized optimization of V-V intervals showed at short/medium-term follow-up, a significant improvement of LV dimensions, systolic function, synchrony, and NYHA class.

P2398 | BEDSIDE
The effect of cardiac resynchronisation therapy on cognitive function in patients with moderate to severe heart failure
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Background: Cognitive impairment in heart failure is common and is associated with the severity of the disease and loss of independence. Cognitive impairment is believed to be due, at least in part, to reduced cardiac output and subsequent cerebral hypoperfusion. Cardiac resynchronisation therapy (CRT) increases systolic blood pressure (SBP) and cardiac output in patients with reduced systolic function and a broad range of heart failure etiologies.

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 psychosexual 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 transthoracic echo pre-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: SBP change was measured at baseline (mean SBP 121±17 mmHg) vs 6 weeks post CRT (159±15 mmHg; p < 0.05). There was a significant increase in SBP of 35±18 mmHg at 6 weeks post CRT (p < 0.05). Significant improvements from baseline were observed in all areas of cognitive function at 6 weeks post CRT insertion. While memory and executive function were unaffected by CRT insertion, significant improvements were observed in the domains of psychomotor speed (mean difference in score 9.3, 95% CI 3.1 to 15.4; p = 0.01), and motor speed (mean difference in score 2.4, 95% CI 0.6 to 4.2; p = 0.03). A significant difference in score 2.4, 95% CI 0.6 to 4.2; p = 0.03). Heart failure related quality of life also improved at 6 weeks (mean difference in score 15.69, 95% CI 7.5 to 23.86, p < 0.004). A significant association was found between improvement in psychomotor speed and change in LVEF at 6 weeks post device implantation (Beta 0.29, 95% CI 0.36–0.76, p = 0.034). The acute rise in SBP was measured using a femoral arterial line at the onset of biventricular pacing.

Table 1

<table>
<thead>
<tr>
<th>Table</th>
<th>Pre-CRT</th>
<th>6 weeks post CRT</th>
<th>Mean difference</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP, mmHg</td>
<td>121±17</td>
<td>159±15</td>
<td>35±18</td>
<td>9.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Active emptying fraction</td>
<td>0.963</td>
<td>0.973</td>
<td>0.01</td>
<td>0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Passive emptying fraction</td>
<td>0.980</td>
<td>0.981</td>
<td>0.01</td>
<td>0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Passive emptying fraction*</td>
<td>0.970</td>
<td>0.973</td>
<td>0.04</td>
<td>0.9</td>
<td>0.8</td>
</tr>
<tr>
<td>Maximum volume</td>
<td>1.023</td>
<td>1.025</td>
<td>0.02</td>
<td>0.9</td>
<td>0.8</td>
</tr>
<tr>
<td>Minimum volume</td>
<td>1.021</td>
<td>1.024</td>
<td>0.02</td>
<td>0.9</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Conclusions: CRT led to clinically significant changes in psychomotor speed in a broad range of heart failure etiologies, ejection fraction, and atrial fibrillation. *Patients in sinus rhythm with a two-lead ECG.
P2399 | BEDSIDE
Single center experience with transseptal endocardial left ventricular lead implantation using transseptal puncture via the subclavian vein
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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 (TSECVL) leads, when transseptal puncture was performed via the subclavian vein in a university heart center.

TSECVL 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 ms pulse duration and 0.9 (0,6; 1,1) V pacing threshold and 942 (851; 1006) Ohm pacing impedance was measured. The number of transseptal puncture attempts was 3 (1; 4). Puncture complication, pericardial effusion was not detected.

If there is no contraindication for anticoagulation therapy, transseptal endocardial left ventricular lead implantation can be a therapeutic option for CRT in special cases.

Acknowledgement/Funding: Medtronic

P2400 | BEDSIDE
Service life of implantable cardioverter-defibrillators for cardiac resynchronization therapy: an analysis of determinants in current clinical practice
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Introduction: Device replacement at the time of battery depletion of implantable cardioverter-defibrillators (ICDs) may carry a considerable risk of complications and engenders costs for healthcare systems. Therefore, ICD device longevity is extremely important both from a clinical and economic standpoint. Cardiac resynchronization therapy defibrillators (CRT-Ds) run out sooner than standard ICDs. In the present study we measured the rate of replacements for battery depletion and we identified possible determinants of early depletion in a series of patients who had undergone implantation of CRT-D devices.

Methods: We retrieved data on 1726 consecutive CRT-D systems implanted from January 2008 to March 2010 in 9 centers.

Results: Five years after a successful CRT-D implantation procedure, 46% of devices were replaced on account of battery depletion. The time to device replacement for battery depletion differed considerably among device manufacturers (log-rank test, p < 0.001). Left ventricular lead output turned out to be an independent determinant of early depletion (hazard ratio, 1.90; 95% confidence interval, 1.51–2.38; p < 0.001). The implantation of a modern-generation device (hazard ratio, 0.46; 95% confidence interval, 0.37–0.56; p < 0.001) and the CRT-D manufacturer (hazard ratio, 0.45; 95% confidence interval, 0.36–0.56; p < 0.001) were additional factors associated with replacement for battery depletion.

Conclusions: The probability of survival at 5 years from battery depletion was 54%. Modern-generation CRT-Ds displayed better longevity, and differences emerged among different manufacturers. High left ventricular lead output was associated with early depletion.

ELECTROCARDIOGRAPHY – CARDIOVERSION – DEFIBRILLATION I

P2401 | BEDSIDE
Difference of mean ventricular fibrillation zone cycle length between appropriate and inappropriate therapy in patients with Brs, ERS and IVF
W.S. Lee, J. Kim, C.H. Kwon, J.H. Choi, U. Jo, Y.R. Kim, G.B. Nam, K.J. Choi, Y.H. Kim. Asan Medical Center, Medical Electrical Engineering, Seoul, Korea, Republic of Background: The implantable cardioverter defibrillator (ICD) is indicated in high risk patients with Brugada syndrome (BS), early regularization syndrome (ERS) and idiopathic ventricular fibrillation (IVF). Though inappropriate ICD therapy occurs frequently in those patients, optimal ICD programming to reduce inappropriate therapy remains to be determined.

Objectives: Aim of this study was to investigate the difference of mean ventricular fibrillation (VF) zone cycle length between appropriate and inappropriate therapy in those patients and to suggest optimal VF zone to minimize inappropriate ICD therapy.

Methods: We enrolled 41 patients (42.6±13.0 years; 35 males) with BS, ERS and IVF (9, 8, and 9 patients, respectively) who experienced ICD therapy between April, 1996 and April, 2014. A total of 244 episodes that activated ICD therapy were reviewed by two independent cardiac electrophysiologists. Mean cycle length of ventricular tachyarrhythmia and supraventricular arrhythmia which an ICD shock were compared.

Results: Of 244 episodes, 180 (73.8%), 64 (26.2%) episodes received appropriate and inappropriate therapies, respectively. Mean VF zone cycle lengths of appropriate and inappropriate therapy were 178.9±28.7 ms and 284.8±24.4 ms (P < 0.001). Discriminating cut off value between appropriate and inappropriate therapy for the highest sensitivity and specificity was 235 ms (sensitivity 98.4%, specificity 95.6%). When we apply single VF zone of 250, 260 or 270 ms in those patients, inappropriate therapy could be reduced by 91.8, 82.0 or 70.5%, respectively and delaying or missing appropriate therapy in 2.8, 2.8 or 1.7%, respectively.

P2402 | BEDSIDE
Are wide complex tachycardia algorithms applicable in adults with congenital heart disease?
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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 electro physiological 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 Vereckei 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 (SVTs) was in 78.2% and VT in 21.8% of the ECGs. The mean age was 38.5±12.6 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 CHDs. The Brugada algorithm correctly predicted the diagnosis 72.7% of the time; the Vereckei algorithm correctly predicted the diagnosis 65.5% of the time 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). kappa Value was 0.85.

Table 1. Results

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brugada algorithm</td>
<td>66.7%</td>
<td>74.4%</td>
<td>42.1%</td>
<td>68.9%</td>
</tr>
<tr>
<td>Vereckei (aVR)</td>
<td>91.7%</td>
<td>58.1%</td>
<td>37.9%</td>
<td>96.2%</td>
</tr>
<tr>
<td>Pava criterion (R wave peak time in i&gt;50ms)</td>
<td>100%</td>
<td>97.7%</td>
<td>92.3%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Conclusion: The Brugada and Vereckei algorithms have low diagnostic accuracy in the adult CHD population. Pava criterion in our cohort was an excellent discriminator between VT and SVT. Specific criteria rather than algorithms should be used to help in diagnosis of WCT in this population.

P2403 | BEDSIDE
Idiopathic ventricular fibrillation - electrocardiographic abnormalities do not predict recurrent arrhythmias
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Background: In patients with cardiac arrest due to idiopathic ventricular fibrillation (VF) the prognosis is unclear. Some studies have suggested a VF recurrence rate...
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 MRI. 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).

<table>
<thead>
<tr>
<th>ECG and ICD therapy</th>
<th>No ICD therapies, n=43</th>
<th>ICD discharge/ATP, n=9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completely normal ECG</td>
<td>13 (30%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>Early repolarization in inferior-lateral leads</td>
<td>4 (9%)</td>
<td>0</td>
</tr>
<tr>
<td>Notched S-shaped in V1</td>
<td>6 (14%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>Left or right axis deviation</td>
<td>5 (12%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>LBBB/RBBB</td>
<td>6 (14%)</td>
<td>1 (11%)</td>
</tr>
<tr>
<td>Negative T waves other than V1 and III</td>
<td>14 (33%)</td>
<td>2 (22%)</td>
</tr>
<tr>
<td>RSR pattern</td>
<td>5 (12%)</td>
<td>2 (22%)</td>
</tr>
</tbody>
</table>

No significant ECG differences between patients with and without ICD therapies.

**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.

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**P2404 | BEDSIDE**

A low fibrillatory wave amplitude predicts sinus node dysfunction after catheter ablation in patients with persistent atrial fibrillation

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**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, electrical cardioversion, 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 SND: 65±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 (0.115±0.086 vs. 0.176±0.077 mV, p=0.009) and larger left atrial volume index (LAVI; 66±31 vs. 66±10 years old, p=0.599) and sex (male; 58% vs. 79%, p=0.186). However, if an attempt was made to recreate a fibrillatory wave amplitude of 0.010 mV (odds ratio=0.84 for 0.010mV decrease, 95% CI: 1.04–1.12, P=0.031) and LAVI (odds ratio=1.08 for 1.0cm3/m2 increase, 95% CI: 1.04–1.12, P=0.001) were independent risk factors for SND.

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**P2405 | BEDSIDE**

Real world usage of direct oral anticoagulants in patients undergoing electrical cardioversion for atrial tachyarrhythmias

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**Introduction:** Direct oral anticoagulants (DOACs) are an alternative to warfarin for stroke prevention in patients with atrial fibrillation (AF). Limited data is available regarding real world usage and safety of DOACs (Dabigatran, Rivaroxaban and Apixaban) in the setting of electrical cardioversion (EC) for atrial tachyarrhythmias.

**Purpose:** Provide information regarding: 1) oral anticoagulation management, and 2) the safety and effectiveness of DOACs on a real world population with AF or atrial flutter (AFL) undergoing EC.

**Methods:** Population-based retrospective cohort study of all patients booked for EC at our Cardiac Arrhythmia Unit between January 2012-September 2014. Patients with non-valvular AF or AFL of ≥48hr receiving any oral anticoagulant (OAC) were included. Main exclusion criteria were severe mitral valve stenosis and mechanical heart valves. Patients were followed for a minimum of 30 days after EC to evaluate thrombo-embolic (TE) events (stroke, TIA, systemic embolism, LA thrombus) and bleeding events.

**Results:** Of 390 patients, 379 were included and 11 (2.9%) were lost to follow-up. 122 (32.2%) received warfarin and 257 (67.8%) DOACs (58.7% Dabigatran, 27.3% Rivaroxaban, 14% Apixaban). Mean age 62 ± 13 ± 71 year male with no significant differences among groups. 19 (7.4%) patients did not undergo EC in the DOACs group (sinus rhythm) and 18 (4.6%) in warfarin group (55.5% due to inadequate anticoagulation or LA thrombus). In patients naive to OACs (28%) time to EC was shorter in DOACs 30 (21–40) days vs 44 (7–70) days p=0.04. Median CHADS2VASc Score was higher in warfarin group 3.03±1.9 vs 2.02±1.5 p=0.01. TE events occurred in 4 (1%) patients: 0 in DOACs group and 4 (3.4%) in warfarin group p=0.01. Major bleeding events occurred in 2 (0.6%) patients: 1 (0.4%) DOACs and 1 (0.8%) warfarin group p=0.52. OAC usage trends varied between 2012–2014 as follows: Warfarin 41.5% to 32.8% p=0.43, Dabigatran 50% to 18.4% p<0.01, Rivaroxaban 8.5% to 24.8% p<0.01, Apixaban 0% to 24% p<0.01.

**Conclusions:** At and academic tertiary center DOACs are used in almost 70% patients undergoing EC, and in a population with a lower thromboembolic risk. Trends in individual DOACs usage varied over time. Adverse events were rare and DOACs appear to be a safe and effective alternative to warfarin in this setting.

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**P2406 | BEDSIDE**

Transient QRS amplitude attenuation in patients with takotsubo cardiomyopathy

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**Background:** Low voltage QRS complexes (LQRSV) and amplitude attenuation of QRS voltage (AAQRV) have been described in takotsubo (TC) patients, and postulated as valuable pre-angiographic markers.

**Purpose:** The aim of this observational study is to evaluate potential diagnostic and prognostic features of QRS amplitude in TC and acute coronary syndrome (ACS) patients.

**Methods:** Fifty-eight patients with TC were matched with 58 patients with ACS according to age, gender, and presence or absence of ST elevation at hospital admission. Twelve-lead ECGs were performed within 12 hours after symptoms onset, the day after coronary angiography (CA) and before hospital discharge. When available, ECGs prior or subsequent to the acute event were also collected.

**Results:** QRS amplitude showed a time related trend, with a first phase characterized by an initial decrease in amplitude in both TC and ACS groups between the first and second ECG (p<0.002). After coronary angiography, TC patients showed a second phase with a progressive increase of QRS amplitude up to pre-event levels, taking the shape of a quadratic curve (quadratic contrast p=0.004), while QRS amplitude in ACS patients showed no significant difference from admission onwards (Figure 1). A similar number of leads with LQRSV was seen in
both groups up until discharge, when TC patients started to show significantly less leads with LQRSV. In TC patients, normalization in AAQRS during hospitalization showed a positive linear association with systolic function recovery.

**Conclusions:** LQRSV 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 transient, and is linearly associated with systolic function recovery.

**P2409 | BEDSIDE**

**Patients who revert to atrial fibrillation after cardioversion demonstrate impaired thrombotic status**

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**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 (DCCV) favourably improves thrombotic profile and reduces stroke risk, is unknown.

**Methods:** We enrolled 40 patients (73% men, 67±13 years) 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 Thromboresist Test. This automated, point-of-care test assesses both platelet reactivity and endogenous thrombolysis 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 endogenous thrombolysis (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 (292±2710 vs. 177±1382±psi, P=0.009), compared to no change in LT between pre- and post-DCCV in those who maintained SR (1891±858 vs. 1480±786±psi, P=0.17). Between groups comparison showed significantly prolonged LT in those who reverted to AF compared to those who maintained SR after DCCV (289±1728±psi vs. 140±1328±psi, 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 CHA2DS2-VASc score.

**Conclusion:** Patients who revert to AF after DCCV exhibit a more pro-thrombotic profile, with impaired endogenous 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

**P2410 | BEDSIDE**

**Implantable cardioverter defibrillator shock does not immediately worsen left ventricular systolic and diastolic function**

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**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 systolic pressure (LVSP), LV end-diastolic pressure (LVEDP), and the tau index 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 (976±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±18±5 vs. 65±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.

**P2409 | BEDSIDE**

**Early repolarization on electrocardiography in survivors after out of hospital cardiac arrest:impact and short-term outcome**

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**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 evidence 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 ≥0.1 mV 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 (≥0.1 mV or ≥0.2 mV).

**Results:** ER was identified in 26 subjects. There was no significant difference in baseline characteristics between two groups. However, 13 subjects with more than 0.2 mV 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**

**Brugada phenocopy: clinical, electrocardiographic and arrhythmic characterization**

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**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 arrhythmical characteristics of the BP associated to hyperkalemia.

**Methods:** We conducted a retrospective observational study of adult 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 BP.

**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%), 5 p of them (4%) presented BP. In the BP group, p were more frequently critically ill (sepsis, diabetic ketoacidosis and 2 out-of-hospital cardiac arrest), had higher serum potassium, were younger, and had lower prevalence of chronic kidney disease (Table). Regarding EKG, BP showed wider QRS, higher positive T wave and abnormal axis. Serious arrhythmias occurred more frequently (60%) in BP (1 high degree AV block and 2 VT) than in the rest of hyperkalemia (25%) (7 high degree AV block, 3 VT and 1 VF).

**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?

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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 aim 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-lead 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 [IQR 25;75]) between A1/PT0 (60 [40;60]) and PT5 (80 [60;100]), A2/PAM0 (0.075 [0;0.2]) and PAM5 (0.1 [0.1;0.1]), A3/ Ptf (4.75 [2.5;6.0]) and Ptf5 (7.9 [6.0;10]). B/Correlations between B1/changes of PT (PT5-PT0) and number of HOSP in 5FU (HOSP5): r=0.28, p<0.0001; B2/changes of PAM (PAM5-PAM0) and HOSP5: r=0.25, p<0.0001; B3/changes of Ptf (Ptf5-Ptf0) and HOSP5: r=0.5, p<0.0001.

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. The difference (ΔPtf, ΔPAM, ΔPT) of the studied parameters correlated with the number of HOSP5 aimed for RSR in our population of patients with AF.

P2412 | BEDSIDE
QT-TQ dynamics in long QT patients during a supine-running test

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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 LQT5, LQT2S 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, QT (QT=RR-TQ), and QTc, 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 supine (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 changed (figure). It resulted in a significant QTc increase during stand-up (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 during stand-up. All four LQT5 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 LQT5, and identifies LQT5 patients with otherwise normal baseline QTc.

P2413 | BEDSIDE
Electrocardiogram characteristics of verapamil-sensitive fascicular ventricular tachycardia

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Purpose: To study the surface electrocardiogram (ECG) characteristics and related electrophysiologic features of verapamil-sensitive idiopathic ventricular tachycardia (VT), 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 electrophysiologic 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 (AV) nodal relationship was recorded. The ECG characteristics were thoroughly analysed.

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 (0.015–0.15s). 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 R/S interval was 57±9.5ms, 4) V1V1 was observed in all preordial and aVR leads, 5) Mean R wave peak time at DIll 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 majorly exhibited R or QR pattern, 8) Lead V6 commonly presented rS or QS pattern, 9) Lead aVr predominantly demonstrated QR pattern. For the left anter- ior ILVTs, the ECG exhibited a right deviation of frontal QRS axis with QR pattern at lead V1 and is 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 VT. 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

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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 electrocardiography (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 guide- lines.

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 (48.8±13.5 vs. 36.7±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

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Background: Experimental studies suggested that transmural differences in early phase of action potential between epicardial and endocardial muscles are responsible for the induction of J-wave. We investigated ECG findings in patients with acute pericarditis which may involve in the subepicardial layer.

Methods: We studied 24 patients (18 males, 59.8±15.0 years) who were diagnosed as 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 >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

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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 indicator of transmural dispersion of repolarization. Tp–e interval and Tp–e/QT ratio have recently determined as the predictors of the development of malignant arrhythmias.

Objectives: To characterize LLBB morphology (in particular QRS/T wave ratio) in patients with chronic LLBB immediately after LLBB onset and compare it to the chronic LLBB.

Methods and results: We analyzed electrocardiograms (EGK) of 14 patients with painful LLBB syndrome (10 published EKG cases, 4 male, age 49±14 years, heart rate 115±14 min-1) and compared it to 443 patients with chronic LLBB, 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 ratio vector. Painful LLBB S/T was 1.48±0.16 (1.1–1.7) while chronic LLBB S/T was 3.92±0.05, range 2.2–4.8 (p<0.001). A subset of chronic LLBB with heart rate >100 (112±5 min-1, n=179) had S/T of 3.67±0.07 (p<0.001 with painful LLBB). There was no overlap between chronic LLBB and painful LLBB at S/T <0.2 of 2.0.

Conclusions: EGK pattern of the painful LLBB within seconds/minutes of onset is characterized by a very low (<1.7) precordial S/T ratio consistent with the “new LLBB” pattern. S/T ratio of 2.0 discriminated between acute onset and chronic LLBB. This finding confirms the validity of LLBB age determination based on QRS/T vectors ratio.

P2418 | BEDSIDE
Is ECG a reliable means of preexcitation syndrome diagnosis?

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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 in 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 conduction 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 36.2±17, 38.2±19, 35.7±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%) (p<0.011) and overt PS (41%) (0.0003). Left posteroseptal AP was as frequent (16, 16, 17%) but right posteroseptal AP 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%) compared to overt PS (14%) (P<0.03). Two patients with unapparent PS presented aborted sudden death. Patients with unapparent and overt PS differ significantly from intermitent 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 VP (108±45 bpm in CS, 168±67 bpm after isoproterenol) than in unapparent PS (191±57, 227±81) and overt PS (197±64, 241±67) (P<0.000).

Conclusion: The diagnosis of PS is not always evident and symptoms should draw attention to minor abnormalities and lead to enlargement indications of EPS that is the on-line changes 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
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Background: The frontal QRS-T angle is defined as the difference between vectors of depolarization and repolarization, which can be easily obtained from 12-lead ECG. A wide QRS-T angle implies either structural abnormalities affecting the depolarization or ionic channels alteration in the repolarization. A previous study reported the association between a wide frontal QRS-T angle and arrhythmogenic cardiopathy in general. We attempted to use frontal QRS-T angle as a predictor of appropriate implantable cardioverter-defibrillator (ICD) therapy in patients with cardiomyopathy.

Methods: The retrospective cohort method was studied in 92 consecutive patients with ischemic and non-ischemic cardiomyopathy (mean age 59±13 year, mean LVEF 32±10.7%). The QRS-T angle was calculated from the frontal QRS and T axis of 12-lead ECG. The frontal QRS-T angle was defined as the angle between the 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% 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 were also predictive of appropriate ICD therapy (hazard ratio 5.25, 95% confidence interval 1.78–15.44, P=0.003 and hazard ratio 11.49, 95% confidence interval 1.19–93.93, 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 ICD therapy in ischemic and non-ischemic cardiomyopathy patients.

P2420 | BEDSIDE
The effect of percutaneous closure of atrial septal defects on the P-wave dispersion
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Objective: The aim of this study is to assess the P-wave dispersion (PD) in patients undergone percutaneous ASC 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 with 12-lead surface electrocardiography, before the procedure and 3 months after procedure. SPSS 12 was used for statistical analysis.

Results: A total of 22 patients were prospectively evaluated; 5 male and 17 females. 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±4.1 ms, Pmin: 42.3±3.7 ms, Pd: 37.2±2.7 ms. Immediate after percutaneous ASD closure: Pmax: 95.3±4.3 ms, Pmin: 48.7±3.9 ms, Pd: 48.3±3.6 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
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Background: Early repolarization pattern (ERP) is an electrocardiogram (ECG) finding characterized by J-point elevation and QRS notchting or slurring in the inferior and/or anterior leads. Its prevalence in Southern Cone of Latin America is unknown.

Purpose: The main objective of the study was to determine the prevalence of ERP according to the Nomenclature suggested by Macfarlane.

Methods: CESCAS I study is an observational prospective cohort study with a 15-year follow-up. A random probabilistic sample of 8000 participants aged 35–74 years from cities representing the Southern Cone of Latin America designed to estimate the prevalence and distribution of and secular trends in major cardiovascular disease events and risk factors.

For the present analysis we use ECGs from 1990 participants, we excluded 18 (0.9%) patients whom ECGs were missing or incomplete. We also excluded 86 subjects with bundle branch block, Wolf–Parkinson–White pattern, atrial fibrillation, cardiac pacing and Brugada pattern.

ERP was defined by an elevation of the J-point ≥1 mm in 2 consecutive leads excluding leads V1 through V3. An ECG was considered ERP positive if there was J-point elevation in ≥2 leads in the inferior (II, II, aVF) and lateral (I, aVL, V4–6) territory. Because the variation in the definition of the ERP the Macfarlane’s classification in five types were used:

Types 1: notch ≥0.1 mV and elevated ST amplitude ≥0.1 mV.

Types 2: notch ≥0.1 mV and elevated ST amplitude <0.1 mV.

Types 3: slr ≥0.1 mV and elevated ST amplitude ST ≥0.1 mV.

Types 4: slr ≥0.1 mV and elevated ST amplitude ST <0.1 mV.

Types 5: ST elevation ≥0.1 mV without notch or slr.

Two trained cardiologists from different blinded to the identity of the patients interpreted the ECGs separately and manually, and recorded the presence of an ERP. Inter-observer reliability was assessed within the observers. The disagreements were judged by the third cardiologist.

Kappa test was used for inter-observer variation.

Results: A total of 1886 ECGs were analysed with a male proportion of 39.8% and a mean age of 54.2 year.

The prevalence of ERP was 4.77% (90/1886). The inferior location was found in 70% of cases (63/836). 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 (25/886).

There was an important strength of agreement between the two initial interpreters (Kappa=0.81).

Conclusions: Consistent with published estimates ranging from 1% to 13% we found an overall prevalence of ERP of 4.77%.

Acknowledgement/Funding: CESCAS I was his work was supported by the National Heart, Lung, and Blood Institute (NHLBI) grant number HHSN282209000029C.
shortening occurs through a decrease in the TpTe interval, indicating reduced repolarization heterogeneity. In contrast, the QTc interval at 1 week trends in the same direction during IC and VP. In patients with ventricular paced rhythms, a formula using the VP QTc interval closely predicts the intrinsically conducted QT interval.

P2423 | BEDSIDE
Identification of the anatomic location of focal atrial tachycardias using synthesized 18 lead electrocardiography
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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. The aim of this study is to evaluate whether synthesized 18 lead ECG gives 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), left arterial root area (n=1), right inferior pulmonary vein (RIPV) (n=2), right superior pulmonary vein (RSPV) (n=2), and left superior pulmonary vein (LSPV) (n=1).

RA ATs except from the TA had positive or biphasic P waves in V3R-5R. We could distinguish CT from CS ostium ATs by checking II,III, and aVF leads. RA posterior ATs had positive P waves in V3R-5R in contrast to the CS ostium, which was negative. AT from the LSPV, RSPV and RIPV had positive P waves in V3R-5R, 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
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Background: Fibrotic scar tissue post infarction may potentially lead to fatal arhythmias, 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 (ECG) 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 Vereckei 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 using visualized using late gadolinium enhancement CMR. Vi/vt on 12-leads ECG were measured manually on each lead and mean of each contiguous leads were included into analysis.

Results: A total of 113 male subjects with average age of 55.7±9.7 years old were enrolled. Myocardial scar were located in 1 territory or more in most of subjects (n=109, 96.6%) and may prompt improvements in patient Health Related Quality of Life (HRQOL) - such as reducing acute mobility restrictions. To date, the HRQOL impact from TPS therapy is unknown.

Conclusion: To evaluate short-term HRQOL impact of TPS following implantation of the pacemaker.
SF-36 results at baseline and at 3 month

<table>
<thead>
<tr>
<th>SF-36 domain</th>
<th>Mean ± Standard deviation</th>
<th>Mean change</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical function</td>
<td>54.75±62.13</td>
<td>68.19±21.56</td>
<td>13.36</td>
</tr>
<tr>
<td>Role physical function</td>
<td>48.03±30.69</td>
<td>65.83±26.26</td>
<td>19.53</td>
</tr>
<tr>
<td>Role emotional function</td>
<td>69.44±29.01</td>
<td>79.45±24.74</td>
<td>9.23</td>
</tr>
<tr>
<td>Vitality</td>
<td>51.13±24.73</td>
<td>62.82±21.82</td>
<td>10.68</td>
</tr>
<tr>
<td>Mental health</td>
<td>71.23±20.25</td>
<td>79.37±16.61</td>
<td>6.55</td>
</tr>
<tr>
<td>Social functioning</td>
<td>72.08±29.77</td>
<td>86.42±21.37</td>
<td>14.01</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>39.65±11.77</td>
<td>41.34±12.67</td>
<td>1.60</td>
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<tr>
<td>General health</td>
<td>58.23±18.76</td>
<td>66.64±21.00</td>
<td>7.82</td>
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</tbody>
</table>

Conclusions: We demonstrated that both CHADS2 and CHA2DS2-VASc scores can be used for predicting long-term outcome in AVB patients undergoing PPM.

P2427 | BEDSIDE
Using the CHADS2 and CHA2DS2-VASc scores for prediction of long-term outcome in patients with atrioventricular block undergoing permanent pacemaker implantation
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Background: Long-term survival for patients with atrioventricular block (AVB) undergoing permanent pacemaker (PPM) implantation 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 endpoints were mortality and occurrence of heart failure.

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 encountering mortality had more percentage of heart failure, vascular diseases, previous stroke/transient ischemic attack, end-stage renal disease, malignancy and more single chamber pacing mode. The CHADS2 and CHA2DS2-VASc scores were significant predictors of mortality with an adjusted HR of 1.316 (p=0.001) and 1.256 (p=0.001) for the CHADS2 and CHA2DS2-VASc scores, respectively.

Table 1. Baseline characteristics of atrioventricular block patients undergoing permanent pacemaker implantation

<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>76.11±7.6</td>
<td>74.71±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 (18.8%)</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>ESRD, n (%)</td>
<td>19 (11.9%)</td>
<td>55 (6.3%)</td>
<td>0.012</td>
</tr>
<tr>
<td>Malignancy, n (%)</td>
<td>32 (20.0%)</td>
<td>96 (11.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHADS2 score</td>
<td>3.8±1.5</td>
<td>3.2±1.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHA2DS2-VASc score</td>
<td>4.5±1.3</td>
<td>4.1±1.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions: We demonstrated that both CHADS2 and CHA2DS2-VASc scores were significant predictors of mortality with an adjusted HR of 1.316 (p=0.001) and 1.256 (p=0.001) for the CHADS2 and CHA2DS2-VASc scores, respectively. CHADS2 and CHA2DS2-VASc scores could be used to predict the long-term outcome of patients with AVB undergoing 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=0.096).

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 pacings 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
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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 center 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 or who had its indication before surgery and those who underwent the implantation of other devices after surgery were excluded.

Results: A total of 91 (0.35%) 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±64.4 and 132.64±64.4 minutes, respectively. The mean hospitalization time in the group who had pacing was significantly lower (16.9±7.3 days) compared to the group with no pacing (19.6±10.7 days) (p=0.001).

Conclusion: PPM implantation had no significant difference between the two subgroups of mitral valve replacement (MVR) and aortic valve replacement (AVR) (25% vs. 27%), and was not there any significant difference when AV was added to MVR (3.6%). Any procedure on the tricuspid valve, whether replacement or repair, significantly increased the risk for pacing in the atrioventricular group (MVR+TVR repair = 4.54%; MVR+AVR+TVR repair = 15.59%). The valvular group had a longer bypass time than the CABG group (143 vs. 99.7 minutes; P value =0.004) and cross-clamp time (93.18 vs. 56; P value <0.001).

Purpose: Prevalence of atrial fibrillation rhythm and bundle branch block and prescription of Digoxin were higher (P value = 0.007) in the valvular group. Low-degree atrioventricular block was more frequent among the CABG patients. Waiting time for PPM implantation was similar between the valvular surgery subgroups. In the valvular subgroups, there were no differences between preoperative electrocardiography, cross-clamp time, bypass time, waiting time or drug prescription.

P2432 | BEDSIDE
Longitudinal strain and twist calculated by Cardiac MRI differs between apical and rvot pacing sites
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The debate regarding the the best position to place a pacing lead within the right ventricle has continued over many years, with conflicting results from many studies.

We aimed to answer this question using cardiac MRI, which is the gold standard method of measuring ventricular performance. We enrolled 50 patients with atrial fibrillation who were having a pace and ablate strategy as part of their clinical care. Each patient was implanted with an Accent MR conditional pacing system with two ventricular leads. One at the apex through the RVOT septum. Each underwent an AV node ablation followed by a dedicated CMR scan. The scan was performed for each pacing site in the same scanning session. Each scan was performed on a 1.5 T Siemens and in a dedicated MRI safe pacing mode.

No complications occurred during the 50 acute scans following the AV node ablation with no clinically significant changes in pacing threshold, impedance or battery voltage.

Standard SSFP sequences were optimised to allow assessment of left ventricular volumes and ejection fractions for each pacing site. Longitudinal strain was calculated in the 2, 3 and 4 chamber views using feature tracking software (Tomtec). Twist was calculated from tagged short-axis MR sequences using the commercially available Intag software and our own in-house excel based software.

The ejection fraction was greater with the RVOT lead compared with the apical lead position, 58±4.1% vs 56±9.85%, p=0.02. Longitudinal strain in the 4 chambers was significantly greater in the RVOT lead 16±6.5 vs, p=0.007, as was Twist 6.8±2.5 vs 6.1±2.7, p=0.05. This study suggests that RVOT pacing has superior hemodynamics to Apical pacing and the differences in longitudinal strain and twist offer a possible mechanism for this. This cohort will be followed up over 18 months to determine if differences found in the acute study persist.

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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
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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 pac ing 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 and asystolic 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 standardised patient referral pathway was hence devised as 90% of patients having the pacemaker implant with a total delay of less than 21 days.

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.

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 2014. 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±42 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?
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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.

Methods: 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 stay in observation and disposition after a standard pacemaker implant or a standard ablation procedure. We divided the population into two groups: Group A, patients were sent home after a protocol discharge after an ambulatory procedure; Group B; patients were admitted and monitored for 24 hs. In both groups the implant technique was identical.

Results: 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.

Conclusions: RFCA is a safe and effective management option for inappropriate shocks due to atrial tachyarrhythmias among patients with an ICD or CRT-D.
Results: Group A – two haematoma and two ventricular lead displacements were detected in three patients. Group B – three haematoma, and one subclavian vein thrombosis, three displacements and three high stimulation thresholds were observed. Group C – one groin haematoma was observed. Group D – one groin haematoma, and three arrhythmia recurrences were detected. No statistical differences were observed between groups.

Conclusions: Ambulatory procedures in selected patients appear to be safe and without complications. Cost effectiveness analysis favors this approach when all safety criteria are met.

P2438 | BEDSIDE
Lead dependent infective endocarditis. How significant is the size of right heart vegetations (RHV)?

Background: Right heart vegetations (RHV) are the main signs of lead dependent infective endocarditis (LDIE). The first-line therapy of LDIE is transvenous leads extraction (TLE). Influence of size of RHV on early effect of TLE and long-term mortality in this patients is relatively little known.

Methods: The comparative analysis of efficacy and safety of TLE in patients with LDIE (52 pts with big RHV ≥2cm and 228 pts with smaller RHV ≤2cm) underwent procedures in single center in years 2006–2013 was conducted. The long term mortality after TLE (mean time of observation: 2,76±1,83 years) was also evaluated.

Results: are demonstrated in the table and figure

<table>
<thead>
<tr>
<th>Age (years) ±SD</th>
<th>Gender, Male (%)</th>
<th>Full procedural success (%)</th>
<th>Clinical success (%)</th>
<th>Major complications (%)</th>
<th>Minor complications (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>65.8±12.0</td>
<td>59.6</td>
<td>82.7</td>
<td>88.5</td>
<td>5.8</td>
<td>1.9</td>
</tr>
<tr>
<td>65.5±15.0</td>
<td>68.0</td>
<td>91.7</td>
<td>98.7</td>
<td>0.4</td>
<td>2.2</td>
</tr>
</tbody>
</table>

Survival after TLE depending on RHV size

Conclusions: Comparison of early effects of TLE demonstrated worse results in patients with bigger vegetations. Moreover, the presence and size of vegetations significantly increased long term mortality after TLE: the mean 2.76 years survival of pts without RHV was 71%, pts with small RHV 62.9%, pts with big RHV 33.8%.

P2439 | BEDSIDE
Major complications of transvenous lead extraction. Risk factors are still ephemeral. An analysis of 1767 procedures
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Methods: From early 2009 to mid-2014, 256 consecutive CRT patients (mean age 68.3±11.6 years, 216 male gender, mean NYHA class 2.3±0.7, EF 35.1±10.8%) were treated at 4 different institutions with TLE. Indications for TLE included systemic (18%) or local (45%) infection (Inf), lead malfunction (24%) (Malfx), or other indications (3%). Demographic, clinical, TLE procedural, and follow-up data were collected prospectively, considering specifically all-cause adverse events (AAE) (death, cardiovascular hospitalization, device-related adverse event) and DAE (distinguished in Inf, Malfx, or other).

Results: TLE was attempted for 614 leads; removal was complete in 607 leads (98.9%), partial in 0.3%, and failed in 5 leads (0.8%). One death after following laceration of superior vena cava (0.2%) occurred. TLE techniques differed and included manual traction (29%), use of mechanical (43%) or laser (28%) sheaths, complemented, if needed, with femoral (2%) or jugular (3%) approaches. Over a mean follow-up of 19±12 months, rate of AAE was 36.3%/year (CI 29.4–44.2%) (Figure). DAE (61) accounted for 38% of all adverse events occurring after TLE, and included recurring Malfx (23; 6.7%/yr, CI 4.5–10.1%), Inf (23; 4.5%/year, CI 2.7–7.3%), and other (15; 3.0%/year, CI 1.6–6.5%).

Conclusions: Even though TLE is safe and effective to treat CRT patients with device-related issues, a high burden of recurring DAE after TLE was observed at mid-term follow-up. Careful evaluation of both patient characteristics as well as implantation strategy is suggested when indicating TLE in a CRT patient.

P2440 | BEDSIDE
Device-assisted transvenous lead extraction (TLE) may result in cardiac and vascular tears and other complications with different degree of severity. Earlier knowledge, which patients need special operating procedure scenario may improve major complications management effectiveness. The aim of the study: Analysis of appearance of major TLE complications (MC). Retrospective analysis of our 8-year TLE data-base.

Methods: Using conventional mechanical systems we have extracted 2963 leads in 1767 pts. Mean dwell implant time was 85.1 months. In 28 (1.6%) MC were noted.

Results: Results are presented in the table. Predominant risk factors of MC included recurring Malfx (23; 6.7%/yr, CI 4.5–10.1%), Inf (23; 4.5%/year, CI 2.7–7.3%), and other (15; 3.0%/year, CI 1.6–6.5%).
Externalization of ICD leads, not only Riata problem

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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. Of these, 143 (33.4%) lead in 137 (52.9%) pts were ICD leads. Indication for TLE in the subgroup were infection in 47 pts, lead failure in 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. A). 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 (96, 39, 117, 73 m. respectively) leads. All externalized leads were successfully extracted using device traction, mechanical telescopic sheaths and autorotational 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.

Clinical features and changes in epidemiology of infective endocarditis on pacemaker devices over a 27-year period (1987-2013)


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 epidemiology, clinical features, management and prognosis were analyzed.

Results: IE-PM represented 6.1% of all IE cases (25 patients), affecting 0.36% of all implanted PM. IE-PM increases from 0% of all IE in 1987–1993 to 5.10% in 1994–2000, 7.69% in 2001–2007 and 9.32% in 2008–2013 (p < 0.001). IE-PM incidence also increased from 0% of all PM implants in the period 1987–1993 to 0.325 in 1994–2000, 0.335 in 2001–2007 and 0.45% in 2008–2013 (p < 0.001). Age of IE-PM patients was 63 years and 80% were male (80%). Causeless microorganisms predominantly were Staphylococcus (84%): S.aureus 48% and S.epidermidis 36%. Rate of severe complications was high: persistent sepsis in 60% of cases, heart failure in 20% and stroke in 12%. Device was removed in 19 patients (76%), mostly by surgery (18 of 19 cases). Early mortality was 24% (33% of medically and 21% of surgically treated patients, 21%, NS).

Conclusion: IE-PM has shown an increasing incidence during the last decades, representing almost 10% of all IE in the last 6 years. This is a severe disease, with a high rate of severe complications and requiring removal of device in most cases. In spite of therapy, early mortality is high.

Detection of Cardiovascular Implantable Electronic Device Infections with Sonication Following Lead Extraction and Generator Change

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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. Survivors of CIED 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 antibiotic prophylaxis at the time of device removal. Diagnosis of CIED infection was made based on clinical findings. After collection, devices were processed and BactoSonics were 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 definitive 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 polymicrobial infections (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 (5x10⁴ vs. 2x10³ CFU/mL, p < 0.001). A cut-off value of 5x10² CFU/mL better identified subjects with infection from those without infection (AUC 0.83; 95% CI 0.73–0.93, p < 0.001).

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.

Risk factors, presentation, treatment and consequences of cardiac device infections; a retrospective analysis

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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 (3±2.5 vs. p=0.14). The most common site of infection 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 histopatho-logic manipulation of device and leads was present in 20 (25%) 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 removed had lower recurrence rates. Mean hospital stay was 15±9 days and mean antibiotic treatment duration was 12±8 days. During in-hospital follow-up 4 (2.8%) patients died.

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. Therefore, appropriate prophylaxis should be taken before and after 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.
P244 | BEDSIDE
Transvenous leads extraction- analysis of factors influencing long-term mortality after procedures
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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 1.501–2.488], the need of remove of ICD leads (due to its dysfunction or LDIE): [HR=1.298; 95% CI 1.090–1.701], 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=1.198; 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=1.038; 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 1.624–2.893]. 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.

P244 | BEDSIDE
Adverse consequences of inappropriate antitachycardia pacing delivered with implantable cardioverter defibrillators: life threatening proarrhythmic effects
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Background: Appropriate antitachycardia pacing (ATP) delivered with implantable cardioverter defibrillators (ICDs) has been shown to be highly effective in terminating ventricular tachycardias (VT); it is currently recommended to program ATP up to a shorter tachycardia cycle length than before in order to avoid ICD therapies. Although the benefits of appropriate ATP therapy are well recognized, the disadvantages of inappropriate ATP therapy in the current ICD setting has yet to be elucidated.

Purpose: This study aimed to elucidate the consequences of inappropriate ATP therapies in clinical practice.

Methods: A total of 243 patients implanted with an ICD (n=177)/CRT-D (n=66) were registered and prospectively followed-up for the last 4 years in terms of all ICD therapies delivered as well as their consequences.

Results: During the follow-up period, 76 patients (31.3%) (60 ICD recipients, 16 CRT-D recipients) received 3,474 appropriate therapies including 79 shocks, 60 ATP + shocks, and 3,335 ATPs. Thirty-three patients (13.5%) (31 ICD recipients, 2 CRT-D recipients) experienced 300 inappropriate therapies: 66 shock events, 11 ATP + shock events, and 223 ATP only events. The inappropriate ATPs were triggered by supraventricular tachyarrhythmias (n=223), T wave oversensing (n=4), and others (n=7). The majority of inappropriate ATP events were asymptomatic (n=232, 99%), however, the remaining two events resulted in syncope as described below. Case 1 was a patient with non-ischemic cardiomyopathy implanted with an ICD for secondary prevention. An ATP (270 pps) delivered during sinus rhythm due to T wave oversensing induced true polymorphic VT, which deteriorated into ventricular fibrillation by the second ATP (250ppm). Finally, sinus rhythm was restored by a 35J shock delivery. Case 2 was a patient with cardiac sarcoidosis implanted with an ICD for secondary prevention. An ATP (275ppm) delivered during sinus rhythm due to frequent atrial premature contractions induced true VT (240bps) that was terminated by a 38J shock therapy.

Conclusions: Although inappropriate ATP events were asymptomatic in the majority of the patients, this study demonstrated two important cases in which ATP delivered during a normal sinus rhythm setting caused true life threatening VTs. This potentially lethal ICD complication, seen in about 1% of inappropriate ATP events, should be noted especially when programming ATP with a short pacing cycle length.

P2447 | BEDSIDE
Five-years microbiologic characteristic of patients with complications of electrotherapy
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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%), Staph. hominis (1,87%), Staph. symphonomis (1,37%), 20 pathogens (2,51%) were found incidentally (1–2 times during 5 years). Cumulative response of the most frequent pathogens for selected antibiotics is presented in the table. Changes in the timeline were found for Staph. epidermidis (Chi2 p=0.002), Staph. hominis (Chi2 Yates p=0.023) and Enterococcus faecalis (Chi2 Yates p=0.045). Most of pathogens were sensitive for Vancomycin and Tigecyclin 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
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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 spatio-temporal resolution. However until now, in most of the previous studies on MCG, measurements have been obtained only from the anterior side of the thorax with the subject supine. We hypothesized that using novel MCG approach with 3-directional recordings capable of delineating the whole heart activation and detecting LV intraventricular conduction delay that is hardly discernible on ECG in DCM patients with narrow QRS duration (GRSD, <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 (GRSD, 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 controls (78±12 vs 60±16, p < 0.001).

Conclusion: Our new MCG approach may allow to evaluate abnormal intraventric-
ular 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
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Background: The heterogeneity of ventricular repolarization across the ventricles is well recognized to be important to initiate and perpetuate polymorphic vent-
tricular tachyarrhythmias, and intravenous magnesium (Mg) is effective for poly-
morphic ventricular tachycardia via homogenization of the transmural ventricular repolarization. However, the relationship between the repolarization parameters and electrolytes 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 [ER] syndromes) with documented episodes of VF and/or ventricular fibrillation were enrolled. Serum electrolyte levels were measured in 95% of J wave syndromes.

Results: The average QT maximum (max), QT minimum (min), QT dispersion (QTd), Tpeak-Tend (Tp-e) interval, Tp-e dispersion (Tp-e/QT), Tp-e/QT ratio, and Tp-e/Td ratio were 405±35ms, 350±35ms, 54±19ms, 102±17ms, 40±11ms, <LQTS, 20 (69%) exhibited TWD in PAC. TWA was significantly associated with elevated TWA and a history of life-threatening ventric-
ular arrhythmias in patients with long QT syndrome (LQTS). However, the response of ventricular action potential (PAC) becomes deformed.

Conclusions: The serum Mg and potassium levels may play an important role in the cardiac repolarization process in J wave syndromes.

P2450 | BEDSIDE
Noninvasive epi-endocardial imaging of cardiac arrhythmias
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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-
rrhythmias 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 Amricard 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; 23 - in the septal position of the RVOT; and 11 patients had AS in the left ventricle outflow tract (LVCT) - 2 - in the boarder of the right and the left sinuses of Valsalva; 3 - in the noncoronary sinus of Valsalva; 2 - in the right sinus of Valsalva; 3 - in the left sinus of Valsalva. The separate epicardial imaging had worse 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 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 only in 3 cases and in patients with paraschism 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 obtained 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 isthmus-dependent atrial flutter.

Conclusions: The accuracy of the noninvasive combined epi-endocardial mapping 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
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Background: We hypothesized that the response of ventricular action potential duration (APD) to premature stimulus is intramanually heterogeneous in patients with long QT syndrome (LQTS) and 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 arrhythmias in patients with long QT syndrome (LQTS).

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 the “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. TWA was significantly higher in patients with TWD than those without (97±123.9 vs. 39.3±12.8 μV, mean±SD, p<0.05). 95% of max TWD lead was in the precordial leads V2–6. Moreover, 70% of max TWD lead was consistent with max TWA lead. In the patient with drug-induced acquired LQTS, transition from TWD to TWA triggered by a short run of PAC was observed. Patients with a history of VTA (n=8) had a significantly higher incidence of TWD than those without (n=21) (100% vs. 57%; p=0.03).

Conclusions: TWD in non-aberrant PAC is common in LQTS patients and associated 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
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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±6 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 (147±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 syncopal episodes (hazard ratio: 3.46; 95% confidence interval: 1.15–10.35).

Conclusion: 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
Arrhythmic region of premature ventricular contraction relates early left ventricular systolic dysfunction
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Background: High burden of premature ventricular contraction (PVC) 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 dysfunctions and reported a superior predictor of outcomes to LV ejection fraction (EF).

Purpose: To elucidate the risk factor for early LV-dys and to detect the influence of the arrhythmogenic region on PVC-induced LV-dys.

Methods: Consecutive 40 patients with normal EF without underlying cardiac diseases, having more than 1000/day of PVC by 24-hour Holter ECG were enrolled. GLS was measured in all patients and control with no PVC (n=8). The relationships between GLS and previous reported risk factors for PVC induced LV-dys were evaluated. The patients were divided into 6 groups depending on the region of PVC focus by 12-lead ECG, including right ventricular outflow tract of septum (RCC+Epi), RV non outflow tract (RV-nOT), LV outflow and non outflow tract (LV-OT and LV-nOT), GLS for each groups were evaluated. The patients were divided into 6 groups depending on the region of PVC focus by 12-lead ECG, including right ventricular outflow tract of septum (RCC+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 (−193±3 vs. −210±3.3±0.05). PVC burden and left bundle branch block type of PVC were selected as statistically significant factor for prediction of GLS (r=0.55, p<0.001). Using univariate regression analysis, GLS of RV-OT was significantly higher (worse) than that of LV-OT (−172±4.2 vs. −20±0.4±0.05). (Figure)

Conclusion: Region of PVC focus is one of the significant risk factor for prediction of PVC-induced early LV-dys. Strain analysis is useful method for detecting fine LV-dys.

P2454 | BEDSIDE
P-wave signal-averaged electrocardiography analysis in acute exacerbation of chronic obstructive pulmonary disease
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Introduction: Chronic obstructive pulmonary disease (COPD) predisposes patients to atrial arrhythmias. There is some evidence that the patients at increased risk of developing AP may have abnormal atrial conduction detected by P wave signal-averaged electrocardiography (SAECG), but there is no data regarding the value of this analysis in arrhythmic risk assessment in patients with COPD.

The aim of the study was to assess the utility of P wave SAECG in identifying patients with acute exacerbation of COPD at risk of developing atrial arrhythmias.

Methods: The study was a prospective analysis on an active group of 40 patients hospitalized for exacerbation of COPD and 52 patients without COPD in the control group. Patients with history of coronary heart disease, heart failure or low left ventricular ejection fraction, cor pulmonale, chronic arrhythmias or on antiarrhythmic drugs were excluded. Filtered P wave duration (FPD), root mean square (RMS) voltage of the terminal 40, 30, 20 ms (RMS40, RMS30, RMS20) of the filtered P wave, RMS voltage of the entire filtered P wave (RMSp), and the integral of the voltages in the entire P wave (integral-p) were analyzed. Atrial late potentials (ALP) were considered present when PD > 132 ms and RMS20 > 2.3 s. A cutoff of > 70 filtered late potentials on 24-hour Holter ECG was considered significant (SPB70).

Results: The mean age was 59±6±12.6 years with no significant difference between groups. Male gender was more prevalent in COPD group (67.5% vs. 42.3±0.03). COPD patients had more supraventricular arrhythmias compared to controls: SPB (505.6±597.75 vs. 403.6±1066.79, p=0.02), SPB burden (0.50±0.72% vs. 0.38±0.10%, p=0.03) and episodes of supraventricular tachycardia (SVT) (5.80±27.41 vs. 2.32±13.15, p=0.02). However, there were no significant differences between the two groups regarding FPD (138.35±43.81 vs. 142.59±23.89, p=0.04), RMS50 (5.82±3.55 vs 5.61±2.21, p=0.17), RMS30 (5.53±3.81 μV vs 4.67±2.59 μV, p=0.7), RMS20 (4.65±3.32 μV vs 3.67±2.05 μV, p=0.2) or integral-p (677.47±254.31 μV vs 710.53±314.81 μV, p=0.5). Percentage of patients with ALP or SPB70 was similar in COPD and control groups (21.15% vs. 22.5%, p=0.9 and 44.23% vs. 62.5%, p=0.12, respectively).

In the COPD group, SPB and SPB burden were the only predictors of SVT identified by ROC curve analysis, with an AUC of 0.680 (95% CI 0.514–0.818, p=0.03) and 0.688 (95% CI 0.522–0.824, p=0.02), respectively.

Conclusion: The diagnosis of paroxysmal supraventricular tachycardia (SVT) frequently is a dilemma, when SVT is too short to be registered. Electrophysiological study (EPS) is the only means to evaluate the nature of symptoms when noninvasive studies remain negative and event recorders are not interpretable. The purpose of the study was to determine the clinical factors of negativity or positivity of EPS in patients suspected of SVT.

Methods: EPS was performed in 2489 patients complaining of tachycardia and suspected of SVT. Transesophageal or intracardiac EPS consisted of programmed atrial stimulation with 1 and 2 extrastimuli in control state and after exercise. Patients were followed from 3 months up to 20 years (mean 5±4 years).

Results: SVT was induced in 1813 patients, 742 males, 1071 females (59%). Mean age 48±19; 260 had associated heart disease (HD) (14%). EPS remained negative in 676 patients, mean age 34±17 (p<0.001), 211 males, 357 females (53%); 24 (3.5%) had associated HD. Feeling of disconnection and syncpe associated with tachycardia was more frequent in patients with negative EPS (283/674 42%) than in patients with SVT (256/1813) (14%) (p<0.0001); 190/283 (67%) with negative EPS and 93/256 (36%) (p<0.000) with SVT were less than 40 years. Feeling of chest pain associated with tachycardia was more frequent in patients with negative EPS (175/676) (26%) than in patients with SVT (231/1813) (12.7%) (p<0.000); 113/175 (64.5%) with negative EPS and 47/231 (20%) (p<0.0001) with SVT were less than 40 years. Association of syncpe and chest pain was present in 71 patients with negative EPS (10.5%) and in 141 patients with SVT (8%) (p<0.03). 4671 (64.8%) with negative EPS and 41/141 (29%) (p<0.0001) with SVT were less than 40 years. The positive predictive value for the prediction of a negative EPS of age <40, chest pain, syncpe or their association was low (63, 26, 42, 10.5%), but negative predictive value was high (67, 67, 86, 92%). At multivariate analysis, age <40 (OR 0.000, OR3.22), absence of HD (0.000, OR3.2), presence of chest pain (0.000, OR5.27) or syncpe (0.000, OR0.286) were independent factors of negative EPS.

Conclusions: Among patients complaining of not documented tachycardia and suspected of paroxysmal supraventricular tachycardia, the association of the feeling of tachycardia with chest pain and/or syncpe with an age <40 years frequently is associated with a negative electrophysiological study.

P2456 | BEDSIDE
Positive Late Potentials are not explained by cardiac MRI findings in patients with ventricular arrhythmias
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Purpose: Late Potentials (LP) is derived from a signal-averaged electrocardio-
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). We therefore investigated the correlation between LP and cMRI findings in patients with verified sustained ventricular tachycardia/fibrillation (VT/ VF).

Methods: We retrospectively collected data from 41 patients examined with LP and those 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 scan 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 difference 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 m²/p-value = 0.85) or RV ejection fraction (56% vs. 58% p-value = 0.57).

Conclusions: In a 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 arrhythmogenicity or, 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
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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 concomitantly relay symptom descriptions from a prepared list, thereby providing a symptom/cardiogram-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 (means±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-syncopes (n=558 patients) and chest pain (n=110 patients). A total of 41,788 (52%) transmissions were made by patients who were in the midst of experiencing the same cardiac complaint(s) for which they were referred. The Cardio R® device displayed a confirmatory disturbance in rhythm in 93% of these cases. The interval between transmission until diagnosis of the recorded rhythm was 9 minutes (range 6–20 minutes), and 2±4 days elapsed until transmission of the first symptomatic episode.

Conclusions: The Cardio R® device enabled prompt ECG interpretations to guide interventions for managing cardiac-relevant complaints.

P2458 | STEMI II
Is there any benefit with beta-blocker therapy in patients with myocardial infarction with left ventricular systolic dysfunction and atrial fibrillation?

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%vs70.0%; P<0.001), but not those in AF (53.3%vs55.3%; 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, male sex, hypertension, diabetes, peripheral artery disease, chronic obstructive pulmonary disease, history of prior AMI, creatinine, STEmI, Killip class, percutaneous 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]=0.58, 95% confidence interval [CI], 0.45–0.77; P<0.001), 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 the recommendation of β-blockers in AMI patients with depressed LVEF and AF.
Conclusions: In patients with AHF caused by ACS, BB therapy had no effect on in-hospital mortality after balancing of overt confounders.

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
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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's 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 (2 points), heart rate >40 or <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.

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P2461 | BEDSIDE
Safety and efficacy of the ESC 0h/3h-protocol for rapid rule-out of myocardial infarction among women and men
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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-cTn), 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-cTnT 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-cTnT (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<0.001). 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 98% (95% CI, 97.1–100%) among men (p<0.001). 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-cTn 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<0.001). 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 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.
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.

**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 should be made to increase the rate of guideline-adherent therapies in these high-risk patients after ACS.

**References:**


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 with and without any cardiovascular (CV) risk factors.

**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 secondary composite endpoint of risk for non-fatal MI, non-fatal stroke, or cardiac death (CVD) was estimated for the first year post-index ACS. Risk and risk factors were assessed by Kaplan-Meier analysis and competing-risk regression based on Fine and Gray’s proportional subhazards modeling, respectively.

**Conclusion:** The presence of CTO and multi-vessel disease are an independent predictor of all-cause mortality between 30 days and 5 years (HR: 1.6, 95% CI: 1.2–2.0, 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, HR: 0.08; 1.3, 95% CI: 1.0–1.8, P=0.08).

**Acknowledgement/Funding:** the Pharmaceuticals and Medical Devices Agency
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 doubled risk vs younger patients. For <75 years one additional risk factor approximately doubled the event rate vs no additional risk factors. 7% of patients had >2 risk factors; which approximately doubling the risk for patients with 0.75 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 compared to younger patients. This indicates the need for closer management of post-MI patients with increased risk, regardless of age.

**Acknowledgement/Funding:** Sponsored by AstraZeneca

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**STEMI II**

**P2468 | BEDSIDE**

**Zowille risk score: the missed opportunity for early discharge after primary percutaneous intervention**

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**Zowille risk score** is well validated to identify low-risk ST elevation myocardial infarction (STEMI) patients who have undergone primary PCI and can safely be discharged from hospital within 72 hours, however this score is not widely adopted and the Length of Stay (LOS) for many low-risk patients remains significantly longer.

**Methods:** The first nationwide Primary Percutaneous Intervention (PCI) Program the Middle East was launched in our state in October 2013. All STEMI in our state are referred to the Heart Hospital for PCI. Demographics, angiographic findings, treatment and outcomes data are prospectively collected and entered in a database. Using this database we compared the clinical profile, in-hospital outcomes and LOS for patients with Zowille score <3 vs those with Zowille score >3.

**Results:** 775 patients underwent PCI between October 2013 and September 2014, among them 605 (80.8%) had a Zowille score <3 and 72 (11.6%) had Zowille score >3 (see table). Patients with score <3 were younger (49.4±8.7 vs. 57.4±11, P=0.001), less likely to have diabetes (50% vs. 43%, P=0.001), hypertension (32% vs. 44%, P=0.003) but more likely to be smokers (49% vs. 31%, P=0.003). The rate of cardiogenic shock post PCI and In-Hospital mortality was significantly lower among patients with score <3 versus those with score >3 (0% vs. 6.2%, P=0.001, 0.6% vs. 16%, P=0.001). The LOS was significantly shorter among patients with Zowille score <3 compared to those with score >3 (mean 3.5±2.8 vs. 7.7±12 days, P=0.001, median 3 vs. 4 days respectively).

**Conclusion:** Zowille score can identify 86% of post PCI patients who are eligible for discharge within 72 hours, however at least half of these low-risk patients stay longer than 3 days. A widespread adoption of this score may substantially reduce the LOS and cut the cost without compromising safety.

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**P2469 | BEDSIDE**

**Postinfarct left ventricular remodeling in male STEMI patients.**

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The TNF superfamily cytokines - receptor activator of TNF-related apoptosis inducing ligand and osteoprotegerin have been proposed to be involved in the pathophysiology of atherosclerosis and heart failure. Aim: To investigate the association of perinfarct TRAIL and OPG serum activity with left ventricular (LV) functional and structural remodeling in male patients during a 6-month follow-up after a first-ever ST segment elevation myocardial infarction (STEMI).

**Methods:** We recruited 150 males (61±10 yrs) with STEMI treated with primary PCI. TRAIL and OPG levels were evaluated at admission and on the 3rd day. Echocardiography was performed on the 7th day and after 6 months.

**Results:** The subgroup of pts with a less favorable perinfarct TRAIL and OPG profile, i.e. with an increase in TRAIL level between baseline and the 3rd day being in the 3rd tertile (increase >9.5 ng/ml) and/or with OPG/TRAIL value at baseline being in the 1st tertile (<0.11) – Group A, demonstrated larger increase in LV end-diastolic dimension and post-systolic strain index, and smaller increase in LV ejection fraction, peak systolic and peak early diastolic myocardial velocities, peak strain and peak early diastolic strain rate than remainder of patients – Group B.

**Conclusions:** The progression of LV functional abnormalities in post-infarct male patients with the perinfarct TNF superfamily cytokines activity: lower OPG/TRAIL ratio suggesting less efficient cardioprotection, as well as larger subsequent increase in TRAIL characterized by cardioinhibitory properties contribute to a poorer of LV functional and structural remodeling at 6 months.

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**P2470 | BEDSIDE**

**TIMI score versus CHAD2VASc: which one does a better job predicting long term mortality in an acute coronary syndrome population?**

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**Background:** The TIMI risk score is validated as a predicting tool for short term prognosis non-ST elevation acute coronary syndromes (ACS) patients. CHA2DS2-VASc is currently used to predict outcomes in a high risk population with atrial fibrillation, but has not been tested in ACS patients. It is unknown whether either of these scores predicts long term prognosis in ACS patients.

**Purpose:** We aimed to assess long term prognosis prediction capability of TIMI score and CHAD2VASc in an ACS population, and to determine which of these scores is better.

**Population and methods:** Retrospective, longitudinal observational study of 4336 patients admitted for ACS [ST-elevation acute myocardial infarction (AMI), non-ST elevation AMI or unstable angina] in a single coronary care unit between May 2004 and November 2012. TIMI risk score was calculated on admission for the entire population. CHAD2VASc was obtained retrospectively and was available for 3939 patients. Primary endpoint was all-cause mortality at follow-up. Receiver operative characteristic (ROC) curves for the primary endpoint were obtained for both scores, and area under the curve (AUC) compared. Both scores were tested in a Cox proportional hazard model.

**Results:** Mean age was 67.3±12.9 years, and 67.4% of patients were male; 1376 patients (31.7%) had ST-elevation AMI. Mean TIMI score was 2.5±4.12 and mean CHAD2VASc score was 2.4±1.55. During a mean follow-up time of 883±691 days, 708 patients (16.3%) died.

The AUC of the ROC curve was significantly higher for CHAD2VASc compared to TIMI score (0.698 vs 0.593, p<0.001). In a Cox regression model, both TIMI score (hazard ratio (HR) 1.078; 95% confidence interval (CI) 1.021–1.139; p=0.008) and CHAD2VASc (HR 1.443; 95% CI 1.376–1.514; p<0.001) were found to be predictors of the primary endpoint. A CHAD2VASc 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, CHAD2VASc performed significantly better, and shows promising results as a risk stratifying tool for long term prognosis in an unselected ACS population.

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**P2471 | BEDSIDE**

**Age and gender differences in place and causes of deaths of acute myocardial infarction in-patients in a 3-year observation after discharge (from nationwide AMI-PL study)**

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**Background and aim:** Despite widespread use of recommended treatment guidelines in acute myocardial infarction (AMI), the mortality after hospital discharge remains relatively high in Poland. Therefore we analysed age and gender differences in place and causes of deaths up to 3 years following AMI hospitalization.

**Methods:** The database of the only, public, obligatory, health insurer in Poland together with the data from National Institute of Public Health, Ministry of the Interior were used. The AMI cases from 2009 were selected based on primary diagnosis...
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 ≥84 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?
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Purpose: About 50% of patients (P) with ST elevation myocardial infarction (STEMI) have multivessel coronary disease (MVD). Primary angioplasty (pPCI) of only the culprit artery (CA) is advised by current guidelines, except in cardiogenic 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 4575 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 294±386ng/ml, p < 0.001). CAO had more extensive CAD (3 vessels: 30% vs 9% vs 24%, p < 0.001), with no differences in CA. Femoral vascular access (36% vs 19% vs 32%, p = 0.001) and bare metal stents (46% vs 23% vs 41%, p < 0.01) were more often used in CAO; but, Gp Ib/IIa inhibitors were less used (32% vs 80% vs 44%, 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±12% vs 12% vs 9%, p = 0.02). CR1 had a higher percentual increase in creatinine (23% vs 28% vs 11%, p = 0.048), but a smaller decrease of hemoglobin (10% vs 8% vs 12%, p < 0.01). No differences were found in dysrhythmic, mechanic or hemorraghic complications. Length of hospitalization was higher in CR2 (5 vs 4 vs 6 days, p < 0.01). CAO had more in-hospital mortality (7% vs 2% vs 0%, p < 0.01). In FU, death and cardiovascular hospitalization were more frequent in CAO (9% vs 5% vs 1%, 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
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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 1- and 3-month 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 (p < 0.001). ProACS risk score showed a good differentiation 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).

Conclusion: 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 multivessel CAD who present without cardiogenic shock
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Background: The optimal revascularization strategy for STEMI patients without cardiogenic shock who are found to have multivessel CAD (approximately 50% of STEMI patients) is not settled. The traditional culprit lesion only PCI strategy is being challenged by recent data that shows advantaged to the preventive and staged PCI strategy.

Purpose: To study the effect of revascularization strategy on 1-year mortality results in STEMI patients with multivessel CAD who present without cardiogenic shock.

Methods: A retrospective study using data from a national ACS survey (compiling 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 multivessel 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 (16% vs 2% vs 12%, p = 0.001). The 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.
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

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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 ST-segment elevation myocardial infarction (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). Multivariable regression analysis confirmed the association of D-dimer 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.

Mechanical chest compressions during prolonged resuscitation for perreperfusion ventricular fibrillation that complicated coronary intervention for ST-elevation myocardial infarction

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Purpose: Ventricular fibrillation (VF) during reperfusion for ST-segment elevation myocardial infarction (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 reperfusion VF and its outcome in patients with reperfusion VF.

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 chest compressions for VF. Patients that demanded mechanical chest compressions tended to suffer more often from VF before reperfusion (30.0% vs. 13.1%, p=0.18), more often had myocardial infarction (MI) history (40.0% vs. 19.3%, p=0.01) and left main stenosis (33.3% vs. 11.7%, p=0.12). They did not differ in female proportion, patients with multivessel disease or MI localization. Two out of 10 patients who received prolonged CPR were discharged alive from hospital without 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.

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 in predicting 12-month MACE, composite of cardiac death, nonfatal MI and stent thrombosis.

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=0.039). 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 occurred 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 rate in patients with STEMI was significantly lower than in patients without STEMI.
survival rate was significantly lower in patients with the lowest quintile compared to patients with other quintiles (Figure).

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

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Background and introduction: Circadian rhythms with regard to time of symptom 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 24h circadian cycle and the prehospital delays, timeliness 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 with prehospital 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-ballon time of 420 min vs 291 min from 12–18h (p <0.001). Patients with onset from 0–6h had a higher prevalence of anterior 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%, p <0.001). 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.

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-ballon times. Those with onset from 18–24h had a higher incidence of heart failure and cardiogenic shock but there wasn’t any 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

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Background: Intravenous (IV) morphine has been shown to be independently associated with adverse clinical outcome in patients with non-STEMI. Currently, there are no data on the association of IV morphine and reperfusion success in STEMI. Thus, we thought to analyse the impact of IV morphine on ischaemic injury. This study aimed to investigate the impact of IV morphine on prehospital delay, first medical contact-to-door time (FMC-CTD) and TIMI frame count (TFC) in STEMI patients.

Methods: STEMI patients reperfused by primary PCI (n=276) within 12 hours of STEMI. Intravenous (IV) morphine administration was recorded in all STEMI patients pairs were successfully matched. Mortality during follow-up was lower 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, Killip class 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 intravascular ultrasound (IVUS) and angiographic scores of antero-septal STEMI.

Methods: Consecutive 37 patients with acute anterior STEMI (mean age = 61 years, 11 women) underwent standard echo and STE-derived Automated Functional 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.

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 the therapies used. Accordingly, long-term outcomes for multiple differing women 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 84 well-organized direct PCI network system


Background: Acute myocardial infarction (AMI) is known crucial disease caus- ing rapid deterioration and death, therefore early admission to cardiac center en- abling emergent percutaneous coronary intervention (PCI) is essential. On this reason emergent ambulance transport to appropriate hospital in shortest time is needed as cooperation system to cover the huge population area.

Objective: To clarify current result of emergency system (Tokyo CCU network) in Tokyo Metropolitan area.

Methods: Tokyo CCU network established in 1978 by 12 CCU centers and emergen- cy 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 hospi- tal admission, and median time from onset to emergent call (EC), to 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 car- ing 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 my-ocardial 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 fre- quently 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 (254±2113 vs. 228±11264; p=0.015). In-hospital and long-term mor- tality was similar between Groups 1 and 2 respectively (3.8% vs. 3.8%; p=0.97; 13.6% vs. 14.5%; p=0.704). Adjusting the outcome to quartile ranges of total ischemic time resulted only a trend for higher mortality in Group 1 with longer reperfusion times (p=0.054).

Conclusion: Physical activity as a trigger of myocardial infarction occurs in ap- proximately 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 | BEDSIDE Time window for clinical benefit from manual thrombus aspiration during percutaneous coronary intervention for acute ST-elevation myocardial infarction

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Background: The benefit of manual thrombus aspiration (TA) during primary per- cutaneous coronary intervention (PCI) in patients with STElevation myocardial infarction (STEMI) remains uncertain.

Objectives: We sought to evaluate clinical impact of TA and time window for clinical benefit from TA during primary PCI.

Methods: We analyzed 5,641 patients with acute STEMI (≤12 hours) from the Korea Acute Myocardial Infarction Registry undergoing primary PCI between De- cember 2007 and December 2012. Patients receiving fibrinolysis and coronary artery bypass graft surgery (CABG) were excluded. Patients were divided into 2 groups according to use of TA during PCI: TA group (n=1,245) and no-TA group (n=4,396). Propensity-matched 12-month clinical outcome was compared between the 2 groups with subgroup analysis according to total ischemic time.

Results: TA group was younger, had lower blood pressure and left ventricular function, more likely to have a totally occluded infarct-related artery and receive glycoprotein IIb/IIIa receptor blocker, and less likely to receive stenting. Twelve-month rates of death and major adverse cardiac events (MACE: composite of death, myocardial infarction, target vessel revascularization, and CABG) were not different between the groups. After propensity score matching (n=1,234 for each group), there were no differences in 12-month clinical outcome between TA and no-TA groups. On subgroup analysis, however, 12-month outcome was significantly different depending on total ischemic time: TA patients with total ischemic time between 4 and 6 hours was associated with lower rates of death (hazard ratio [HR]: 0.53, 95% confidence interval [CI]: 0.24 to 1.19, p for inter- action = 0.01) and MACE (HR: 0.34, 95% CI: 0.16 to 0.69, p for interaction = 0.02).

Conclusions: Manual TA during primary PCI was not associated with improved clinical outcome at 12 months. TA may benefit patients with acute STEMI under- going reperfusion between 4 and 6 hours after symptom onset.

P2486 | BEDSIDE Association between hyperglycemia at admission and microvascular obstruction in patients with ST-segment elevation myocardial infarction

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Background: Blood glucose level at admission in ST-segment elevation my- ocardial infarction (STEMI) is a predictor of heart failure and mortality. Previous study showed the association between hyperglycemia and microvascular dys- function using microangiographic technique. Limited evidence for microvascular enhancement (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 hy-
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 to 1.04 to 1.09, p=0.003). The occurrence of MVO was significantly higher in the patients with glucose level 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

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**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=0.022) and hypertension (57.6% vs. 50.5%; p=0.007), 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. 11.6%; 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 0.368–0.921) 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% and 93.0% in early and late presenters, respectively; p=0.017).

**Conclusion:** In this real-world cohort of STEMI-patients, female sex and diabetes were independently associated with diagnostic lag in STEMI, whereas 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?

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**Background:** GRACE risk score is the risk stratification score in acute coronary syndromes using 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). The 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.

**Results:** We included 3170 patients, with a mean age of 64±13 years, 71% males, 62.2% with ST-segment elevation myocardial infarction. Hospital mortal-

**P2490 | BEDSIDE**

The association of epicardial fat thickness with stress hyperglycemia in patients with ST elevation myocardial infarction

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**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 (β=−0.362 p<0.001), CRP levels (β=−0.291 P=0.003) and peak CKMB (β=−0.288, p=0.004). In multivariate analysis, EFT was demonstrated as an independent predictor of SH (OR: 1.490 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.

**P2491 | BEDSIDE**

Intravascular ultrasound guidance versus angiographic guidance in primary percutaneous coronary intervention for segment ST-elevation myocardial infarction

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**Background:** In the setting of elective percutaneous coronary intervention (PCI), intravascular ultrasound (IVUS)-guided PCI 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.
Methods: In the CREDO-Kyoto acute myocardial infarction (AMI) registry that enrolled consecutive 5429 AMI patients in 26 centers between 2005 and 2007, the current study population consisted of 3026 STEMI patients with primary PCI within 24 hours of symptom-onset. We compared 5-year clinical outcomes between 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 mortality was significantly lower in the IVUS-guided PCI group (3.4% versus 7.8%, log-rank P = 0.001). In addition, the rates of MACE were significantly lower in the IVUS-guided PCI group at 30 days and at a median 224 (range 30 – 441) days of follow-up.

Conclusion: IVUS-guided PCI was not associated with a lower risk for TVR as well as ST in STEMI patients who underwent primary PCI.

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P2492 | BEDSIDE

Bioresorbable vascular scaffolds for ST-segment elevation myocardial infarction treatment

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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) defined as all-cause death, myocardial infarction, repeat target vessel revascularization at 30 days and at a median 224 (range 30 – 441) days of follow-up.

Results: Five (4.7%) patients presented with Killip class III-IV at admission. Multi-vessel PCI with BVS in acute phase was performed in 2 (1.9%) patients due to unstable hemodynamics after infrarenal artery-related trauma. 29.0% of patients received multiple scaffolds in the infarct-related artery. 34.6% of BVS implantations were IVUS-guided. All patients had successful scaffold implantation with TIMI-3 flow achieved in 94.4% of cases. The MACE rate at 30 days was 0%. At a median 224 (range 30 – 441) days of follow-up there was one (0.9%) non-cardiac death and one (0.9%) Q-wave myocardial infarction in non-target vessel. There was no scaffold thrombosis. The overall rate of major adverse cardiac events at follow-up was 1.9%.

Conclusions: PCI with bioresorbable vascular scaffolds in STEMI is technically feasible and safe with favorable short-term and mid-term outcomes.

P2493 | 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

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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

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P2496 | 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 (CMR) in patients with STEMI undergoing primary PCI.

Methods: We analyzed CMR data from 306 consecutive patients treated with primary PCI for STEMI. They were divided into two groups based on initial shock index: shock index > 0.7 (n=188) 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 > 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 > 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 CMR analysis, shock index > 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 > 0.7 was independently associated with large myocardial infarction (odds ratio: 3.34, 95% confidence interval: 1.76 to 6.36).

Conclusions: Shock index is an independent predictor of myocardial injury and infarct size in STEMI patients undergoing primary PCI.

Odds ratios comparing predictive effect

Conclusion: Initial shock index may be a reliable predictor for myocardial injury in STEMI patients undergoing primary PCI.

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

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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: Intracoronary Doppler flow velocity measurements were obtained both before and directly after 90 minute balloon occlusion, with subsequent reperfusion, of the circumflex 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 6 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

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Background: The serum total bilirubin (TB) level has been inversely related with stable coronary artery disease. However, the relation between TB concentration and clinical outcomes in patients with STEMI is not known.

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 were divided into high TB group (n=816) and low TB group (n=295) 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...
were not found after hospital discharge. In the multivariate model, high TB was an independent predictor of in-hospital MACE (HR 2.72 [1.67–4.44], p=0.012) and in-hospital cardiac death (HR 2.72 [1.67–4.44], p=0.012) after adjusting for age, gender, left ventricular ejection fraction, Killip class, creatinine clearance, and in-hospital cardiac death before discharge. 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


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 and oxidative stress are not fully determined.

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, cuff deflation and vascular assessment at 5 min after 2nd cuff deflation (T2). We measured aortic crosssectional area, flow-mediated dilation (FMD), endothelium-dependent vasodilatation (EDV), endothelium-independent vasodilatation (EIVD), arterial stiffness, systolic blood pressure (SBP) by Complior b perfusion boundary region (PBR) micrometers) of the sublingual arterial microvessels (ranged from 5–25 micrometers) using Sideview, Darkfield imaging (Microman, Glycocheck). Increased PBR was considered an accurate non-invasive index of reduced endothelial glyocalyx thickness c malondialdehyde plasma levels (MDA) as marker of oxidative stress

Results: AMI patients had higher PWV, CBF, AI, and PBR and MDA than healthy controls (p<0.05). CBF Al and PBR increased after 1st cuff inflation compared to baseline but return to baseline values after 2nd cuff inflation in AMI patients (CBF: 119±19 vs. 121±21 vs. 118±21mmHg. AI: 8±21 vs. 13±23 vs. 9±21%, PBR: 1.99±0.3 vs. 2.3±0.2 vs. 1.93±0.14, p<0.05 for all comparisons). Conversely, in healthy controls, AI, CBF and PBR remained unchanged throughout the study (p>0.05). MDA was reduced after 2nd cuff inflation compared to baseline (3.65±3.13 vs. 2.6±1.38, p=0.02) in AMI while it remained unchanged in healthy controls (2.7±1.5 vs. 2.2±1.8 p=0.09).

Conclusion: Endothelial glyocalyx and aortic elastic properties are impaired in AMI compared to controls. In our remote ischemic conditioning protocol, the first episode of remote ischemia appears to deteriorate vascular function but also appears to act as conditioning stimulus for the following ischemic episode after which there is improvement of vascular function instead of further deterioration. Thus, remote ischemic conditioning confers acute short-term improvement of vascular function and endothelial glyocalyx, likely through reduction of oxidative stress

P2500 | BEDSIDE
Crucial components of the characteristics for ST-segment elevation myocardial infarction in acute coronary syndrome

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Background: ST-segment elevation myocardial infarction (STEMI) results in larger size of myocardial necrosis and have been reported to cause in-hospital cardiovascular mortality. However, few studies have compared with those with NSTEMI ACS and to identify the most potent combination of the characteristics using the Limitless-Arity Multiple-testing Procedure (LAMP) which is the novel algorithm to reduce the effect of multiple testing correction and minimizes false negative by calibrating Bonferroni correction.

Methods and results: We analyzed the data set of 3597 patients with ACS as signed in PACIFIC registry, a multicenter prospective observational cohort study performed in Japan. We focused on 2761 patients, 1800 with STEMI and 961 with NSTEMI. We used LAMP and then compared with those with NSTEMI ACS and to identify the most potent combination of the characteristics using the Limitless-Arity Multiple-testing Procedure (LAMP) which is the novel algorithm to reduce the effect of multiple testing correction and minimizes false negative by calibrating Bonferroni correction.

Methods and results: We analyzed the data set of 3597 patients with ACS as signed in PACIFIC registry, a multicenter prospective observational cohort study performed in Japan. We focused on 2761 patients, 1800 with STEMI and 961 with NSTEMI. We used LAMP and then compared with those with NSTEMI ACS and to identify the most potent combination of the characteristics using the Limitless-Arity Multiple-testing Procedure (LAMP) which is the novel algorithm to reduce the effect of multiple testing correction and minimizes false negative by calibrating Bonferroni correction.

Purpose: The present study was undertaken to clarify the characteristics of the patients with STEMI compared with those with NSTEMI ACS and to identify the most potent combination of the characteristics using the Limitless-Arity Multipletesting Procedure (LAMP) which is the novel algorithm to reduce the effect of multiple testing correction and minimizes false negative by calibrating Bonferroni correction.

Methods and results: We analyzed the data set of 3597 patients with ACS as signed in PACIFIC registry, a multicenter prospective observational cohort study performed in Japan. We focused on 2761 patients, 1800 with STEMI and 961 with NSTEMI. We used LAMP and then compared with those with NSTEMI ACS and to identify the most potent combination of the characteristics using the Limitless-Arity Multipletesting Procedure (LAMP) which is the novel algorithm to reduce the effect of multiple testing correction and minimizes false negative by calibrating Bonferroni correction.

To the primary end-point was all-cause in-hospital mortality. Results: The new score has a good discriminative ability in the development population to all patients was not statistically significant between the periods (p=0.176).

Conclusion: We speculate that Ramadan fasting does not increase acute coronary heart disease events and that the fasting is a protective factor. We believe that further prospective studies should provide an opportunity to examine the relation of fasting to coronary events.

P2502 | BEDSIDE
ProACS score: an early and simple score for risk stratification of patients with Acute Coronary Syndrome

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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 internal validation cohort (AUC 0.785, 95% CI 0.767–0.803, p=0.333). In the external validation cohort, there was also no significant difference when compared with other myocardial infarction (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
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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 elevation 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 antiplatelet 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
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Rationale: The clinical relevance of complete revascularisation at the acute stage of myocardial infarction (AMI) is currently debated.

Aim and methods: We assessed 5-year mortality according to completeness of revascularisation in 1,165 patients consecutively included in 223 centers participating in the French nationwide FAST-MI 2005 registry, without history of CABG, undergoing PCI during the index hospital stay, and discharged alive after STEMI or NSTEMI; 5-year follow-up was available in 97%.

Results: 1,426 patients (66%) had complete revascularisation (CR). CR patients had more 1-VD (74.5% vs 25.5%), and were younger (62 vs 66 years), with less comorbidity, and less frequently had a prior history of CAD. Five-year survival was 87% vs 78% in the absence of CR (P < 0.001).

After Cox multivariate adjustment CR was associated with a decreased risk of 5-year death (HR 0.70, 95% CI 0.56–0.87, P=0.001). Interestingly, in STEMI patients with x-VD, CR during the initial procedure was associated with decreased mortality (HR 0.33, 0.17–0.62), while CR achieved by staged procedures was not (HR 2.48, 1.39–4.42). In contrast, staged procedures in NSTEMI patients were also associated with decreased 5-year death (HR 0.12, 0.02–0.84).

P2505 | BEDSIDE
Determinants and clinical relevance of polyhydroid content in intracoronary thrombus formed during acute myocardial infarction
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Background: Recently it has been demonstrated that clot contraction is associated with fibrin exposure on its surface and erythrocyte compression in the interior core into the tightly-packed arrays of polyhydroids, detectable in the intracoronary thrombus (ICT) of ST-segment elevation myocardial infarction (STEMI) patients.

Purpose: We sought to investigate determinants and clinical relevance of polyhydroid content in ICT.

Methods: We assessed the content of fibrin, platelets and erythrocytes including polyhydroids 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 TTPMP 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. Polyhydroids were found in 16 (20%) thrombi. They covered ≥50% of fields of view covered by polyhydroids on ICT surface (40 vs. 70%, P=0.014) or in the interior portion (41 vs. 69%, P=0.016) compared with those with <50%. In patients with lumen diameter of infarct-related artery of ≥3.5 mm, thrombi rich in polyhydroids were detected more frequently both on ICT surface (6/24 vs. 2/56, P=0.003) 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 polyhydroids in the inside core (8/37 vs. 3/43, P=0.058) as compared with time of ischemia of <5h. Patients with and without polyhydroids 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 TTMMP-2/3 myocardial perfusion (75.0 vs. 72.6%, P=0.85) 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±4.5 vs. 7.8±5.11x10^4 IU/Lh, P=0.99).

Conclusions: Our findings suggest that polyhydroids 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.

P2506 | BEDSIDE
Early discharge of low-risk patients after successful PCI treatment of ST-segment elevation myocardial infarction - 12 month clinical follow-up data (analysis from PL-ACS and AMI-PL registries)

ESC guidelines suggest that early discharge may be considered in selected low-risk patients.

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 V 417 patients) and the AMI-PL registry, which retrospectively collected 1,426 patients (66%) who were consecutively included in 223 centers participating in the French nationwide FAST-MI 2005 registry, without history of CABG, undergoing PCI during the index hospital stay, and discharged alive after STEMI or NSTEMI; 5-year follow-up was available in 97%.
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 performed (table). The 30-day mortality was low in both groups (0.4%) with similar 12-month mortality (2%).

**Conclusion:** Early discharge of low-risk patients after successful PCI treatment for STEMI is safe with similar incidence of cardiovascular events during 12 months following STEMI.
Conclusions: In low risk patients with STEMI, using landiolol during pPCI may attenuate myocardial reperfusion injury and reduce adverse events.

P2510 | BEDSIDE
Acute coronary syndrome in elderly - what is the place for invasive strategy?
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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-dependent 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±4 years, 1025P (90.9%) 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 27.7%; 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 GII 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 (0.01% vs 0.005) and major bleeding (3.5% vs 1.9%; p < 0.002). 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), haemoglobin 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 < 0.001), stroke (OR 0.50; p < 0.002), dementia (OR 0.28; p < 0.001), heart rate (OR 0.99; p < 0.003) and EF -50% (OR 0.68; p < 0.001). Hospital mortality was inferior in GI (8.3% vs 16.3%; p < 0.001), being STEMI (OR 2.21; p < 0.001), dementia (OR 2.15; p < 0.021), inotropics (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
Prognostic impact of anemia on admission in Japanese patients with acute myocardial infarction: a multi-center study of Tokyo CCU network
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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 g/dL <Hb≤10.0 g/dL) and severe anemia group (Hb<10.0 g/dL). The result of Cox-regression analysis showed that even mild anemia was a predictor of short-term mortality. Kaplan-Meier for the revealed gradual increase among the 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
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Background: The occurrence of cardiac magnetic resonance imaging defined microvascular injury (MVI) after angiographically successful primary percutaneous coronary intervention (PCI) is an important predictor of subsequent development of microvascular injury (MVI) - and has the potential to identify patients at risk for MVI at the time of primary percutaneous coronary intervention (PCI) who might benefit from interventions to improve myocardial perfusion.

Objective: 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 (HDVPS) and zero flow pressure (PZF) were calculated. HDVPS 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 extravascular 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 HDVPS and PZF were related.

Results: PZF was significantly higher in patients with MVI in comparison to patients without MVI (4.56±2.87 vs. 1.04±0.62 mmHg; p < 0.018). In patients with extensive MVI, defined as more than 2.0 cm² MVI, PZF was and 48.5±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 HDVPS and PZF (r=0.29, p>0.13). HDVPS did not discriminate between patients with or without the development of MVI (1.47 (IQR 0.82–2.69) vs. 1.39 (IQR 0.99–2.55) mmHg·cm⁻¹·s⁻¹ respectively, p=0.77).

Conclusions: PZF, but not HDVPS, was related to the presence and extent of MVI indicating a way to identify patients at risk of developing MVI directly following primary PCI. It is conceivable that in patients with MVI, elevated interstitial compressive forces caused by intramyocardial edema and hemorrhage underlie the elevated PZF.

P2513 | BEDSIDE
Patient’s delay in seeking care do not affect one-year post-discharge mortality in STEMI treated with primary coronary angioplasty
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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 then 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. 857 consecutive patients, who met criteria for the invasive treatment at risk of transmission 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

Multivariate analysis showed that landiolol use was an independent predictor of STR (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
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Aim: In this study, we aimed to investigate the relationship between ST segment resolution (STR) obtained in the post-procedural 60th minute and long term (median follow-up, 59 months) cardiovascular events in patients with ST segment elevation myocardial infarction (STEMI), treated with primary percutaneous coronary intervention (p-PCI).

Study protocol: The study population consisted of 3090 patients (792 female, median age 57 years) treated with p-PCI for STEMI, who achieved TIMI 3 flow 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), 0.51–0.99, p = 0.01], p-PCI treated before PCI (OR 0.61, 95% CI 0.48–0.85, p = 0.009), baseline anemia (OR 2.04, 95% CI 1.43–3.11, p = 0.001), baseline SYNATX score -18 (OR 1.58, 95% CI 1.15–2.87, p = 0.021), TIMI trombus score: -4 (OR 2.94, 95% CI 1.54–4.97, p = 0.001), pain-to-balloon time - 4h (OR 1.82, 95% CI 1.29–2.65, p = 0.001) and neutrophil to lymphocyte ratio > 5 (OR 1.82, 95% CI 1.34–2.30, p = 0.007) were identified as independent predictors of no-STR. In hospital death (11.8% vs 7.5% vs 13.3%), chest pain (19.6% vs 17% vs 18.5%), reinfarction (14.1% vs 12% vs 8.8%) were higher in the no-STR group compared to the complete STR and incomplete STR groups (p < 0.001 for both).

Conclusion: Complete STR in patients with STEMI is associated with better in-hospital and long term clinical outcomes. Pts with STEMI who did not achieve STR at the post-procedural 60th minute may have higher early and long term complications and mortality compared to pts who achieved STR.

P2515 | BEDSIDE
Comparison of the in-hospital complications and mortality in patients with Takotsubo cardiomyopathy and ST segment elevation myocardial infarction
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Background: Takotsubo cardiomyopathy (TTC) mimics acute coronary syndrome. The symptoms are similar but the prognosis is generally favourable in TTC patients (pts). However, some complications which may occur could be fatal. Purpose: The aim of our study was to compare in-hospital complications and in-hospital mortality in pts with TTC and myocardial infarction with ST segment elevation (STEMI).

Patients and methods: Ninety consecutive female pts with TTC were compared to 90 consecutive female pts with STEMI. The mean age was 68.7 years in pts with TTC and 69.9 years in STEMI group. Chest pain before hospitalisation occurred in the same numbers of pts with TTC and STEMI. Pts with TTC had dyspnoea more 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: Patients with STEMI had a higher incidence of serious complications compared to TTC 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 records and phone interviews. The figures represent any number of patients with complete 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 unspecified 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 no mortality. The Kaplan-Meier curves for survival showed excellent mortality. Besides, long-term prognosis is excellent if the patient stands for 12 hours after P-PCI.

Conclusions: Clinical presentation and P-PCI are paramount in AMI due to ULM occlusion even with a highly successful intervention. The figures mean absolute important factors associated with survival. Besides, long-term prognosis is excellent if the patient stands for 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


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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 2106 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 than 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 2.69–6.10, p<0.001) and more than a three-fold increased risk of one-year mortality (HR 3.58, 95% CI 2.60–4.93, p<0.001). When adjusted for baseline clinical characteristics, new-onset AF remained independently associated with both 30-day (HR 2.38, 95% CI 1.55–3.67, 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?

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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 461 consecutive patients undergoing PPCI for acute STEMI and matching eligibility criteria of the study between January 2010 and December 2011 were included in the study. Patients were divided into two groups: 61 (13.1%) with AVDE and 404 patients without AVDE based on angiograms performed during PPCI.

Results: Longer stent length, higher balloon diameter, low Syntax score (SxS), low LVEF, high neutrophil/lymphocyte ratio and chronic renal failure were seemed to be associated with AVDE in univariate analysis and these variables were entered into multivariate analyzes. Syntax score, stent length, LVEF and low SxS were found to be associated with AVDE (OR: 0.11, 95% CI: 1.06–1.16, p<0.01; OR: 0.80, 95% CI: 0.80–0.91, p<0.01; OR: 0.85, 95% CI: 0.79–0.91, p<0.01, respectively).

Conclusions: This study concluded that low SxS, longer stent length, low LVEF were predicting risk factors associated with the development of AVDE in patients undergoing PPCI. Low SxS associated with AVDE may be linked to the strong relation between AVDE and high thrombus burden and composition of atherosclerotic plaque rather than complex coronary lesions.

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STEMI VII

Risk factors of contrast-induced nephropathy development in patients with ST-elevated myocardial infarction while performing percutaneous coronary intervention


Purpose: To detect the risk of CIN development, to determine its role in the implementation of adverse outcomes in patients with STEMI.

Materials and methods: The study enrolled 954 STEMI patients admitted for up to 24 hours since the moment of symptoms onset. In multivariate analysis, stent length, LVEF and low SxS were found to be associated with AVDE from a common group underwent intraaortic balloon counterpulsation procedures for up to 24 hours since the moment of symptoms onset. At admission all the patients were estimated serum creatinine level, GFR was calculated by MDRD formula. Cases of CIN were determined under increase of creatinine level for more than 25% or for 0.5 mg/dL (44 mcmol/l) as compared to the baseline within 48–72 hours after intravascular administration of contrast in the absence of an alternative cause.

Results: Development of CIN was detected in 52 (7.2%) STEMI patients, depending on its presence the patients were divided into two groups. While analyzing the clinical and anamnestic characteristics of groups of STEMI patients with and without CIN, a significantly greater frequency of DM (28.85% vs 15.37%, p<0.04) occurrence and CKD (55.7% vs 41.34%, p=0.03) occurrence were detected in patients with nephropathy. The predominance of II–IV classes of AHF by Killip (32.69% vs 17.91%, p=0.008) and lower ejection fraction in a group with CIN (47% vs 50%, p=0.02) were noted as compared to the patient with normal renal function. By the method of univariate regression analysis it was determined that a presence of AHF of II–IV classes by Killip increased the chances of CIN development 2.2-fold, DM – 2.2-fold. By the method of multivariate logistic regression it was also detected a true impact of DM and AHF II–IV classes by Killip on the probability of CIN development. Analyses of a number of adverse outcomes in hospital period detected statistically significant increase in deaths (23.0% vs 6.8%, p=0.003), recurrent MI (27.0% vs 6.7%, p=0.05), EPIA (23% vs 10.6%, p=0.006) among the patients with CIN as compared to a group of patients without renal function disorder. Thus the chances of EPIA development while having CIN increased 2.5-fold (95%, CI 1.26–5.05), recurrent MI – 5.4-fold (95%, CI 2.69–10.6), total complications – 4.95-fold (95%, CI 1.99–8.29), and nonfatal complications – 5.1-fold (95%, CI 2.85–9.17).

Conclusion: CIN was detected in 7.2% patients, was associated with DM, a history of CKD, evident AHF and reduction of left ventricular ejection fraction. DM
and clinically apparent AHF (II-IV class by Killip) were independent predictors of CN 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)

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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 novel predictors for mortality through this prospective, nationwide, multicenter, observational registry in the real world of Chinese patients.

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% (9886) had received emergency revascularization and 79.9% (4796) of them was primary PCI; of those NSTEMI patients 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 (7.6%), diabetes (7.7%), severe smoking (8.90%), and chronic kidney history (9.9%), chronic renal insufficiency (12.05%), chronic pulmonary diseases (12.54%), ST elevation (6.81%), anterior wall involving (7.75%), heart failure (5.77%), cardiac arrest (33.16%) or cardiac shock (36.44%) when admission, and patients who received emergency revascularization: 17.3%. As an example, female patients (14.04%) and age ≥75 (7.75%) were two of the most significant factors to affect the negative outcomes of AMI.

Conclusions: Among selected 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

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Background: Thrombin generation is a central step of the coagulation system involved in hemostatic and thrombotic roles, from promotion and inhibition of 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 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 endogenous thrombin potential (ETP), peak, and velocity index. Baseline characteristics significantly associated to delayed PCI included older age, female sex, diabetes, atypical symptoms, higher Killip class, longer time from symptom onset to FMC, and cardiac arrest before pPCI, all indicating a higher risk profile. Organisational factors significantly associated to timely PCI were pre-hospital ECG and direct admission to Cath Lab. Other factors indicated by the attending cardiologist as main responsible for the delay are shown in the Table.

Conclusions: This study identified several organisational and patient characteristics associated to delay. The former can be improved, while the latter, although non-modifiable, can be taken into consideration in order to minimize the repertusion delay.

P2524 | BEDSIDE

Relative survival potential of platelets is differentially associated with CXC4-CXC7R and modulates clinical outcome following STEMI

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Background: The chemokine receptors CXC4-CXC7R which ligate SDF-1 mediate the differentiation of progenitor megakaryocytes and variably regulate the thrombotic–haemostatic functions of platelets and their survival. Surface expression of CXC7R on circulating platelets is significantly enhanced in acute coronary syndrome (ACS) and significantly correlates with improved myocardial function following ACS. Moreover, high CXC4 surface expression on platelets is associated with better survival and less re-infarction rates in patients with symptomatic CAD. Since regenerative or inflammatory attributes of platelets depend on their survival in circulation, this study was designed to investigate the possible correlation between apoptotic/survival potential of platelets with respect to the relative surface expression of CXC4-CXC7R and the clinical outcome in patients with STElevation myocardial infarction (STEMI).

Subjects and methods: For the cohort study, we included 78 consecutive STEMI patients. Apoptosis in platelets was ascertained by flowcytometry evaluating the externalization of phosphatidylserine (Annexin V binding) and mitochondrial transmembrane potential loss (△ψm by TMRE) among resting platelets at baseline levels. Surface expression of CXCR4-CXCR7 on circulating platelets was assessed by whole blood flowcytometry gating for CD42b+ platelet population. Patient’s blood was taken at the time of pre-cutaneous coronary intervention (PCI) and was immediately analysed. Patients were admitted to cardiac magnetic resonance tomography (CMR) at intrahospital stay and after 6 months to evaluate cardiac mechanics (left ventricular function - LVEF) and infarct size. Correlations were assessed by Spearman’s rank correlation coefficient (r). Normally distributed data were compared using independent Student’s t-test.

Results: Platelet TMRE correlated significantly and positively with platelet CXCR7 (r=0.302, p=0.039) and inversely with platelet CXCR4 (r=-0.363, p=0.027). Furthermore, platelet Annexin V levels < median were associated with better LVEF% after 6 months as compared to Annexin V levels ≥ median (59.8% vs. 51.3%, p=0.05).

Conclusions: The present results suggest a possible influence of platelet survival on platelet expression levels of CXCR4 and CXCR7. Furthermore, enhanced platelet survival might improve LVEF% recovery after myocardial infarction. Large scale studies are however warranted to certify these results.
P2525 | BEDSIDE
Relationship between inferior artery location, acute total coronary occlusion and mortality in STEMI and NSTEMI patients

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Purpose: We compared angiographic findings and mortality in patients with non-ST-segment elevation myocardial infarction (NSTEMI) versus STE-segment elevation myocardial infarction (STEMI) undergoing percutaneous revascularization in STEMI.

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 0 flow – 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 related artery (IRA) in STEMI group was RCA 49.37% (LAD 37.84%, LCX 12.78%) whereas in NSTEMI group was RCA 43.30% (LAD 32.96%, LCX 23.85%). Pts with TO had higher mortality during all 36-mnth follow up but only in STEMI group, mortality in NSTEMI group was comparable between TO and nTO pts. LCX pts with TO had higher in-hospital mortality both STEMI and NSTEMI patient groups. There were not differences in mortality between RCA TO and nTO pts both STEMI and NSTEMI patient 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 coronary 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-mnth follow up and had impact on only in-hospital mortality LCX-related MI pts, both STEMI and NSTEMI.

P2526 | BEDSIDE
Diabetes Mellitus type 2 is an important risk factor for sudden cardiac arrest in patients with STEMI

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Background and introduction: Sudden cardiac arrest (SCA) is the most serious complication of STE 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 [47.5%]) with confirmed STEMI as the LCX among patients and without T2DM and evaluated the occurrence of prehospital SCA. Then, we performed comparative analysis between these groups.

Results: We observed 137 (30.5%) cases of T2DM (we provided 15 diagnoses during the follow-up period, according to the current criteria of 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/0 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).

P2527 | BEDSIDE
Factors influencing the patient delay in STEMI

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Background: Many papers showed that patient delay defined as time from the onset 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 in a 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=0.007), not smoking in the period preceding the illness (avg. + 71 min., + 40.1%, p=0.004), never ever smoking cigarettes (avg. + 57 min., + 29.5%, p=0.037). 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 one 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
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 pertension, hypercholesterolemia, diabetes, obesity, overweight, history of CAD (myocardial infarction, interventional treatment) on the patient’s delay was determined.
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/1.73 m² 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): 0.669 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): 0.723 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.

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**P2530 | BEDSIDE**

**Infarct size in staged versus immediate complete revascularization for multivessel disease:**

**Methods:** In the prospective CVLPRIT-CMR substudy, 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 end-point was IS on 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 MS and LVEF were lower with staged CR. At follow-up CMR, prevalence and extent of reversible ischaemia and MACE incidence were similar (Table 1).

**Table 1. Baseline, CMR and clinical results**

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>62.8±11.7</th>
<th>66.0±10.3</th>
<th>0.37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex (n, %)</td>
<td>52/60 (86.7)</td>
<td>28/30 (93.3)</td>
<td>0.34</td>
</tr>
<tr>
<td>Anterior infarct (n, %)</td>
<td>21/60 (35.0)</td>
<td>11/30 (36.7)</td>
<td>0.88</td>
</tr>
<tr>
<td>Symptom-PPCI time (min)</td>
<td>179 (127–305)</td>
<td>203 (151–296)</td>
<td>0.93</td>
</tr>
<tr>
<td>Time to acute CMR (d)</td>
<td>3.2 (1.3–7.6)</td>
<td>4.1 (2.7–5.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%) on acute CMR scan</td>
<td>47±9.4</td>
<td>42±10.2</td>
<td>0.023</td>
</tr>
<tr>
<td>Total infarct size (% left ventricular mass) on acute CMR scan</td>
<td>11.3 (5.4–17.4)</td>
<td>19.1 (8.8–32.6)</td>
<td>0.014</td>
</tr>
<tr>
<td>Myocardial salvage index (%) on acute CMR</td>
<td>61.7 (36.4–76.2)</td>
<td>35.1 (5.9–66.4)</td>
<td>0.011</td>
</tr>
<tr>
<td>Presence of ischaemia (n, %) on follow-up CMR</td>
<td>10/49 (20.4)</td>
<td>7/26 (26.9)</td>
<td>0.52</td>
</tr>
<tr>
<td>Global ischaemic burden (% left ventricular mass) on follow-up CMR</td>
<td>12.8±10.9</td>
<td>19.2±17.3</td>
<td>0.36</td>
</tr>
<tr>
<td>Major adverse cardiovascular events (n, %)</td>
<td>4/60 (6.7)</td>
<td>4/30 (13.3)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

**Conclusions:** This is the first CMR study comparing revascularisation for multivessel disease at PCPI. Staged in-hospital CR was associated with increased irreversible injury, which may impact on long-term outcome.

**Acknowledgement/Funding:** National Institute for Health Research (NIHR), British Heart Foundation (BHF)

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**P2531 | BEDSIDE**

**Transradial vs. Transfemoral Coronary Intervention for ST Elevation Myocardial Infarction**

**Methods:** We have studied 1808 consecutive patients that 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 clinical 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% or 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 4.9% lower 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 TFA strategy (14.6% Vs 22.1%; 95% CI [0.43–0.78], p<0.001). Cumulative survival curves were created to illustrate findings.

**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 coronary intervention in STEMI patients. TRA was associated with sustained mortality benefit after two years.

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**P2532 | BEDSIDE**

**Diagnostic accuracy of focused cardiac ultrasound performed by emergency physicians for the assessment of ascending aorta dilatation 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 was evaluated in parasternal long-axis view. Aorta diameter <40 mm was accepted as normal dimension determined by CTA.

**Objectives:** The diagnostic performance of transthoracic focus cardiac ultrasound (FoCUS) performed by emergency physicians (EP) to estimate ascending aorta dimensions in the acute setting has not been prospectively studied. We investigated the diagnostic accuracy and the interobserver variability of EP-performed FoCUS to evaluate thoracic aortic dilatation and aneurysm compared with computed tomography angiography (CTA).

**Methods:** This was a prospective single-centre cohort study of a convenience sample of patients that underwent CTA. FoCUS was performed to estimate thoracic aortic dilatation and aneurysm with computed tomography angiography (CTA).

**Results:** 140 patients were enrolled in the study. Ascending aorta dilatation 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 65.6–89.6) and 99.2% (95% CI 85.1–97.3) respectively for ascending aorta dilatation, 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 k=0.82.

**Conclusions:** FoCUS performed by EP is specific for ascending aorta dilatation and aneurysm when compared to CTA and appears as a reproducible technique.

**Acknowledgement/Funding:** ADVISED study group

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**P2533 | BENCH**

**Inferior vena cava compression (IVC) maneuver as a novel technique to detect patent foramen ovale: transesophageal echocardiographic study**


**Background:** Valsalva maneuver, the most sensitive testing to identify patent foramen ovale (PFO), cannot be performed by the patient independently during transesophageal echocardiography (TEE) especially under sedation or cognitive disorder. We aimed to investigate the effectiveness of newly-invented “inferior vena cava compression (IVC) maneuver” to diagnose PFO compared with Valsalva maneuver.

**Methods:** We prospectively enrolled 217 consecutive patients with paroxysmal AF schedule to undergo left atrial catheter ablation. All the patients received TEE prior to ablation. Except for 3 patients newly diagnosed as atrial septal defect by TEE and performed saline injection under sedation following 3 conditions: Valsalva maneuver without or under minimal sedation, at rest and IVCC maneuver under sedation. IVCC maneuver defined as manual compression of 5cm right side of epigastric region during 30 seconds and releasing the compression immediately.
mediately 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 < 0.0001) which was not inferior to Valsalva 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 Valsalva maneuver. Especially when Valsalva 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?
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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 tissue Doppler derived main pulmonary arterial 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 (MPVESV, MPLSV), right pulmonary artery early and late velocities (RPESV, RPLSV), 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 velocity (p < 0.05) (Table 1). Using regression analysis, we were able to create the formulas, 84.9 − [193 x ESV − 0.21 x TIBSP] and 58.6 − [137.8 x ESV – 0.29 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>MPESV (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 (ms)</td>
<td>66±20</td>
<td>52±16</td>
<td>0.001</td>
</tr>
<tr>
<td>MPTIBSP (ms)</td>
<td>141±30</td>
<td>111±24</td>
<td></td>
</tr>
<tr>
<td>RPSV (cm/s)</td>
<td>8±2</td>
<td>6±2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>RPSV (cm/s)</td>
<td>3±1</td>
<td>6±3</td>
<td>AD</td>
</tr>
<tr>
<td>RPSAS (ms)</td>
<td>34±9</td>
<td>38±12</td>
<td>0.01</td>
</tr>
<tr>
<td>RPTIBSP (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
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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 atherosclerosis.
Purpose: The aim of this study was to assess whether the AVP (Figure 1) was

Abstract P2535 – Table 1. Comparison of 3DE and 2DE to CMR RV

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Correlation Coefficient</th>
<th>P value</th>
<th>Bland-Altman difference of means (bias)</th>
<th>Bland-Altman limits of agreement</th>
<th>Linear regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>3DE RVEDV vs. CMR RVEDV (ml)</td>
<td>0.94</td>
<td>-0.0001</td>
<td>-3.5 ml</td>
<td>-18.7 to 11.6</td>
<td>y = 0.93x + 11.98</td>
</tr>
<tr>
<td>3DE RVESV vs. CMR RVESV (ml)</td>
<td>0.87</td>
<td>-0.0001</td>
<td>-0.8 ml</td>
<td>-16.4 to 14.9</td>
<td>y = 1.67x - 2.79</td>
</tr>
<tr>
<td>3DE RVEDV vs. CMR RVEDV (%)</td>
<td>0.51</td>
<td>-0.003</td>
<td>11.7%</td>
<td>-12.7 to 10.5</td>
<td>y = 0.66x + 20.5</td>
</tr>
<tr>
<td>2DE RVEDV vs. CMR RVEDV (ml)</td>
<td>0.51</td>
<td>-0.0035</td>
<td>-33.1 ml</td>
<td>-81.9 to 15.7</td>
<td>y = 0.49x + 77.8</td>
</tr>
<tr>
<td>2DE RVESV vs. CMR RVESV (ml)</td>
<td>0.53</td>
<td>-0.0021</td>
<td>-18.7 ml</td>
<td>-48.9 to 11.6</td>
<td>y = 0.65x + 30.5</td>
</tr>
<tr>
<td>2DE RVEDV vs. CMR RVEDV (%)</td>
<td>0.25</td>
<td>ns</td>
<td>5.5%</td>
<td>-9.3 to 19.4</td>
<td>y = 0.26x + 41.4</td>
</tr>
</tbody>
</table>

Figure 1. Measurement of descending aorta propagation velocity (AVP) in a subject in control group (a) and in a patient with obstructive sleep apnea syndrome (b).

Figure 1. Measurement of descending aorta propagation velocity (AVP) in a subject in control group (a) and in a patient with obstructive sleep apnea syndrome (b).

P2536 | BEDSIDE
Comparison of right ventricular volumes, ejection fraction and mechanical indices derived automatically from 3D speckle tracking to cardiac magnetic resonance imaging
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Background: Automated border tracking algorithms for calculating right ventricular (RV) volumes and function are often difficult to implement due to the complex anatomy and over editing needed for effective border tracking of RV endocardium. Recently, a simplified 3D speckle tracking method (TomTec 3D Function 2.0) has been developed requiring minimal operator input (mitral valve, tricuspid valve, apex, aortic valve) for RV volume determination which requires validation.
Methods: 31 normal subjects (16F, 15M) ages 30 to 93 years, average 65.3±15 years were recruited after IRB approval and underwent 2D echocardiography (2DE), full volume real-time 3D echocardiography (3DE) and cardiac magnetic resonance imaging (CMR) within 24 hours. 3DE RV end-diastolic and end-systolic volumes (RVEDV, RVESV) and ejection fraction (RVEF) were automatically calculated based on 3D speckle tracking. In addition, longitudinal septal and RV free-wall strains and tricuspid annular plane excursion (TAPSE) were automatically derived and compared to CMR and 2DE results.
Results: Mean BSA 1.73±0.21 m². Mean CMR RVEDV 120.3±24.5 ml. Mean CMR RVESV 51.7 ± 16.9 ml. Mean CMR RVEF 58±5.5%. Mean values of 2DE and 3DE RVEDV and 2DE RVESV and 2D RVEF differed significantly from CMR results whereas 3DE RVESV and 3DE RVEF did not. Correlations between 3DE,2DE and CMR results using Spearman-Rank correlation coefficients. ANOVA, paired t tests, Bland-Altman and simple linear regression analyses were performed as appropriate (Table).
Conclusions: 1) 3DE RV volumes correlated more closely with CMR than 2DE RV volumes. 2) Correlations for RVEF were significant but limited by a narrow range (48–68%), 3) Septal and RV free-wall strains and tricuspid annular plane excursion (TAPSE) did not correlate with CMR RVEF or 3DE RVEF.

P2537 | BEDSIDE
Echocardiographic marker of arterial stiffness in OSAS
N. Watanabe1, H. Oe1, Y. Ohno1, Y. Sakatani2, A. Ueoka2, T. Miyoshi2, N. Nishi2, K. Nakamur2, H. Morita2, H. Ito2, Okayama University Hospital, 2Okayama University, Dept. of Cardiovascular Medicine, Okayama, Japan
Background: In patients with aortic stiffness (AS) and atrial fibrillation (AF), the
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
Validation of novel vendor-independent software algorithm for left ventricular volumes and ejection fraction by three-dimensional echocardiography: impact of manual correction versus automated tracking

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1 University of Medicine and Pharmacy Carol Davila, Bucharest, Romania; 2 University Hospital Padova, Cardiology, Padua, Italy

Background: Despite three-dimensional echocardiography (3DE) is the recommended method for measuring the left ventricle (LV) by the ASE/EACVI guidelines, it still remains underused due to time constrain and need of different vendor-specific software tools. A faster and vendor-independent 3DE algorithm for LV quantification requiring minimal human input is now commercially available. Our aim was to assess the reproducibility and the accuracy of this 3DE algorithm versus cardiac magnetic resonance (CMR).

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 correction 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 algorithm showed more underestimation of LV EDV (20±22 vs 5±13 ml), stroke volume (21±19 vs 2±11 ml), and EF (7.7±9.2 vs 7.5±2.4% vs 0.001), but EF was similar (54±11% vs 53±12% vs 0.118), Semi-automated 3DE algorithm provided LV measurements with excellent correlations and agreement (bias±SD; CMR (r=0.97 and 9.71±4 ml), stroke volume (21±19 vs 2±11 ml), EF (7.7±9.2 vs 7.5±2.4% vs 0.001), but EF was similar (54±11% vs 53±12% vs 0.118), Semi-automated 3DE algorithm provided LV measurements with excellent correlations and agreement.
the maximum difference in rotation angle between the base and apex (unit is °). Torsion was defined as LV twist/long axis length (unit is °). Time-LV twist curve was obtained from 3D-STE. LV torsion was derived from time-twist curve and integrated by long axis length for each instance in time (each frame). Time to peak torsion was expressed as % systole by dividing the time by a total systolic period.

**Results:** LV ejection fraction (EF) in HHD was reduced compared to control and HTN (control: 58±7, HTN 59±10, HHD: 39±9%, **p** =0.05 vs control). The amplitudes of peak torsion at 3 layers were correlated with LVEF in 81 subjects (endocardium: **r** =0.41, midwall: **r** =0.33, epicardium: **r** =0.25, **p** =0.05). Endocardial peak torsion was significantly greater than the corresponding midwall and epicardial torsion by 50% and 77%. LV torsion in HHD was higher in all 3 layers compared to control and HHD. The decreasing torsion from endocardium to epicardium was observed in control, HTN and HHD (endocardium: control: 2.36±0.34, HTN: 2.63±0.45°, HHD: 2.12±0.31°; midwall: control: 1.12±0.19, HTN: 1.36±0.29°, HHD: 1.07±0.21°; and epicardium: control: 0.56±0.18, HTN: 0.64±0.26, HHD: 0.43±0.18°). Time to peak torsion was earliest at epicardial layer in HHD and latest at endocardial layer in HTN (90±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 HHD and smaller in HHF. The differences in LV torsion among the 3 layers seemed to diminish in association with LV systolic dysfunction.

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**NEW INSIGHTS INTO VALVULAR HEART DISEASE**

**P2554 | 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.


**Background:** ASEE/AECVI guidelines recommend using three-dimensional echocardiography (3DE) to measure left ventricular (LV) volumes and ejection fraction (EF) in echocardiography with experience with this technique. However, in multivendor echocardiographers, 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 30%, valvular 25%, cardiomyopathy 27%, and other cardiac diseases 16%) were enrolled. LV full volume data sets were acquired using Vivid 99 (GE Vivid, Horten, N) and E33 (Philips Medical System, Andover, MA) scanners during the same echo session. A single researcher analyzed the 3DE data sets with VS and VI software packages in row, one week apart from each vendor to the other. Then he performed a second set of measurements with 4D LV Analysis 3.1 software (TomTec) 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 (EF 18–79%). Differences between LV volumes obtained from different vendors to reduce the differences in LV volumes and EF were found to offer the best prediction for severity of pulmonary regurge. Significant regurge of 0.8 has sensitivity of 86.36% and specificity of 100% (AUC=0.924) and no flow time of >64 msec has specificity of 81% and specificity of 100% (AUC=0.894) in identifying significant pulmonary regurge. Compared to controls, patients after TTO repair showed significantly lower right ventricle myocardial velocities, higher E/ E' ratio and prolonged MPI. Among the patients, MPI, VS MPI and VI MPI showed significant negative correlation (**r** =−0.402; **p** =0.008) with tricuspid annulus peak systolic velocity (S) and significant positive correlation (**r** =0.413; **P** =0.04) with right ventricle stroke volume by CMR.

**Conclusion:** Conventional echocardiography can offer a simple, readily available and accurate tool for quantification of pulmonary regurge and right ventricular function during mid-term follow up after surgical repair of tetralogy of Fallot.

**P2543 | BEDSIDE**

**Dynamics of mitral valve annulus in patients with mitral regurgitation due to fibro-elastic deficiency or barlow’s disease**


**Background:** The dynamics of the mitral valve annulus in organic mitral regurgitation (MR) may differ significantly between the various entities. The present evaluation characterizes the mitral annulus dynamics in patients with MR due to Barlow disease (BD) or fibro-elastic deficiency (FED) using 3-dimensional (3D) modeling.

**Methods:** 49 patients with moderate to severe organic MR (29 male, age 63±20 years, 23 FED 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 axis ratio (AH-WCR)) were measured along the systole. MR was 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 FED 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 with late systolic MR, all of them with BD, suggesting more enhanced movement and flattening of the mitral annulus during late systole compared with FED.

**Conclusion:** BD is associated with more pronounced changes in mitral valve annulus geometry along the systole compared with FED 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 (r=0.93, p<0.001, 2SD: 9.9±1.5 cm² by 3D-PISA; r=0.76, p<0.001, 2SD: 19.7±LM. When used to classiﬁer 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.

Subgroup analysis according to the AR

Conclusion: Automated quantification of AR using the 3D-FVCDE method is clinically feasible and more accurate than the current 2D-based method. AR quantification by 2D-PISA significantly misclassified AR grade in patients with eccentric or multiple jets. This study demonstrates that 3D-FVCDE is a valuable tool to accurately measure AR volume regardless of AR characteristics.

Acknowledgement/Funding: Authors have no conflict of interest

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).

P2545 | BEDSIDE

Determinants of normal tricuspid annulus area in healthy volunteers: a three-dimensional echocardiographic study


1 University of Padova, Department of Cardiac, Thoracic and Vascular Sciences, Padua, Italy; 2 University of Bologna, Department of Cardiac, Thoracic and Vascular Sciences, Padua, Italy; 3 University of Chicago, Chicago, United States of America; 4 University of Padova, Department of Cardiac, Thoracic and Vascular Sciences, Padua, Italy; 5 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 coronary artery bypass 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 identiﬁer 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 CT 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 s (range 24–57). TA area decreased from 4.92±0.75 cm² to 4.37±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); however this difference disappeared after BSA indexation (6.1±0.5 cm² vs. 6.0±0.5 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


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 with wide variability and time consuming. A specialized TEE reconstruction tool has recently been introduced, which allows automatically 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 (0.606–0.862), (r: 0.742, p<0.01)) and AA area ((ICC): 0.723 (0.495–0.856), (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
the assessment of AA in TAVR patients with higher correlation with MDCD than the manual measurements. Our results support its use in clinical practice, and may be an alternative to MDCD for patient's selection. Further studies are needed to evaluate additional clinical benefit in this group of patients.

### Table 1. Correlation and interobserver variability between the automated and manual measurements of the AA with MDCD

<table>
<thead>
<tr>
<th>Method</th>
<th>r</th>
<th>p</th>
<th>ICC</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual assessment vs MDCD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA diameter</td>
<td>0.830</td>
<td>0.000</td>
<td>0.779</td>
<td>0.333–0.940</td>
</tr>
<tr>
<td>AA area</td>
<td>0.670</td>
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<td>0.624</td>
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<tr>
<td>AA diameter</td>
<td>0.901</td>
<td>0.000</td>
<td>0.941</td>
<td>0.761–0.985</td>
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<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>

### Purpose

Assume the color flow method allows accurate quantification of MR.

### 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 intraobserver and interobserver 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.

### 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.

### Table 1. Correlation and intermethods agreement analysis using 3D PISA EROA as gold standard

<table>
<thead>
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<td>EROA 3D PISA, EROA 2D volumes</td>
<td>0.32</td>
<td>0.10</td>
<td>0.29</td>
<td>0.24–0.33</td>
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<tr>
<td>EROA 3D PISA, EROA 3D volumes</td>
<td>0.753</td>
<td>0.87</td>
<td>0.85</td>
<td>0.97–0.92</td>
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<td>EROA 3D PISA, EROA 3D volumes</td>
<td>0.98</td>
<td>0.95</td>
<td>0.96</td>
<td>0.95–0.98</td>
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### Conclusion

A 3D color flow model provides a new tool that measures the flow that passes through cardiac valves.

### Purpose

To explore the potentiality of 3D transthoracic echo (3DTE) in the education, planning and decision-making.

### Methods

- 3D datasets have been used to simulate/plan cardiac surgery. Recently, transoesophageal 3D datasets have been used to obtain 3D printed models of mitral valves. However, the lack of dedicated software to quantitate the complex morphology of the tricuspid valve (TV) hampered the possibility to obtain 3D models of TV to be used to plan annuloplasty procedures.

### Purpose

To explore the feasibility of using transthoracic 3D echo data to generate a 3D patient-specific model of TV.

### Methods

- 3D dataset of the TV (32 volumes/s) acquired using Vivid E9 scanner from the apical approach was analyzed with dedicated custom software (Figure, A, B). Coordinates of the annulus and the leaflets were imported into Mesh-Lab (Visual Computing Lab IST-CNR) software to construct a solid model (Figure, C) which was converted to stereolithographic file format and 3D printed by a commercially available MakerBot Replicator 2 3D printer (Figure D).

### Results

Total time for generating the 3D model of TV was 30 min. The resulting model closely mimicked the original 3D rendered images and postprocessed TV model provided by the software (Figure). The tangible 3D model of TV enhanced the perception of the complex 3D shape of the TV.

### Conclusion

3D printing of TV from transthoracic 3D echocardiography is feasible, with highly preserved fidelity. Given the short turn-around time and the possibility to use 3D datasets obtained from transthoracic approach, this technique has the potential for rapid integration into clinical practice to assist with surgical education, planning and decision-making.

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changes and functional abnormalities. LA size is often used as a surrogate marker of LA function in clinical practice. However, whether LA 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 <60ml/min/1.73m²) 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-LAe) 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 1).

**Conclusions**: LA function and stiffness are significantly impaired 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 patients (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 = 56.9±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/ocipital 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) were obtained in apical 4-, 3- and 2-chamber views, using speckle tracking echocardiography. Simultaneously, 30 volunteers were studied with the same protocol.

**Results**: 1,866 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, A-B) when compared with normal values (Fig. 1).

**Conclusion**: Using TTE, the baseline echographic features of the ACP are represented by 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 TEE in the routine follow-up of these devices remains to be approved.

### P2555 | BEDSIDE

**Use of transthoracic echocardiography in patients implanted with Amplatz atrial appendage plugs**

M. Kubala, S. Traullie, S. Quenum, O. Buicic, J.S. Hermida. Amiens University Hospital - Hospital Sud, Amiens, France

**Background**: Transcatheter occlusion of left atrial appendage (LAA) with Amplatzer cardiac plug (ACP) has been recently demonstrated as an alternative to oral anticoagulants in selected patients. Transesophageal echocardiogram (TEE) is currently used to facilitate the ACP positioning and to detect complications including thrombosis, plug dislodgement or peri-device leaks during the follow-up. Baseline ultrasound features of the ACP evaluated by transthoracic echocardiography (TTE) have not been described till now.

**Methods**: During the first month following the device implantation we performed TTE in 24 pts (13 men) mean age=73±11y, mean CHA2DS2VASc score=4.7±1.3 and HAS-BLED score=3.6±1.1 implanted with 16–28 mm devices.

**Results**: The mean LA size was 32±8 cm². Using a modified 4-chamber view, a similar 8 shape like look of the ACP was seen in all cases in front of the LAA ostium (Fig 1) showing a proper sealing of the LAA orifice. The first 8 ring near the mitral valve measured 11.5±1.7x1.1±2.2 mm and the second one 12.4±1.7x11.8±2.1 mm. The distances between the 8 circles and the mitral valve plan, the left atrial roof and the left atrial free wall were respectively of 3.8±1 mm, 23.5±4 mm and 7.7±2.6 mm. Five patients (21%) had mild para-device leaks of 2–3 mm maximal diameter detected by TEE during the follow-up. All leaks were also viewed using TTE-doppler zoomed 4-chamber view. There were not any thrombus detected.
Table 1. LA volume and S and SR parameters

<table>
<thead>
<tr>
<th></th>
<th>LA biv and volume (mL)</th>
<th>LASe</th>
<th>LA Sa</th>
<th>LASRe</th>
<th>LAS Ra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-surgery group</td>
<td>67.7±5.3</td>
<td>18.2±0.7</td>
<td>3.6±0.15</td>
<td>−0.6±0.03</td>
<td>−0.4±0.03</td>
</tr>
<tr>
<td>Control group</td>
<td>26.0±0.7</td>
<td>42.6±1.5</td>
<td>16.8±0.56</td>
<td>−1.06±0.06</td>
<td>−1.7±0.06</td>
</tr>
</tbody>
</table>

1.2. C-D; Table 1). After 17±2 months of mean follow up, LA volume (≥64mL/m²) was the only independent predictor of recurrence (p=0.03).

Conclusion: In our previous study, we have demonstrated that the 2D- and 3D-speckle tracking echocardiography (2D-STE) parameters in prediction of the AF recurrence after SA during VHD surgery when compared with normal patterns. LA volume was larger in patients with AF recurrence; however, no differences were found regarding myocardiak deformation parameters.

P2555 | BEDSIDE

The application of a novel three-dimensional transesophageal echocardiographic technique for the assessment of left atrial appendage anatomy in transcatheater LAA closure


Purpose: We sought to explore the clinical value of two dimensional (2D) and three dimensional transesophageal echocardiography (3D-TEE) for the left atrial appendage closure (LAA) procedure by a precise evaluation and measurement of the anatomic morphology of the LAA.

Material and methods: Transesophageal echocardiographic (TEE) and 3D echocardiographic examinations were performed to assess the LA and LAA anatomy and morphology. In particular, the maximal and minimal LAA ostial dimensions and the plane distribution patterns were analyzed. Twenty of fifty-one patients had CHADS2 risk scores of 1 or more and were eligible for LAA closure. The correlation between the closure device size and the LA landing zone dimension measured by 2D-TEE, 3D-TEE, and fluoroscopy were analyzed to determine each individual modality efficiency for the assessment of the LAA ostial dimension for the occlusion.

Results: Among fifty-one AF patients, the LAA ostial dimension measured by 2D-TEE was slightly different at 0°, 45°, 90° and 135°, and the maximal dimensions were found at 135°. A 3D-TEE slice revealed that the maximal LAA ostial dimension was distributed within the 30°-160° plane, and 88% presented within the 90°-120° LAA closure.

Conclusion: Compared with routine 2D-TEE, RT3D-TEE allows for more precise assessments of left atrial appendage anatomy and device delivery in LAA closure procedures.

P2556 | BEDSIDE

Which is better for assessing recurrence risk of atrial fibrillation after catheter ablation, 2D- or 3D-speckle tracking echocardiography?

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Background: Several studies have shown utility of left atrial (LA) function determined by three-dimensional speckle tracking echocardiography (3D-STE) for identifying the patients with paroxysmal atrial fibrillation (AF). However, whether 3D-STE is applicable for prediction of the recurrence of AF after catheter ablation (CA) remains unknown.

Objective: We examined whether any of 3D-STE parameters is better than 2D-STE parameters in prediction of the AF recurrence.

Methods: Twenty-two patients with paroxysmal AF (age 60±9 years, 73% male) underwent the 2D- and 3D-STE just before the first CA in our institute. LA peak longitudinal, circumferential and area strains in systole (3D-Ls, CSs, ASs) and those in late diastole (3D-Lsa, CSa, ASA) were determined by 2D-STE, and standard deviations of times to peaks of regional LA strains (SD-Ls, CSs, ASs, Lsa, Sa, Asa) were calculated as indices of LA dysfunction. In 2D-STE, LA peak longitudinal strains in systole (2D-Ls) and late diastole (2D-Lsa) were determined by 2D-STE. Cox proportional hazards regression analysis was used to determine whether recurrence of AF is predicted by any of demographic and echocardiographic parameters, serum biomarkers and medications.

Results: During follow-up of 43±262 days, six patients (27%) had AF recurrence. In univariate analysis, age (hazard ratio [HR]: 1.31, p=0.002), 3D-Ls (HR: 0.74, p=0.021), CSs (HR: 0.88, p=0.014), CSa (HR: 0.76, p=0.037), ASs (HR: 0.93, p=0.0064), ASa (HR: 0.89, p=0.022) and 2D-ASs (HR: 1.12, p=0.022) were the predictors of AF recurrence, though association of the recurrence with 2D-Ls (p=0.49), 2D-Lsa (p=0.60), or 3D-LA volume (p=0.73) was not significant on the ROC curve. In multivariate Cox proportional hazards regression analysis, age and 3D-ASs were independent predictors of AF recurrence (HR: 1.37, p=0.005 and HR: 0.93, p=0.016, respectively). ROC analysis indicated that optimal cutoff value of age was 64 years, of which sensitivity and specificity were 83% and 75% (AUC: 0.87), respectively, and optimal cutoff value of 3D-ASs was 22.6%, of which sensitivity and specificity were 83% and 81% (AUC: 0.85), respectively. Kaplan-Meier curves showed that patients with 3D-ASs >22.6% had higher recurrence-free rate than the others at 1 years after the CA procedure (89% vs. 77%, p=0.04).

Conclusions: LA strain determined by 3D-STE may be a novel and better predictor of AF recurrence after CA than those determined by 2D-STE or the other known predictors.

P2557 | BEDSIDE

Left atrial global longitudinal strain, a new and early cardiotoxicity marker?

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Background: 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 shown to be a marker of cardiac toxicity, however, there are no studies analyzing LA morphologic parameters.

Purpose: Our aim was to evaluate the effect of a first dose of potential cardiotoxic drugs in LVGLS and left atrial global longitudinal strain (LAGLS) from breast cancer patients in order to test if left atrial (LA) muscle is more sensitive to the effect of these drugs than left ventricular muscle.

Methods: A pilot, non-interventional, observational, prospective study in newly diagnosed breast cancer patients to receive potential antitumoral cardiotoxic agents (doxorubicin or trastuzumab) was designed. A complete echocardiogram, includ-

Echocardiographic parameters

<table>
<thead>
<tr>
<th>Before chemotherapy</th>
<th>After chemotherapy</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDD</td>
<td>45.61</td>
<td>45.2941</td>
</tr>
<tr>
<td>LVESD</td>
<td>27.61</td>
<td>28.75</td>
</tr>
<tr>
<td>LVEF</td>
<td>60.86</td>
<td>59.80</td>
</tr>
<tr>
<td>LAIV</td>
<td>18.42</td>
<td>22.27</td>
</tr>
<tr>
<td>LV GLS</td>
<td>6.85</td>
<td>6.80</td>
</tr>
<tr>
<td>LVGLS</td>
<td>−17.41</td>
<td>−17.19</td>
</tr>
<tr>
<td>LAGLS</td>
<td>35.16</td>
<td>27.20</td>
</tr>
</tbody>
</table>

Echocardiographic parameters

VOLVED, left ventricular end diastolic diameter; LVESD, left ventricular end systolic diameter; LVEF, left ventricular ejection fraction; LAGLS, left atrial global longitudinal strain; LVLGS, left atrial (LA) index volume.

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 manual border outlining 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 with semiautomatic software (4D AutoLVQ). These volumes were compared with atrial volumes determined by the QLAB 9.1 software using 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.

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LA volumes indexed by body surface area were similar in men and women and were calculated. (Vmin) and pre-A (VpreA) volumes using 4D LA Analysis (TomTec Imaging Systems, D). Maximal (MaxVol), minimal (MinVol) and volume at P wave on the ECG (preAVol) were measured and total, passive, and active emptying fractions were calculated.

Results: 3DE LA volumes were significantly smaller than those calculated with 2DE (Table). The average differences ranged from 5 ml (MinVol) to 13 ml (MaxVol) and had clinically significant implications for the definition of normality. The upper limit of normality for 3DE LA volumes was in a range of values that would define severe dilatation by 2DE. Differences in LA emptying fractions calculated by 2DE vs 3DE were also significant (Table).

LA reference values by 3DE vs 2DE

<table>
<thead>
<tr>
<th></th>
<th>3DE</th>
<th>2DE</th>
<th>p value</th>
<th>3DE RL</th>
<th>2DE RL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max Volume</td>
<td>57±15 ml</td>
<td>44±11 ml</td>
<td>&lt;0.0001</td>
<td>46 ml/m²</td>
<td>34 ml/m²</td>
</tr>
<tr>
<td>Min Volume</td>
<td>19±7 ml</td>
<td>14±6 ml</td>
<td>&lt;0.0001</td>
<td>17 ml/m²</td>
<td>14 ml/m²</td>
</tr>
<tr>
<td>PreA Volume</td>
<td>32±11 ml</td>
<td>26±9 ml</td>
<td>&lt;0.0001</td>
<td>28 ml/m²</td>
<td>25 ml/m²</td>
</tr>
<tr>
<td>Total EF</td>
<td>67±8%</td>
<td>69±8%</td>
<td>&lt;0.05</td>
<td>55%</td>
<td>51%</td>
</tr>
<tr>
<td>Passive EF</td>
<td>44±9%</td>
<td>47±10%</td>
<td>&lt;0.001</td>
<td>26%</td>
<td>21%</td>
</tr>
<tr>
<td>Active EF</td>
<td>39±10%</td>
<td>47±10%</td>
<td>&lt;0.05</td>
<td>19%</td>
<td>27%</td>
</tr>
</tbody>
</table>

EF: ejection fraction; RL, reference limit (upper or lower).

Conclusions: Implementation of 3DE to measure LA volumes and function in clinical practice requires specific reference values in order to discriminate between normal and dilated LA. This is clinically relevant, as interpreting LA size, since the application of 2DE upper limit of normality to LA 3DE volumes would lead to misclassification of many normal LAs as severely dilated.

NEW TECHNIQUES IN CORONARY, CAROTID AND HYPERTENSIVE DISEASE

P2561 | BEDSIDE
Clinical value of right atrial strain in predicting early hemodynamic deterioration in patients with pulmonary hypertension
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Objectives: Right atrium (RA) dilatation is an important prognostic factor for patients with pulmonary hypertension (PH). Strain by 2D (two-dimensional) speckle-tracking echocardiography (STE) is a new developed technique helpful to identify RA remodelling. The aim of this study is to explore the value of RA 2D TE as early predictor of hemodynamic deterioration in patients with PH.

Methods: Patients with suspected PH, referred to our center for first line cardiac catheterization (RHC) underwent conventional 2D echocardiography in 48h of RHC. Specially, RA function was assessed with 2D STE from standard 4-chamber apical view. Echocardiographic parameters were compared to cardiac index (CI), pulmonary vascular resistances (PVR) and mean pulmonary artery pressure (mPAP) RHC-derived. Patients underwent clinical and functional evaluation. Healthy matched subjects were included as controls. Results: We included 43 patients (mean age 69±12 years) and 16 controls. RA 2D STE was significantly worse than controls (p<0.001). Regression analysis showed that RA 2D STE but not RA volume strongly correlated with RHC measurements of C.I (p=0.001) and PVR (p=0.007). RA 2D STE inversely correlated with functional class (p=0.027), BNP (p=0.002) and directly correlated with 6MWT (p=0.011). Multivariate analysis including RA volume, TAPSE, LA strain and RA showed that RA 2DSTE had the highest overall performance for the prediction of
P2562 | BEDSIDE
Carotid plaque neovascularization is independently associated with atheromatous plaques in South Asians vs Europeans: A possible mechanism underlying the greater cardiovascular disease burden in South Asians

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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 prognosticator for major CVD events. However, our group has recently shown that there were 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 cardiovascular event rate in South Asians. We aimed to investigate the extent of neovessels. Presence of IPN was graded semiquantitatively 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±8.9 yrs and 140 (80%) were male. There were 96 Northen 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: Our first study to demonstrate 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
Echoluent carotid plaque is useful for assessment of residual risk in patients with history of myocardial infarction on statin therapy


Background: Ultrasound assessment of either intima-media thickness (IMT) or plaque echolucency of the carotid artery provides prognostic information on coronary events. Although lipid-lowering treatment using statin therapy reduced coronary 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 echolucency of the carotid artery may provide additional residual risk information. We performed a post-hoc analysis of a large echocardiographic database and aimed to assess the incremental risk stratification provided by plaque echolucency score in patients with a history of myocardial infarction (MI).

Methods: Ultrasound assessment of either carotid IMT or plaque echolucency was performed in 192 patients with history of MI who had undergone carotid ultrasound examination during a 12 month period before MI. Patients were classified into two groups (stage I and stages II). Stage I: The plaque echolucency score is ≥3 and/or the IMT of the maximum thickness plaque is ≥0.9 mm. Stage II: The plaque echolucency score is ≥3 and/or the IMT of the maximum thickness plaque is <0.9 mm. Our primary endpoint was the occurrence of cardiovascular events (CVD) defined as death from coronary artery disease, non-fatal myocardial infarction, or unstable angina requiring unplanned revascularization as determined by JNC 7. All subjects underwent echocardiography with use of GE Medical Vivid 7. Results: The study included 90 patients (54 males, 60%) with a mean age of 48.57±6.82. TAPS measurement did not show any significant differences between the 3 groups (control, stage I HTN and stage II HTN) patients. Patients data demonstrated that a difference in plaque vulnerability may account for the observed increased CVD events. Intra-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. Results: A total of 175 patients underwent B-mode and CEUS carotid ultrasonography. Mean age was 64.7±8.9 yrs and 140 (80%) were male. There were 96 Northen 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: Our first study to demonstrate 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

P2564 | SPOTLIGHT
Right ventricular function: the neglected issue in systemic hypertension

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Background: The right ventricle (RV) is neglected in clinical practice. The aim of this study is to assess 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' velocities of tricuspid annulus (E/A'). Isovolumetric relaxation time (ms) was determined by pulse Doppler echocardiography. Tissue Doppler echocardiography is a useful tool in detecting right ventricular systolic dysfunction even with normal TAPSE measurements.

Results: The study included 90 patients (54 males, 60%) with a mean age of 48.57±6.82. TAPS measurement did not show any significant differences between the 3 groups (control, stage I HTN and stage II HTN) patients. Doppler data obtained at the tricuspid valve in the 3 studied groups showed statistically significant results regarding E (p<0.001), 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 and stage II HTN we found statistically significant differences for S (14.97±0.81 vs. 12.37±0.72 vs. 10.63±1.07 cm/sec respectively; p<0.001) while E measurements were (16.93±1.17 vs. 14.07±0.64 vs. 12.17±0.75; p<0.001) and A' measurements were (16.73±1.23 vs. 17.47±1.07 vs. 17.51±1.71 cm/sec respectively; p=0.018). Similarly significant values were found in the A' to E/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 treatment with measuring coronary flow velocity reserve at the peak of exercise

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Assessment of coronary flow is used only during pharmacological tests. Nevertheless, supine bicycle tests have allowed the application of coronary 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 at rest (CFAV) and at the peak of exercise (CEAV) during exercise tests (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±7.02 vs. 70.26±7.01 cm/s, p<0.01), 0.1722±0.023 vs. 0.174±0.027, p<0.002). CFVR (1.3±0.4 vs. 2.0±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 (59.27±7.02 vs. 70.26±7.01 cm/s, p<0.01). CFVR (1.3±0.4 vs. 2.0±0.7, p<0.00001) to other patients. Among the group with CFVR<2.0, 0% had myocardial infarction, death or coronary artery bypass grafting, and 17% 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
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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 differentiation of left ventricular (LV) functional improvement 12 months after myocardial infarction (MI) treated with primary percutaneous intervention (pPCI).

Material and methods: 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 passive postystolic 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 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, left ventricular ejection fraction) and 2D speckle tracking parameters (global SLS, STS, PLS, PTS, SLR, 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 0.0002–0.995) 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 values of CKMB mass are predictive for LV functional improvement, while global PLS 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 percutaneous intervention (pPCI). There are no studies evaluating the value of coronary flow reserve (CFR) in medically treated 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 stenosis (visual assessment 50–70%) on non-infarct related artery (LAD or RCA). All patients were followed for 2–15 months. CFR was defined as the ratio of maximal velocity of diastolic coronary blood flow during maximal hyperemia and baseline velocity measured during steady state at baseline.

Results: LV dilation was associated with CFR ≤ 2 (p=0.0001) and CFR > 2 (p=0.006). LV dilation was more frequently seen in patients with CFR ≤ 2 (75% CI: 62.7–87.3%) compared to patients with CFR > 2 (95% CI: 12.7–77.6%; p=0.001, respectively).

Conclusions: Measurement of resting coronary flow reserve applied early post STEMI as well as maximal values of CKMB mass are predictive for LV functional improvement, while global PLS 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
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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 ischemic 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 area strain (GAS), and global radial strain (GSR) were quantified by 3D STE. Receiver operating characteristic curves (ROC) were computed to determine optimal strain cutoff values to predict severe multi-vessel coronary stenosis. Observers 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 stenosis group (stenosis of ≥2 and more than 2 coronary arteries ≥50%, at least one branch coronary stenosis ≥75%, n=38). 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 group of severe coronary stenosis group were more dramatically decreased (GLS: 2.9±2.19 vs. 13.35±2.89, GCS: 12.32±5.2 vs. 17.16±5.01, GAS: 18.58±9.3 vs. 26.11±5.25, GRS: 29.06±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 stenosis group compared to the severe single-vessel coronary stenosis group, whereas only GLS and GAS 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 cutoff value of magnitude < -11% with 84.2% sensitivity and 3D GAS cutoff value of magnitude < -19% with 91.9% specificity predicted severe multi-vessel coronary stenosis (severe multi-vessel coronary 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
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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 DCE. Furthermore, we examined the ability of 3DSTE to differentiate between patients with ischemic and patients with non-ischemic LV dysfunction.

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.

Table 1: 3DSTE (%) - mean±SD of ischemic and non-ischemic patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ischemic (%)</th>
<th>Non-ischemic (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLS</td>
<td>-15.4±8.5</td>
<td>-16.7±9.2</td>
<td>0.25</td>
</tr>
<tr>
<td>GCS</td>
<td>-15.1±6.7</td>
<td>-15.0±7.1</td>
<td>0.91</td>
</tr>
<tr>
<td>GAS</td>
<td>-13.4±5.8</td>
<td>-11.9±7.0</td>
<td>0.03</td>
</tr>
<tr>
<td>3DS (%)</td>
<td>26.1±15</td>
<td>25.7±16</td>
<td>0.91</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.

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P2570 | BEDSIDE
3D myocardial strain measurement after reperfusion therapy is useful to predict future clinical events in patients with ST-segment elevation myocardial infarction

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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 outcome.

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 electrocardiography 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 the hospital, and 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 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 echocardiographic 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

VASCULAR BIOLOGY

P2571 | BENCH
Translational potential of cardiac regeneration: from fish & mice to men?

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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 2D gel electrophoresis, we observed a mirror 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 over-expression of DNA synthesis-related proteins in the cardiac proteome of the adult zebrafish heart similar to neonatal and 4–5 day post-fertilization (DPF) zebrafish, 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, myogenin-2 (also known as cardiac myogenic regulatory factor-like myofibers) are highly expressed in the zebrafish heart, 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 analysis of zebrafish and mammalian hearts challenges the assertions on the translational potential of cardiac regeneration in the zebrafish model. The immature myoflament composition of the fish heart may explain why adult mouse and human cardiomyocytes lack this endogenous repair mechanism.

Acknowledgement/Funding: No funding

P2572 | BEDSIDE
ADMA and arginine derivatives in relation to non-invasive vascular function measurement in the general population

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Background: Nitric oxide produced from L-arginine is central to vascular homeostasis. However, little is known on the relation of arginine derivatives including asymmetric dimethylarginine (ADMA) to non-invasive vascular function measurements in the general population.

Methods: We included 6,500 participants from the general population (mean age 55±11 years, age range 35–74 years, 49% women) in the Gutenberg Health Study. We measured circulating L-arginine and the arginine derivatives ADMA, N-monomethyl-L-arginine (NNMA) and symmetric dimethylarginine (SDMA) in relation to brachial artery diameter and flow-mediated dilatation (FMD). Arginine derivatives were quantified by liquid chromatographic-tandem mass spectrometry. FMD was assessed by the Endo-FTX2000 finger tip device. Brachial artery diameter was recorded by two-dimensional high-resolution ultrasound images (Philips HDI1XE CV, Netherlands).

Results: Statistically significant bivariate correlations were observed for all biomarkers except for L-arginine and FMD respectively for SDMA and PAT ratio. Linear regression analysis showed significant associations for all measured arginine derivatives with baseline pulse amplitude. In addition, ADMA was negatively related to PAT ratio (beta −0.078, p<0.0001) and FMD (beta −0.075, p<0.0001) and positively with brachial artery diameter (beta 0.094, p<0.0001). After adjustment for age, sex and cardiovascular risk factors, ADMA was no longer associated with any of the vascular function measures except of PAT ratio (p<0.01) and baseline pulse amplitude (p<0.05). Also, L-arginine/ADMA was significantly associated with baseline pulse amplitude (beta −0.093, 95% confidence interval (CI) −0.119–−0.067 age/sex adjusted and beta −0.065, CI −0.090–−0.040 risk factor adjusted; respectively) and PAT ratio (beta 0.098, CI 0.070/0.125 age/sex adjusted and beta 0.071, CI 0.044/0.098 risk factor adjusted; respectively). Associations were comparable with additional stratification for creatinine, gender and prevalent cardiovascular disease.

Conclusions: Adjusted for age, sex and cardiovascular risk factors, L-arginine/ADMA but not ADMA alone was consistently related to baseline pulse amplitude and PAT ratio in the general population. These findings support a complex interplay of nitric oxide generation and inhibition. Whether an optimization of the L-arginine/ADMA ratio improves vascular function needs to be shown.

P2573 | BENCH
Dysfunction of skeletal muscle pericytes from type 2 diabetic patients with chronic limb ischemia is associated with altered oxidative status

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Background: Efficient tissue healing requires the parallel activation of angiogenesis and myogenesis through restorative cooperation between muscular pericytes (MPs), endothelial cells, and myocytes.

Purpose: Assess whether type 2 diabetes mellitus (T2D) negatively impacts on functional properties of human MPs.

Methods: Muscle biopsies from healthy controls, diabetes, T2D and T2D + chronic limb ischemia (CLI-MPs) were isolated. ADMA and arginine derivatives in relation to non-invasive vascular function measurements in the general population.

Acknowledgement/Funding: No funding

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lar result was obtained treating HUVECs with T2D+CLI-MPs-conditioned medium (11.8±1.04 vs 16.1±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 0.97±0.04), and p68SGC (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 musculoskeletal 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 (CRAVE) study

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**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 51.9±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-femoral pulse wave velocity (cfPWV), 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:** 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, 0.14%/year for 1 RF and ~0.39%/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

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**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 aerosol solution of FA (2.4 mg/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 (1.80–2.60) pg/ml; *p=0.63] and in RANTES levels [12.25 (8.17–17.70) 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 (20.47–47.52) pg/ml; *p=0.58] in TNFα levels [2.10 (1.70–5.89) pg/ml vs. 0.32 (0.06–1.14) pg/ml; *p=0.21] and in RANTES levels [13.09 (10.43–20.42) 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 stimuli of a diet rich in cholesterol. These findings further elucidate the effects of folic acid administration in subjects with increased cardiovascular risk.

P2576 | BENCH

Metformin and vildagliptin: from blood glucose lowering to nephroprotection

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**Background:** Prevention of diabetic nephropathy (DN) progression could lead to a decrease in cardiovascular mortality and morbidity. 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 nicotineamide (NA, 230 mg/kg) and streptozotocin (STZ,65 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 group was considerably higher compared to ND (4.6±1.2%). 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 μmol/min/kg; 25±4.6 mg/24h, respectively) compared to P group (65±3.6; 3.23±0.21; 38±8.25, P=0.05 each), urinary levels of KIM-1 (589±93.3 ng/ml) and NGAL (1544.9±100.6 pg/ml) in metformin-treated animals were significantly lower than those in diabetic rats without treatment (KIM-1: 1386.9±651.1; 1918.6±118.1, respectively, P=0.05 each). Moreover, renoprotection in the study groups was confirmed by histological examination and electron 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.

P2577 | BENCH

Evidence of protozoan biofilm communities in atheromatous debris: a metagenomic analysis

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**Introduction:** Evidence that vascular inflammation is an important mechanism involved in all stages of atherogenesis continues to accumulate. We hypothesize that common complex microbial involvement may be present in atheromatous debris removed from treated lesions. We evaluated this debris with metagenomic analysis.

**Purpose and methods:** After informed consent, fifteen cases of vascular aspirates and filter from patients undergoing carotid stenting (3 MoMa, 10 embolic filters). One case was in a saphenous vein graft intervention (aspirate and filter) and one case was after SFA orbital atherectomy (aspirate and filter). Fluorescence microscopy, bacterial and
PMP induced thrombin formation is associated with coronary artery CAC.

In patients with severe CAC score (100% vs. 50%). AVC (4417±3994 and 437±55 n=27). Likewise, significant coronary artery disease was more prevalent as compared to patients with less severe CAC (Agatston Score of 1.5% isoflurane). A small chest wall incision, expanded with retractors, facilitated the adhesive (VetBond) positioning of a specially designed tissue stator.

**Conclusion:** The present study showed that procoagulant activity of circulating MPs was assessed using a two-step amidolytic assay for thrombin formation. Patients with CAC Score above the median.

**Methods:**

**Hypothesis:** Procoagulant activity of circulating MPs mediates CAC via enhanced thrombin formation.

**Results:**

**Level of PMPs (R=0.461, p=0.001) and CD62E+ EMPS (R=0.300, p=0.046) correlated positively with MP-induced thrombin formation. Level of PMPs (R=0.6984, p<0.001) and CD62E+ EMPS (R=0.438, 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 disease independent of valvular calcification creating a potential vicious cycle.

**P2578 | BENCH**

**Microparticle-induced thrombin formation predicts severity of coronary artery calcification in patients with severe aortic valve stenosis**

**Purpose:** Cell-based strategies to regenerate injured myocardial tissue have emerged over the past decade, but the optimum cell type is still under scrutiny. In this context, human adult epicardial fat surrounding the heart has been characterized as a reservoir of mesenchymal-like progenitor cells (cardiac ADTPCs) with potential benefits on cardiac function. However, additional data on the possibility that these cells could trigger a deleterious immune response following implantation are needed. Thus, in the presented study, we took advantage of the well-established low immunogenicity of umbilical cord blood-derived mesenchymal stem cells (UCBMSCs) to comparatively assess the immunomodulatory properties of cardiac ADTPCs.

**Methods:** T cell alloproliferation was determined in an in vitro allostimulatory assay using allogeneic mature monocyte-derived dendritic cells (MDDCs) cocultured with either cardiac ADTPCs or UCBMSCs. Cytokines present in supernatants collected from alloproliferation assays were measured using the CBA human Th1/Th2 Cytokine kit II.

**Results:** Similar to UCBMSCs, increasing amounts of seeded cardiac ADTPCs suppressed the alloproliferation of T cells in a dose-dependent manner. Secretion of pro-inflammatory cytokines (IL6, TNFα) was also specifically modulated by the different numbers of cardiac ADTPCs co-cultured (Figure 1).

**Conclusions:** In summary, we show that cardiac ADTPCs abrogate T cell alloproliferation upon stimulation with allogeneic mature MDDCs. This suggests that these cells could further regulate a possible harmful immune response in vivo, being valid for future use in cell therapy to regenerate injured myocardium.

**P2581 | BENCH**

**Glucagon-like peptide 1 (GLP1) improves disseminated intravasal coagulation (DIC) and vascular function in LPS-induced endotoxemia**

**Methods:** While stem cell (SC)-based therapy following myocardial infarction has emerged, clinical success is compromised by poor SC homing to the heart following infusion. One solution is to identify strategies to increase SC capture by coronary microvessels. We have routinely used intravital microscopy (IVM) to monitor SC trafficking in murine organs in vivo. To do so in the heart would facilitate research aimed at improving SC delivery to this organ. However, IVM of the mouse beating heart remains technically challenging due to difficulties accessing the organ and an impractical degree of motion. This study presents a means for intravascularly monitoring the beating heart using a 3D-printed stabilizing device.

**Results:** Microparticles (kryptonite/yellow); in vivo were artificially ventilated using a small rodent ventilator which delivered oxygen containing gaseous anaesthetic (1.5% isoflurane). A small chest wall incision, expanded with retractors, facilitated the adhesive (VetBond) positioning of a specially designed tissue stator.

**Conclusions:** We present a working model to intravascularly image the mouse beating heart in real-time in vivo. This method may be useful in monitoring SC dynamics and microvascular disturbances in the damaged heart at the single cell level.

**Acknowledgement/Funding:** British Heart Foundation

**Figure 1. Cytokine production levels**
is a growing body of evidence for an immunemodulatory effect by DPP4i therapy and GLP1a stimulation with GLP1a administration may improve sepsis associated vascular complications and disseminated intravascular coagulation.

Methods: C57BL/6J, DPP4−/− and GLP1 receptor−/− mice were used. DPP4i (linagliptin) and GLP1a (ligulitide) were applied s.c. Sepsis was induced by lipopolysaccharide (LPS) injection. Fluorescence-activated imaging technique was used to detect microvascular occlusion in lungs. Vascular function was tested by isometric tension recording. Aorta and heart tissue was used for Western blotting and immunohistochemistry. Platelet function (thrombin burst (CAT), aggregation) 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 significantly increased in P1 of CAD, but not in ACS patients. The oxidative burst measured by GLP1a and DPP4i stimulation in platelet-rich plasma (PRP), cell count and quantification of oxidative stress were tested.

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 inhibition of GLP1 receptor−/− animals as compared to untreated wild-type mice, and this endothelial dysfunction was evident. Although there were more monocytes, P1 in P2 and P3 mice not modified at all by GLP1a supplementation. DPP4i, GLP1a therapy and DPP4i-knockout reduced aortic mRNAs levels of P-selectin and IL-6 in endotoxemia, whereas isolated platelets of GLP1 receptor−/− animals showed increased activation in monocytes in P1 of CAD, but not in ACS patients.

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

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Background: Inflammation and inflammatory cells plays a vital role in tissue repair process and in defence against infectious agents, yet an unresolved immuno- inflammatory reaction may be harmful to the human organism. In recent years it became important to study inflammasomes as role players in different diseases such as atherosclerosis. Although there have been more IL-20 inflammatory cell populations 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 patients compared to healthy subjects. Additionally, the ACS patients showed a significant higher amount of CD14+ cells in comparison with CAD patients. The isolated monocytes were lysed in Giazol and total RNA was isolated and reverse transcribed to mRNA (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-) 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.

Caspase1 and inflammasome expression has been shown to be downregulated in monocyte subtypes of patients with CAD and ACS. Interestingly, a significant expression of mir-223 mirrored the NLRP3 increase only in ACS but not in CAD patients. mir-181a demonstrates a similar expression pattern to mir-223 in ACS and CAD 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.

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P2583 | BENCH Premature vascular aging in aldosterone-associated hypertension: role of Nox1


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Premature vascular aging in aldosterone-associated hypertension: role of Nox1

Background: There has been recently shown that aneurysmal ascending aorta (Asca) exhibit increased stiffness, but their effect on the left ventricle has not been studied yet. Speckle tracking echocardiography (STE) is an established non-invasive method which detects subtle changes in myocardial function, before they become overt and influence traditional indices, such as ejection fraction (EF).

Our aim was to investigate left ventricular (LV) mechanics by two dimensional echocardiography (2DE) longitudinal strain in subjects with dilated Asca (<21mm²/m²).

We studied 50 patients (pts) (male/female ratio 1.25, mean age 60.9±11.2y) with dilated Asca and 50 matched by sex and age pts (male/female ratio 1.25, mean age 60.7±7.1y) with Asca within the normal limits. Limitation includes criteria for pts in the study population was the diagnosis of isolated, essential arterial hypertension with sufficient treatment for blood pressure (BP) control. None of the included pts suffered from end-organ damage. Exclusion criteria were diabetes mellitus, atrial fibrillation, history of angina pectoris, coronary artery disease, valvular diseases, Marfan syndrome or other connective tissue disorder. Additionally, the presence of bicuspid aortic valve. In addition to conventional echocardiographic measurements, global longitudinal strain of the LV (LVS) was estimated off-line from the three apical views by 2D-STE using EchoPac 110. 4D strain assessment (systolic and diastolic strain of the left ventricle, LVES, LVED, LVEF, LVS) between the two groups with pth density differences between the two groups (SBP 132±2 vs 130±7mmHg, p=0.08, DBP 76±5 vs 76±6mmHg, p=0.07 and HR 71±18bpm vs 66±12bpm, p=0.31). Additionally the two groups did not significantly differ neither in the LV and diastolic diameters (47.9±15 vs 48.1±16.5mm, p=0.79) nor in the LVEF (60.3±8±7 vs 61.4±4.3, p=0.27). On the contrary, there were noteworthy differences in indexed diameters of the Asca (22.0±2.04mm²/m² vs 17.9±2.14 mm²/m², p<0.0001) and LVS between the two groups. Pts with Asca had significantly increased LVS (−2.40±1.72% vs −18.2±7.14%, p<0.0001). A correlation analysis showed that LVS is independently associated with Asca (r=−0.495, p=0.009) in the whole study population.

VASOCA REMODELLING

P2584 | BEDSIDE Effect of dilated ascending aorta on LV deformation mechanics. A 2D speckle tracking echocardiography study

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Effect of dilated ascending aorta on LV deformation mechanics. A 2D speckle tracking echocardiography study

We studied 50 patients (pts) (male/female ratio 1.25, mean age 60.9±11.2y) with dilated Asca and 50 matched by sex and age pts (male/female ratio 1.25, mean age 60.7±7.1y) with Asca within the normal limits. Limitation includes criteria for pts in the study population was the diagnosis of isolated, essential arterial hypertension with sufficient treatment for blood pressure (BP) control. None of the included pts suffered from end-organ damage. Exclusion criteria were diabetes mellitus, atrial fibrillation, history of angina pectoris, coronary artery disease, valvular diseases, Marfan syndrome or other connective tissue disorder. Additionally, the presence of bicuspid aortic valve. In addition to conventional echocardiographic measurements, global longitudinal strain of the LV (LVS) was estimated off-line from the three apical views by 2D-STE using EchoPac 110. 4D strain assessment (systolic and diastolic strain of the left ventricle, LVES, LVED, LVEF, LVS) between the two groups with pth density differences between the two groups (SBP 132±2 vs 130±7mmHg, p=0.08, DBP 76±5 vs 76±6mmHg, p=0.07 and HR 71±18bpm vs 66±12bpm, p=0.31). Additionally the two groups did not significantly differ neither in the LV and diastolic diameters (47.9±15 vs 48.1±16.5mm, p=0.79) nor in the LVEF (60.3±8±7 vs 61.4±4.3, p=0.27). On the contrary, there were noteworthy differences in indexed diameters of the Asca (22.0±2.04mm²/m² vs 17.9±2.14 mm²/m², p<0.0001) and LVS between the two groups. Pts with Asca had significantly increased LVS (−2.40±1.72% vs −18.2±7.14%, p<0.0001). A correlation analysis showed that LVS is independently associated with Asca (r=−0.495, p=0.009) in the whole study population.
LVGLS is supranormal in pts with diluted 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 pathophysiological interaction of the left ventricle and the aorta.

P2585 | BEDSIDE
CMR assessment of arterial stiffness in patients with large vessel vasculitis
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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±SD, 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, 7 with polyarteritis nodosa and 7 with other systemic disease associated with LVV. Clinical outcome was defined as a composite end point of major cardiovascular events including all-cause mortality, myocardial infarction, stroke or transient ischemic attack, aortic or arterial valve surgery, and heart failure hospitalization. Mean aortic PWV was 10.0±3.4 m/s; PWV was highest in patients with polymyalgia rheumatica 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).

Conclusions: 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
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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, supporting NO bioactivity. 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 sildenafil (1.4 mg/kg/day ip, n=12) or saline (n=12). Then rats were anaesthetized with saturated NaCl (100mM), and the right 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).

Results: Mean aortic PWV was 10.0±3.4 m/s; PWV was highest in patients with polymyalgia rheumatica 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).

Conclusions: CMR-derived aortic PWV is a powerful independent predictor of major cardiovascular events in patients with LVV.

P2587 | BENCH
Vascular aldosterone synthase contributes to phosphate-induced osteogenic transformation of vascular smooth muscle cells
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Background: Aging, chronic kidney disease and a variety of other conditions cause vascular calcification. The calcification is promoted by osteogenic transformation of vascular smooth muscle cells (VSMC), an active process triggered by hyperphosphatemia. Elevated phosphate levels are predictive for heart failure, cardiac remodeling and risk of death. Vascular calcification is a determinant of mortality in chronic kidney disease, a state of accelerated vascular aging. Mineralocorticoid receptor (MR) activation accelerates vascular aging and osteoinductive transformation of VSMCs.

Purpose: To investigate a possible role of local aldosterone synthase expression during vascular osteoinductive transformation of VSMCs.

Methods: Experiments were performed in primary human aortic smooth muscle cells (HaSMCs) and in klotho hypomorphic mice (kikii) and corresponding wild-type mice.

Results: Even in the absence of exogenous aldosterone, spironolactone, eplerenone and MR silencing ameliorated phosphate-induced osteogenic transformation of HaSMCs. Increased expression of CYP11B2 was observed in aortic tissue of hyperphosphemic kikii mice. In right coronary artery tissue of patients with reduced and maintained renal function, CYP11B2 mRNA expression was correlated with CBFAT mRNA levels. In HaSMCs, silencing of CYP11B2 ameliorated phosphate-induced osteogenic reprogramming and calcification. Phospho-eNADPH oxidase and nuclear export of the transcriptional repressor APEX1. Silencing of APEX1 upregulated CYP11B2 expression and mimicked the effects of phosphate in HaSMCs. Spironolactone treatment abrogated the effects of phosphate on osteoinductive transformation without modifying increased CYP11B2 expression in HaSMCs. Conversely, APEX1 overexpression reduced phosphate-induced HaSMCs transformation. Early stage aortic osteoinductive reprogramming of kikii mice following discontinuation of dietary rescue was ameliorated by spironolactone treatment, but not by adrenalectomy. In the adrenalectomy kikii mice, spironolactone was still able to mitigate the aortic osteogenic transformation.

Conclusions: VSMCs are able to express aldosterone synthase promoted by phosphate-induced dysregulation of APEX1. Aldosterone may promote osteoinductive transformation of VSMCs and therefore vascular calcification independent of circulating aldosterone levels, offering new opportunities for vascular-protective interventions in chronic kidney disease.

P2588 | BENCH
MicroRNA-216a induces a premature senescence-like phenotype and regulates angiogenic activity in human vascular endothelial cells
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Background: Among the age-associated functional and structural changes, of particular note is cellular senescence of endothelial cells, which plays a key role in age-associated dysfunction and atherogenesis. But the molecular basis of which is not fully defined. We have shown that a particular microRNA, mir-216a, is up-regulated in senescent endothelial cells, here, the present study aimed to determine the role of mir-216a in regulating premature senescence and angiogenic activity of endothelial cells.

Methods and results: Human umbilical vein endothelial cells (HUVECs) were cultured and population-doubling levels (PDLs) were calculated over passages. Briefly, PDLs was computed as Log2 (Cs/Ch), where Cs was the number of viable cells at harvest and Ch was the number of cells seeded. PDL44 were respectively identified as young and senescent HUVECs, 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 15 days. We also found that telomerase activity was dependent on APEX1 induced by mir-216a levels, which confirms a crucial role for miR-216a 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 angiogenic 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). There was no significant impairment of tube formation in the Matrigel assay.

Conclusions: Our data indicated that miR-216a can promote the premature endothelial senescence and may serve as a target in regulating endothelial dysfunction associated with atherosclerosis.
P2589 | BENCH
Deregulation of thioredoxin system contributes to monocyte dysfunction in diabetes mellitus: Implications for impaired arteriogenesis in type2 diabetic patients
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Purpose: Arteriogenesis is a process encompassing the growth of pre-existing collateral blood vessels to form functional arteries. 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 VEGF1 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 (Tx1 and 2) and Tx-interacting protein (Tnip) were detected by qPCR and WB. Activites of protein tyrosine phosphatase (PTP) (pTP) and Trx 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 cell based-polyoxybenzylamine chamber assay (induced by PI)-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 Tx1/2 and an upregulation of Tnip expression in monocytes. Likewise, Tx activity in diabetic monocytes was impaired. As a consequence, the total PTP activity was downregulated in hyperglycemia in a Trx-dependent fashion which resulted in VEGF resistance in monocytes ex vivo. On the other hand, improving Tx activity in hyperglycemia (diabetic patients and db/db mice) with the use of TMP significantly reversed monocyte dysfunction in an ex vivo assay. Daily administration of TMP to db/db mice resulted in significantly improved hindlimb perfusion in respect to db/db mice receiving placebo.

Conclusions: Deregulated Tx system contributes to higher oxidative stress-related deregulation of PTP activity in hyperglycemic monocytes. Improving Tx function by supplementing Tx mimetic reversed monocyte dysfunction in diabetics. Most importantly, hindlimb perfusion improved in db/db mice with HLI following treatment with Tx mimetic 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 proper arteriogenesis response in the diabetic environment.

P2589 | BENCH
Selective PPARα agonist, K-877 suppresses macrophage activation and experimental arterial lesion formation

Background: We tested the hypothesis that nuclear receptor PPARα suppresses macrophage activation and the development of arterial disease using the highly-selective, novel PPARα agonist K-877.

Methods and results: Silencing of PPARα induced pro-inflammatory gene products TNFα and IL1b in macrophage cell line THP-1 cells, suggesting anti-inflammatory effects of PPARα. The network prediction analysis revealed a close relationship between PPARα 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 TNFα, INOS, IL-1β 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 promoted the release of co-activators for PPARα gene expression (e.g., PGC-1α, SRC1) at 1 μM. 1000-fold lower than that of a conventional PPARα agonist fenofibric acid. K-877 also rescued IFNg-induced suppression of co-repressors of inflammation, NcoR1 and NcoR2/SMRT. Furthermore, in vivo administration of K-877 for 28 days LDL receptor −/− mice after femoral artery mechanical injury attenuated neointima formation and macrophage accumulation.

Conclusion: These results indicate anti-inflammatory properties of the PPARα 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)

P2590 | BENCH
Inhibition of BET bromodomains attenuates smooth muscle cell proliferation and prevents neointima formation

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 α-smooth muscle actin (α-SMA) content. Selective inhibition of BET bromodomains by (+)-JQ1 (10 μM) via a self-degrading thermosensitive Pluronic F-127 resulted in a significantly attenuated neoimal 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)

P2591 | BENCH
Selective PPARα agonist, K-877 suppresses macrophage activation and experimental arterial lesion formation

Background: We tested the hypothesis that nuclear receptor PPARα suppresses macrophage activation and the development of arterial disease using the highly-selective, novel PPARα agonist K-877.

Methods and results: Silencing of PPARα induced pro-inflammatory gene products TNFα and IL1b in macrophage cell line THP-1 cells, suggesting anti-inflammatory effects of PPARα. The network prediction analysis revealed a close relationship between PPARα 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 TNFα, INOS, IL-1β 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 promoted the release of co-activators for PPARα gene expression (e.g., PGC-1α, SRC1) at 1 μM. 1000-fold lower than that of a conventional PPARα agonist fenofibric acid. K-877 also rescued IFNg-induced suppression of co-repressors of inflammation, NcoR1 and NcoR2/SMRT. Furthermore, in vivo administration of K-877 for 28 days LDL receptor −/− mice after femoral artery mechanical injury attenuated neointima formation and macrophage accumulation.

Conclusion: These results indicate anti-inflammatory properties of the PPARα 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)

P2592 | BENCH
Inhibition of collateral formation by activated protein c in murine hindlimb ischemia model

Inflammation is one of the key mediators and promoters in the process of arteriogenesis. Small arteries are remodeled to collateral arteries. Endogenous anti-inflammatory mediators could negatively affect this process. Thus, anti-inflammatory and proinflammatory effects of activated protein C (aPC) are known, in addition to its anticoagulant effect. We hypothesized that aPC has an inhibitory effect on arteriogenesis. We ligated the right femoral artery of C57/Bl6 mice in addition to its anticoagulant effect. We hypothesized that aPC has an inhibitory effect on arteriogenesis. We ligated the right femoral artery of C57/Bl6 mice in addition to its anticoagulant effect. We hypothesized that aPC has an inhibitory effect on arteriogenesis. We ligated the right femoral artery of C57/Bl6 mice in addition to its anticoagulant effect. We hypothesized that aPC has an inhibitory effect on arteriogenesis. We ligated the right femoral artery of C57/Bl6 mice in addition to its anticoagulant effect. We hypothesized that aPC has an inhibitory effect on arteriogenesis.

Conclusion: This work was 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 vs. 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 ligation in the aPC-high group. Ctr. 1.3 vs. 3.7 aPC-high on day 7. Over the time clinical outcome between the groups was more substantial (day 14; Ctr. 1.0 vs. 1.3 aPC-high) and day 21 (0.17 ct. vs. 3.7 aPC-high (p<0.05, n=6). In our experiments of activated protein C has an inhibitory effect on arteriogenesis. This seems to be due to its anti-inflammatory property. Whether aPC is part of a negative feedback-regulation to reduce the formation of collaterals is currently under investigation.

P2593 | BENCH
A comparative quantitative histopathological study in aneurysms of the ascending aorta with special emphasis on Marfan’s syndrome

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Introduction: There are only limited studies focussing on and comparing histopathological features in aortic aneurysms with respect to different underly- ing pathologies including Marfan syndrome (MS).

Methods: We searched our database from 2014 backwards for aortic aneurysms of the ascending aorta with atherosclerosis (AS) (n=29, 17 males, mean age 70 years) and MS as underlying pathologies (n=25, 14 males, mean age 40 years). Aortic biopsies from Marfan donors served as controls (n=30, 14 males, mean age 48 years). Aortic dissections were excluded from the analysis. Formalin-fixed paraffin-embedded tissue sections were re-evaluated on conventional histology and on stained slides highlighting the different components of the interstitial mater- nal. The quantity of the different components was measured using a purpose-built imaging software under visual control. Group comparisons were tested with the Kruskal-Wallis test followed by Mann-Whitney test using the Dunn-Bonferroni ad- justment for multiple comparisons.

Results: Consistent with other studies, the main histopathological hallmark of MS - the mean quantity of mucopolysaccharides (MPs) - differed significantly, in comparison to both the control group (p=0,034, 34% vs 27%) and the AS group (p<0,001, 34% vs 23%), although normal minimal values in the MS group and normal maximum quantities in AS cases were observed. Furthermore, nearly double the collagen content than in the donors (p<0,001) was observed in AS and MS patients, without a statistically significant difference between the two patholo- gies (p=0,091).

Conclusion: Our data indicate that the quantity of MPs is not as consistent a marker in MS as assumed but appears to be rather a visual phenomenon due to its accumulation from different interstitial layers. On the other hand, in the proper clinical setting, the additionally observed elevated collagen content could add to diagnosis of MS in younger patients.

VASCULAR INFLAMMATION

P2594 | BEDSIDE
Total antioxidant capacity of diet and plasma markers of oxidant-antioxidant status are associated with low-grade chronic inflammation: the rotterdam study

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Background: Plasma oxidant-antioxidant balance as well dietary antioxidants have been suggested to play a role in low-grade chronic inflammation, an es- tablished risk factor for cardiovascular disease. Dietary ferric reducing antioxidant potential (FRAP) has been suggested to capture the overall antioxidant capacity of a diet, while uric acid (UA) and gamma glutamyltransferase (GGT) have been suggested to be major endogenous markers of oxidant and antioxidant plasma sta- tus.

Objectives: We examined whether FRAP, UA and GGT were associated with markers of low-grade chronic inflammation and whether these associations differ by gender.

Methods: A total of 4,506 participants age ≥55 years from the Rotterdam Study were eligible for analyses. FRAP score was assessed at baseline by a food fre- quency questionnaire. UA and GGT were assessed at baseline. High sensitiv- ity C-reactive protein (hs-CRP) was assessed at baseline and 10 years later, whereas adiponectin, leptin, plasminogen activator inhibitor-1 (PAI-1) and resistin were assessed 10 years later in a subgroup of participants (n=798). Multivariable regression coefficients (β) and 95% confidence intervals (CI) were calculated.

Results: A high FRAP score was associated with lower levels of both UA and GGT. FRAP was not associated with hs-CRP levels overall. However, in women (p-interaction with sex=−0.01) a high dietary FRAP score was associated with lower levels of hs-CRP (β=−0.01, 95% CI: −0.02; −0.003) whereas no association was observed in men. Furthermore, FRAP score was inversely associated with leptin (β=−0.01, 95% CI: −0.02; −0.00) and positively associated with adiponectin (β=+0.01, 95% CI: 0.002; 0.01), assoc- iations that did not differ by sex. No association was observed between FRAP and resistin in either sex. Increased levels of UA were positively associated with hs-CRP (β=+0.15, 95% CI: 0.12; 0.18), PAI-1 (β=+0.17, 95% CI: 0.11; 0.22), leptin (β=−0.11, 95% CI: 0.06; 0.16) and inversely associated with adiponectin (β=−0.07, 95% CI: −0.10; −0.03). No association was observed between UA and resistin. Similarly, GGT was positively associated with hs-CRP (β=+0.19, 95% CI: 0.15; 0.22) and PAI-1 (β=+0.09, 95% CI: 0.03; 0.14) whereas no association was ob- served between GGT and other markers of inflammation. No sex differences were observed in any of these associations.

Conclusion: The results of this study suggest that high overall dietary antioxidant capacity and lower levels of both UA and GGT are associated with diminished chronic inflammation.

P2595 | BENCH
Exploring the obesity paradox in secondary prevention: a new biological role of femoral adipose tissue in humans

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Background: Obese individuals (as defined by body mass index) have better clin- ical outcome in secondary prevention. This “obesity paradox” reflects the inability of the current anthropometric measures of obesity to describe adipose tissue (AT) biology, further to its small mass.

Purpose: Establish a novel index describing the quality of adipose tissue by quantifying the expansion of femoral AT (FemAT), and linking it with vascular func- tion and systemic oxidative stress.

Methods: FemAT thickness was measured by U/S in 185 pts undergoing coro- nary bypass surgery (CABG), and defined as the average AT thickness at the an- terior and lateral surface of the 2 thighs, at the mid-point of the distance between the iliac crest and the knee. FemAT biopsies from these patients were cultured ex vivo for secretome and gene expression studies. Malondialdehyde (MDA), an ox- idative stress marker, was measured in plasma and FemAT culture supernatants. Brachial flow mediated dilatation (FMD) and distensibility were assessed by U/S.

Results: FemAT thickness was only weakly correlated with BMI (r=0.235, p<0.001) and waist-to-hip ratio (WHR, r=−0.179, p<0.05). BMI did not predict systemic oxidative stress or vascular function, while WHR was weakly correlated with FMD (rho=−0.156, p<0.05). Patients with increased FemAT thickness had lower plasma (A) and FemAT-derived MDA (B), lower expression of IL6-R (C) & CD68 (D) in FemAT, higher FMD (E) and greater brachial distensibility (F).

Conclusions: Quantification of FemAT accumulation provides valuable informa- tion on AT and systemic inflammation, predicting vascular function in human atherosclerosis. This new marker of adiposity partly explains the “obesity para-adox”, and can be used for risk prediction in secondary prevention.

P2596 | BENCH
Antimicrobial peptide LL37 RNA complexes stimulate Toll-like receptor 3 upon shock wave therapy of ischemic muscle

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Background: Shock wave therapy (SWT) induces angiogenesis in ischemic heart disease. It is mediated via Toll-like receptor 3 (TLR3), an endosomal recep- tor of the innate immune system recognizing RNA. How TLR3 is activated upon SWT remains unknown. The antimicrobial peptide LL37 has been shown to be released after mechanical stress and to form complexes with RNA.

Purpose: We hypothesized that mechanical stimulation upon SWT leads to LL37 release, which forms complexes with RNA and leads to activation of endosomal TLR3.

Methods: Supernatant of treated human umbilical vein endothelial cells (HUVEC) was transferred onto TLR3 reporter cells and TLR3 activation was measured. To find out whether protein/RNA complexes play a role after SWT, supernatants
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. Laser Doppler perfusion imaging and histological quantification of vessels was performed. 

Results: Supernatants of treated cells activated TLR3 reporter cells (CTR 31.67±28.17 vs. SWT 19757±1054, p = 0.001). Supernatants of treated cells activated TLR3 reporter cells (CTR 0.48±0.01, p = 0.021) in treated muscles. 

Conclusion: TLR3 activation upon SWT is mediated via the release of LL37. This study in mice subjected to hind limb ischemia suggests that LL37 plays a role in angiogenesis and may be a potential target for treatments for ischemic heart disease. 

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P2597 | BENCH
Expression of sVEGFR3 decoy receptor alters lipid accumulation and changes cardiac lymphatic vessel organization in these mice, it does not seem to affect the functionality of the heart. 

P2598 | BENCH
IL-6 modulates angiogenesis through bone marrow derived cells activation 
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Background: Inflammatory reaction was involved in neovascularization in a mouse model for femoral artery flow-restriction by ligation. On the other hands, bone marrow derived cells were also known to be involved in neovascularization after femoral artery ligation. However, the relationship of inflammatory cytokine, interleukin-6 (IL-6) and bone marrow derived cells to neovascularization still remained unknown. 

In this study, we evaluated the detail role of IL-6 and bone marrow derived cells to the angiogenic effect using mice hindlimb ischemia model. 

Methods: We performed femoral arterial ligation to wild type (WT) mice or IL-6 knockout (KO) mice to evaluate neovascularization. Bone marrow cells from both kinds of mice were isolated, cultured and detected the ability of transdifferentiation to smooth muscle like cells. 

Results: In KO mice, the blood flow estimated by Laser Doppler Analysis was significantly decreased than WT mice at 1 and 3 weeks after femoral arterial ligation (p < 0.01, respectively). Moreover, infiltration of inflammatory cells was also significantly decreased compared WT mice. 

Conclusion: Our data indicated that inflammatory cytokines, IL-6 modulates angiogenesis through bone marrow derived 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. 

P2599 | BENCH
Delayed overexpression of vascular endothelial growth factor in the right ventricular myocardium accelerates irreversable cardiac remodeling in pulmonary arterial hypertension 
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Objective: We have reported on right ventricular (RV) remodeling prior to the plextiform formation in pulmonary arterial hypertension (PAH). The aim of this study was to elucidate the precise mechanisms of the hypoxia-induced RV remodeling in PAH model rats and to evaluate chronological changes of vascular endothelial growth factor (VEGF) mRNA expression and its downstream signal transduction in human pulmonary artery endothelial cells (HPAECs) and human pulmonary artery smooth muscle cells (HPASMCs). 

Methods: Male Sprague-Dawley rats were exposed to hypoxia (10% O2) for 2 weeks after a single subcutaneous injection of VEGF receptor blocker (Sugen5416, 20 mg/kg; SU-Hypo) or solution (V+Hypo). HPAECs were co-cultured with HPASMCs and incubated under hypoxic conditions (37°C, 1% O2). 

Results: our data indicated that inflammatory cytokines, IL-6 modulates angiogenesis through bone marrow derived 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. 

P2600 | BENCH
miRNA126 regulates the Tissue Factor isoform expression in endothelial cells under inflammatory conditions

Introduction: Tissue factor (TF) is the primary initiator of blood coagulation. Side coagulation TF plays an important role in vessel wall hemostasis, angio- genesis and thrombosis. TF exists in 2 isoforms, the membrane bound “full length” (fTF) and a soluble “alternatively spliced” (as)TF. Recently, we could show that the isoform expression is regulated by post transcriptional alternative splicing activity. We identified enzymes, such as Cdc2-like kinases and
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 TFf, asTF and miRNA126 under normal conditions. The treatment with TNFα for 2h and 6h reduced the expression of miRNA126 and induced mRNA expression of ITF and asTF (p<0.05). The asTF and asTF protein expression was increased 24h post stimulation with TNFα. The miRNA126 mimic for 2h significantly reduced the ITF and asTF protein expression compared to the co mimics and inhibitors, 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: The miRNA126 targets it self and asTF and induces a decreased 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).

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**P2601 | BENCH**

**CD14+CD16+ patrolling monocytes expressing LRP5 are internalized in advanced coronary atherosclerosis**

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**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 in their macrophage markers are believed to differentiate from monocytes recruited from circulating blood. We have recently shown that LRP5 (low-density lipoprotein receptor-related protein 5), a member of the LDL family of receptors, regulates monocyte to macrophage differentiation and triggers the VEGF 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 in M1 macrophages derived from classical CD14+CD16- monocytes. Circulating monocytes from WT mice also show increased expression of LRP5 in CD11b+GR1-low monocytes, the mice equivalent for human patrolling monocytes. M2-high-LRP5-expressing macrophages secrete anti-inflammatory cytokines as opposed to M1-low-LRP5-expressing macrophages that secrete large amounts of proinflammatory cytokines supporting an anti-inflammatory role for the M2/LRP5+ macrophage subset. LRP5 is not found in healthy vessel or arterial intimal thickening but is found in advanced human atherosclerotic lesions co-localizing only with the M2 macrophage subset. LRP5-expressing macrophages infiltrate the deep layers of atherosclerotic plaque towards the intima-media boundaries showing increased migratory activity.

**Conclusions:** These results demonstrate that anti-inflammatory M2 macrophages found in atherosclerotic human plaques express LRP5 suggesting that M2 macrophages in advanced atherosclerotic plaques trigger the anti-inflammatory, defensive and repair response through LRP5 signalling.

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**P2602 | BENCH**

**TGFβeta signalling as modulator of endothelial-to-mesenchymal transition during chronic thromboembolic pulmonary hypertension**


**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 TGFβf, released from activated platelets, during CTEPH and to determine whether it may promote pulmonary fibrosis via induction of mesenchymal transition (EndMT).

**Methods:** Endarterectomy specimens from CTEPH patients are processed for paraffin and cryo-embedding followed by histological and immunohistochemical analysis (including confocal microscopy), and for RNA isolation followed by quantitative real time PCR examination (qPCR). Furthermore, cells from CTEPH tissue and circulating monocytes from WT mice were expanded under different culture conditions and processed for expression and functional analysis.

**Results:** To confirm the presence of EndMT, double-fluorescence staining was performed on cryo-preserved CTEPH tissue and on cells outgrown from it, demonstrating cells simultaneously expressing endothelial (VE-cadherin, CD31) and mesenchymal (SM, FSP1) markers. Also, transcription factors known to be involved in mesenchymal differentiation, such as Snail and Twist, were found to be highly expressed. Immunohistochemical staining and qPCR analysis revealed that several of the known TGFβf receptors (i.e. TGFBR1, endothelial, BM-PRII, ALK1 and ALK5) are expressed in CTEPH tissue, particularly in endothelial cells. Moreover, within the endarterectomy specimens rich in endothelial cells and/or myofibroblasts were found to be strongly positive for phospho-SMAD2 and phospho-SMAD5 indicating active TGFβf signaling. QPCR and immunohistochemical expression analysis suggested that activation of TGFβf signaling occurs primarily through TGFβ1 or BMP's (BMP2 and BMP4), whereas TGFβ3 or the TGFβ3 antagonist BMP7 were not detected. To study the chronic remodelling response to and the chronic remodeling and the role of TGFβf in AT, mice with platelet-specific TGFβ1 deletion (P4.Cre x TGFβ1flx/tlox) 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 over 3 weeks.

**Conclusions:** Our findings suggest that TGFβf induced signalling events in endothelial cells and myofibroblasts may enhance post-thrombotic fibrosis in CTEPH by promoting EndMT.

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**P2603 | BENCH**

**Fish oils, eicosapentaenoic acid and docosahexanoic acid, attenuate oxidative stress-induced DNA damage in vascular endothelial cells**

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**Background:** Accumulative evidence has suggested that omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexanoic acid, 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 (100 μM) 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 other 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 (38% and 54%, respectively). To further investigate the anti-oxidative effect of EPA and DHA, nuclear factor erythroid 2-related factor 2-related factor (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 NAD(P)H quinone oxidoreductase 1, were significantly upregulated by both 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

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Background: Accelerated arterial stiffening is a major complication of diabetes in the absence of 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-mycograph; 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.

Figure 1. Pressure-diameter curves; +/db ctr

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.

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P2605 | BENCH

A DPP4 inhibitor, vildagliptin, attenuates monocyte inflammatory response through suppression of MAP kinase pathways and ameliorates CaCIZ-induced vascular remodeling in mice

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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 monocyte aorta induced by CaCIZ.

Methods: The effects of vildagliptin were investigated in a monocye cell line, U937 cells. The expression of DPP4 in U937 was knocked down by siRNA. As a model of inflammatory vascular remodeling, CaCIZ-induced atherosclerotic aortic dilation was used. After application of 0.5 M CaCIZ to the infrarenal aorta, then mice received oral vildagliptin (30mg/kg/day, n=10) or a vehicle (n=10) for six weeks. The glucose tolerance test showed no difference in glucose change among three groups.

Results: In vitro experiments, induction of interleukin-6 by lipopolysaccharide in U937 cells was suppressed by vildagliptin alone (20μM-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 CaCIZ. Then, vildagliptin significantly attenuated aortic dilatation (external diameters: 1.1±0.06 mm [CaCIZ] vs. 0.95±0.05 mm [CaCIZ-vildagliptin]; p<0.05, respectively). Histological analysis showed that the recruitment of macrophages into media and adventitia in CaCIZ group was significantly greater than that in vildagliptin group (3.3±2.0 cell/mm² vs. 1.2±2.2 cell/mm²; p<0.05). 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)

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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 (SPP1) 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 SPP1 and IBSP was performed by reverse transcriptase-polymerase chain (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 SPP1 and IBSP were also increased 4.3-fold and 5.3-fold, respectively for AngI 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 AngI and AngII, respectively (p<0.01) stimulation. No changes in ACE and AT1R mRNA expression after AngI 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

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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 <0.6cm²/m² and LVEF >50%, 88 (80±7 years, 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/m². LVOT area was also measured by 3-dimensional echocardiography. The 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. 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. 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. 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. 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. 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. 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.

Redclassifying aortic stenosis severity.
Conclusion: The aortic valve calcium, calcium density and calcium index were not significantly different between the 2 low-gradient groups and between those reclassified to true moderate AS versus those reclassified to low gradient.

P2600 | BEDSIDE
Transcatheter mitral valve-in-ring implantation with the direct flow medical valve
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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 an attractive 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 used for mitral annuloplasty.

Aim of the study: 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 valve-in-ring implantation for severe mitral regurgitation following failed 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 DF; 2) Edwards Physio 30mm, perimeter of 75.6mm, 27mm DF; 3) Medtronic CG Future 26mm, perimeter 65.8mm, 25mm DF. All cases were performed via the transapical approach with a 24F sheath. The DFM was successfully positioned within the mitral ring in all 3 cases resulting in excellent sealing, 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 responstivable and retrievable valve within a failed mitral annuloplasty ring with excellent acute hemodynamic outcomes.

P2601 | 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
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Background: Presence of functional mitral regurgitation (MR) is known to be associated with poor prognosis in coronary artery disease. Revascularisation 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 (45.1%) presented with the left anterior descending coronary artery bypass grafting. 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, postoperatively 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.

P2601 | BEDSIDE
Cutoff mitral gradient and systolic pulmonary artery pressure predictive of dyspnea on Doppler stress in mitral stenosis
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Background: In mitral stenosis (MS), the American Recommendations AHA/ACC advocate percutaneous mitral commissurotomy (PMC), when in stress echo Doppler the mean gradient (MGM) or the systolic pulmonary artery pressure (SPAP) are respectively above 15 mmHg and 60 mmHg at peak stress. However, these thresholds are controversial. Objective: In Doppler cardiac stress, determine the thresholds of MGM and SPAP in prediction of the dyspnea justifying percutaneous mitral dilatation in patients with MS.

Method and results: Were included 300 patients with mitral area <2cm2 and NYHA II-III. A. stress test treadmill has been systematically to distinguish dyspneic patients (n=182) of non dyspneic patients (n=118). The thresholds of the MGM and SPAP predictive dyspnea justifying the PMC were sought using the tables of stress echocardiography. In no dyspneic patients, the MGM was >33.5 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 33.5 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.

Conclusion: This is the first and largest study that looked at stress echo Doppler the thresholds MGM and SPAP predictive dyspnea justifying the PMC. Our results suggest that the low specificity of the MGM and SPAP peak effort with the values of the AHA/ACC Guidelines. Optimal thresholds Predictive of dyspnea obtained in this study at the peak of the effort are 33.5 mmHg for MGM and 75.5 mmHg for the SPAP.
**P2610** | **BEDSIDE**
Impact of atrial fibrillation 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 fibrillation (AF) is common in patients with degenerative mitral regurgitation (DMR) due to mitral valve prolapse, associated with atrial remodelling 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 included 34 patients with severe DMR and AF (DMR-AF), 64 patients with severe DMR and SR (DMR-SR), and 29 normal subjects were prospectively studied using real-time 3-dimensional (3D) transoesophageal 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±9y, 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:** 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, U01HL69015, and U01HL60913

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**Table 1**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normal (n=29)</th>
<th>DMR-SR (n=64)</th>
<th>DMR-AF (n=34)</th>
<th>ANCOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annular height, mm</td>
<td>7.8±1.9</td>
<td>7.4±1.9</td>
<td>6.1±1.9</td>
<td>&lt;0.0001</td>
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<tr>
<td>Commissural width, mm</td>
<td>33.2±3.8</td>
<td>38.0±4.7</td>
<td>39.6±5.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Annular height-to-commissural width ratio (normality index), %</td>
<td>23.7±5.5</td>
<td>15.3±3.3*</td>
<td>12.4±3.3* †</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Anteroposterior diameter, mm</td>
<td>27.8±2.5</td>
<td>35.4±3.8</td>
<td>38.3±4.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Annular area, mm2</td>
<td>737±129</td>
<td>1063±251*</td>
<td>1207±333* †</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Left atrial maximal volume, ml</td>
<td>43±10</td>
<td>108±40*</td>
<td>186±73*   †</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Left atrial peak systolic longitudinal strain, %</td>
<td>31±9</td>
<td>27±7*</td>
<td>17±6* †</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*P<0.05 vs. normal subjects. †P<0.05 vs. DMR-SR group.

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**P2614** | **BEDSIDE**
Mitral clip versus heartport mitral valve annuloplasty in very severe heart failure
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**Background:** Functional mitral regurgitation (FMR) worsens prognosis in patients with heart failure. Catheter-based Mitraclip implantation and surgical Heartport technique are minimally invasive approaches to repair FMR.

**Purpose:** To compare mid-term efficacy and outcomes of Mitraclip and Heartport techniques in matched patients with very severe systolic heart failure and FMR.

**Methods:** A total of 23 patients (Mitraclip; 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 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 (LVEDD −1.5mm vs −1.8mm; LVEF +25% vs +114%; NS) during follow up.

**Conclusions:** In patients with systolic heart failure and significant FMR, both Mitraclip 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.

---

**Table 1**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mitraclip</th>
<th>Heartport</th>
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</thead>
<tbody>
<tr>
<td>MR III-IV</td>
<td>Baseline</td>
<td>Follow-up</td>
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<tr>
<td>Baseline</td>
<td>77%</td>
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</tr>
<tr>
<td>NYHA III-IV</td>
<td>91%</td>
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</tr>
</tbody>
</table>

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**P2615** | **BEDSIDE**
Long term outcome of balloon mitral valvotomy in patients with atrial fibrillation
G. Cherni, I. Mechi, M. Mahjoub, M. Hassine, M. Ben Messoud, Z. Dridi, F. Bettbou, H. Gama. Fattouma Bourguiba University Hospital, Department of Cardiology A, Monastir, Tunisia

**Background:** The immediate and particularly the long term outcome of Balloon Mitral Valvotomy (BMV) in patients with atrial fibrillation (AF) is not well known compared to that in patients with normal sinus rhythm (NSR).

**Objectives:** We sought to evaluate the effect of AF on the immediate and long-term (23 years) outcome of patients undergoing BMV.

**Methods:** The immediate procedural and the long-term clinical outcome after BMV of 139 patients with AF were collected and compared with those of 381 patients in NSR.

**Results:** Patients with AF were older (43.3 vs. 29.7 years; p<0.001), had frequently a history of systemic embolism (9.4% vs. 1.6%, p<0.001) and of mitral commissurotomy (28.1% vs. 19.4%, p=0.035). Symptoms were similar between...
Atriectomy (41 cm² vs 32 cm², p=0.001) and a lower transmitral gradient (11.1 mmHg vs 16.6 mmHg, 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 < 2 cm² (OR: 2.5, 95% CI [1.2; 5.18], p=0.014), procedural complications including severe mitral regurgitation and tamponade (OR: 1.05, 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 <2 cm², procedural complications and NYHA ≥ II predict adverse events during follow up.

AORTIC VALVE DISEASE

P2616 | BEDSIDE

Impact of pre-operative moderate/severe functional tricuspid regurgitation in TAVI population and its post-procedural modifications

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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 2007 to 2014, 529 TAVI pts were screened. Clinical and echocardiographic baseline data were collected. Echocardiographic follow up was collected between 1 to 6 months after TAVI. FTR severity was graded using a multi-parametric approach. A composite endpoint (hospitalization for heart failure or all-cause mortality) was evaluated at 1 year follow up. Pts were divided in 2 groups: FTR≥2 (group 1) and FTR<2 (group 2); according to FTR improvement<1 degree after TAVI pts were also divided in 2 subgroups: FTR improved group, FTR no change group.

Results: Among 529 pts (mean age 79.9±7.5, male 46.7%), 161 (30.4%) had FTR≥2. At one year clinical follow up, no significant differences were found in the composite endpoint in the 2 study groups (group 1 event rate 80.7% vs group 2 81.5%, log rank p=0.97). In group 1, 110 (68%) had follow up echo after procedure. Echocardiographic follow up showed improvement of FTR grade in 55% pts. At the multivariate analysis, absence of chronic obstructive pulmonary disease (COPD) was found to be an independent prognostic factor for FTR improvement (p = 0.064, OR 0.25, CI 95% 0.07–0.83; p=0.024). There was no significant difference in the composite endpoint between FTR improved group vs FTR no change group (95.8% vs 86.7%, log rank p=0.20).

Conclusion: Moderate/severe functional TR is a frequent finding in TAVI population, although improving after this procedure. COPD is an independent predictor of FTR non-improvement. The presence of more than moderate FTR, even if not improving after TAVI, does not affect prognosis, so it should not influence patients’ candidacy to TAVI.

P2619 | BEDSIDE

Transcatheter aortic valve implantation in patients with reduced ejection fraction and low transvalvular gradient: the rule of 40

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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). Conclusion: At least one parameter (LVEF or MTG x systolic pressure) 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.

P2618 | BEDSIDE

Determinants of functional capacity in aortic stenosis patients

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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 symptoms not certainly related to valvular disease. Patients underwent a symptom-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/VCO2 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 output x systolic pressure) and higher peak-rest transaortic mean gradient difference (ΔMAG). At multivariate analysis, only ΔMAG resulted independently associated with impaired functional capacity (p=0.048; CI 1.001–1.323).

P2617 | BEDSIDE

Impact of reduced ejection fraction and low transvalvular gradient on cardiac functional capacity in patients with severe AS

A. Margonato, A. Colombo, E. Agricola, A. Latib, M. Montorfano, A. Chieffo, M. Barletta, S. Miyazaki, I. Rosa, C. Marini, A. Chieffo, M. Montorfano, A. Latib, A. Margonato, A. Colombo, E. Agricola. San Raffaele Hospital of Milan (IRCCS), Milan, Italy

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 symptoms not certainly related to valvular disease. Patients underwent a symptom-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/VCO2 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 output x systolic pressure) and higher peak-rest transaortic mean gradient difference (ΔMAG). At multivariate analysis, only ΔMAG 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 stenosity severity. These results suggest the role of isotropic and contractile reserve supporting the routine evaluation of cardiac reserve as a determinant of symptoms development.
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 0.611; 95% CI 0.628–0.753) and for the combined endpoint of mortality, cardiac декompensation, and cardiac rehospitalisation (AUC 0.61; 95% CI 0.562–0.671). Clinical factors associated with the combined endpoint were NYHA class, pre-operative aortic valve area, atrial fibrillation, impaired renal function (GFR <45), diabetes, low BMI, and chronic obstructive pulmonary disease. Multivariate analysis revealed that the level of NT-proBNP on the third day after TAVR is an independent predictor of mortality, cardiac декompensation, and cardiac rehospitalisation 12 months after TAVR. After setting the optimal cut-off level for NT-proBNP on the third day after TAVR to 12,000 pg/ml, the multivariate analysis showed an AUC of 0.709 (95% CI 0.646–0.772).

Conclusion: The serum level of NT-proBNP 3 days after TAVR is an independent predictor of long-term mortality and morbidity in patients undergoing TAVR.

Results: After 6 months of treatment, there was no difference in the baseline adjusted left ventricular end diastolic volume between patients allocated to metoprolol and those allocated to placebo (Figure). At follow-up, the mean adjusted left ventricular ejection fraction was 2.7 percentage points (0.1–5.3 percentage points; p=0.04) higher in the metoprolol group than in the placebo group. The exercise capacity and peak oxygen consumption did not differ between treatment arms; whereas, serum levels of N-terminal pro-B-type natriuretic peptide were higher in the metoprolol group. There were no serious adverse events in either treatment arm.

Conclusions: 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.
**P2624 | BEDSIDE** Rapid deployment balloon-expandable aortic valve replacement: rates of major paravalvular leak and new permanent pacemaker implantation

T. Wahlers¹, G. Laufer², M. Borger³, M. Shrestha⁴, A. Kocher², T. Walther⁵, F. Mohr⁶, C. Schmitz⁷, F. Duah⁶, A. Haverich¹.¹ University of Cologne, Cologne, Germany;²Medical University of Vienna, Vienna, Austria;³Columbia University Medical Center, New York;⁴University of Minnesota Medical School, Minneapolis, Minnesota, USA;⁵Hannover Medical School, Hannover, Germany;⁶Kerckhoff Clinic, Bad Nauheim, Germany;⁷Heart Center of Leipzig, Leipzig, Germany; University Hospital of Munich, Munich, Germany; Edwards 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 TAR 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 needed to expand the frame within 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.

**Results**: 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. Wittaker, F. Matcham, M. Gunning, S. Block, P. MacCarthy, O. Wender. 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 total was 33,319GBP (36,647GBP and 28,465GBP for surgically and medically treated patients, respectively) and for Cohort 2 was 32,048GBP (37,061GBP and 25,492GBP for surgically and medically treated patients, respectively).

**Conclusions**: 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

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**Background**: Ross procedure in aortic valve endocarditis, avoiding prosthetic valve implantation in septic context. We sought to assess long-term outcome after 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 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, with a good functional status for all patients with NYHA II, <50% exercise intolerance and echocardiographic follow-up of this population.

**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.
P2627 | BEDSIDE
Current clinical presentation, management and long-term outcome of infectious endocarditis: results from a contemporary registry in 2 referral centres
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Background: Infective endocarditis (IE) has a relatively low incidence but clinical presentation, management and outcome is changing due to the aging of the general population and the increase of invasive procedures and use of intracardiac devices. In this study we evaluated the current clinical presentation, management and outcome of IE in a long-term registry in the Ghent diabetics, stroke and reduced kidney function. Importantly, pts undergoing device/catheter extraction and pts treated medically also had a significant higher mortality during long-term follow-up as compared to pts undergoing cardiac surgery.

Methods: We evaluated all patients with definite IE (Duke Criteria) admitted or followed between 2006 and 2012 to 2 centers performing cardiac surgery in Belgium. Data on clinical characteristics, EUROSCORE II, in-hospital treatment and in-hospital mortality were collected in all patients. After discharge pts were followed for all-cause mortality during a mean follow-up of 47±22 months

Results: In total 174 patients (age 62±15 years, 29% women) with definite IE were included. Native valve IE was present in 69%, prosthetic valve IE in 24% and 12% presented with device or catheter infection. Staphylococcus species were found in 40% and 29% had an invasive procedure less than 3 months before admission. Overall in-hospital mortality was 19%, varying from 11% in pts undergoing cardiac surgery (74% of all pts), to 27% mortality in pts undergoing device/catheter extraction (5% of all pts) and 48% mortality in pts treated medically (18% of all pts) (overall p-value <0.001). The AUC of EUROSCORE II for the prediction of in-hospital mortality for pts undergoing surgery was 0.77 (95% CI 0.67–0.87, p<0.001). After discharge 1 year survival was 92%, 3 year survival 82% and 5 year survival 69%. Independent predictors for all-cause mortality during long-term follow-up as compared to pts undergoing cardiac surgery. (HR 2.82, 95% CI 1.33–5.98), diabetes (HR 2.31, 95% CI 1.17–4.88) and reduced kidney function (HR 2.39, 95% CI 1.17–4.88). Pts undergoing device/catheter extraction and pts treated medically also had a significantly higher mortality during long-term follow-up as compared to pts undergoing cardiac surgery. (Log Rank 29.01, p <0.001).

Conclusion: The results of this contemporary registry indicate that IE is still associated with a high in-hospital mortality (19%) and that long-term outcome after discharge is mainly related to age and comorbidities including diabetes, stroke and reduced kidney function. Importantly, pts undergoing device/catheter extraction and pts treated medically had a significantly higher in-hospital and long-term mortality as compared to pts undergoing cardiac surgery.

P2628 | BEDSIDE
Regulatory T cell subsets in patients with rheumatic heart disease: relation to disease severity
M.I. Salama, H.M. Hassoba, A.F . Abdelhai, H.M. Kamal, S.E. Younis. Suez Canal University, Faculty of Medicine, Ismailia, Egypt

Background: Rheumatic heart disease (RHD) is an autoimmune progressively destructive valvular disorder that develops as a sequel of acute rheumatic fever (RF). The CD4+ CD25+ Foxp3+ regulatory T cells are essential for the induction/maintenance of self-tolerance and prevention of autoimmunity. Decreased number and/or altered status of Treg cells have been implicated in the pathogenesis of some autoimmune diseases.

Purpose: To assess the frequency of CD4+ CD25+ Foxp3+ Tregs in patients with RHD, and its correlation with the disease severity.

Patients and methods: A case-control study was carried out on RHD with univalvular lesions (n=13) and multivalvular lesions (n=27). Thirty normal healthy persons served as a control group. Immunophenotyping of Treg cells was performed using the surface markers CD4 and CD25 as well as the transcription factor Foxp3.

Results: A significant decrease was observed in the frequency of Tregs subpopulations (CD4+CD25+Foxp3+), (CD4+CD25+Foxp3+), and (CD4+CD25+Foxp3+) in RHD patients compared to healthy controls (p-value<0.001, 0.03 and 0.03 respectively). However, no correlation between the frequency of Treg subsets and the severity of cardiac involvement was observed. Tregs were able to discriminate RHD patients from normal control at a cut off values of 102, 88, 23 cell/mm² for the subpopulations (CD4+CD25+Foxp3+), (CD4+CD25+Foxp3+), and (CD4+CD25+Foxp3+) respectively with p<0.001 each.

Conclusion: Our study confirms the role of Treg deficiency in the development of RHD. This would support the possibility of using Treg-based therapy to restore the level of Treg cells in patients with RF as a possible way to prevent the development of RHD.

P2629 | BEDSIDE
Role of reversibility assessment of pulmonary vascular resistance index (PVRI) and echocardiography in management of valvular heart disease (VHD)
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Background: VHD leading to pulmonary hypertension (PHT) is an important predictor of in-hospital, ventricular failure and mortality 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 15min).

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. Reversibility was assessed in only 30 patients (30%). Seventeen (53%) of our patients were responders and had 25% 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 PHTN 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
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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 the current 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 a significantly lower eGFR (95% CI 1.88–4.98; p<0.001).

The results of this contemporary registry indicate that IE is still 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 the current knowledge.

Conclusion: Reversibility of AKI and this complication is less well defined. This study aimed to fill this gap in the current knowledge.

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 (years)</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 (PVRI)</td>
<td>7.9 W/m²/L</td>
<td>11 W/m²/L</td>
</tr>
<tr>
<td>Change in PVRI post Reversibility test with iloprost</td>
<td>3.3 W/m²/L</td>
<td>0.03 W/m²/L</td>
</tr>
<tr>
<td>Cardiac Index (L/min/m²)</td>
<td>2.54 L/min/m²</td>
<td>2.04 L/min/m²</td>
</tr>
<tr>
<td>Left Ventricle diastolic dimension on transthoracic echo. Pre-study</td>
<td>53 millimetre</td>
<td>60 millimetre</td>
</tr>
<tr>
<td>RV Tricuspid Annular Plane Systolic Excursion (TAPSE) on transthoracic echo. Pre-Study</td>
<td>1.8 cm (range 2.3–4.0)</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 transcatheater 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 (15.0–36.5)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.

P2633 | BEDSIDE
Risk scores and biomarkers for the prediction of 1-year outcome after transcatheater aortic valve replacement
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Background: Up to 50 percent of the patients still die or have to be rehospitalized during the first year after transcatheater 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 rehospitalization (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). We applied the 3 different risk scores to predict all-cause mortality and rehospitalisation after TAVI.

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.

CARDIOMYOPATHIES

P2634 | BENCH
Selumetinib, an oral anti-neoplastic drug, may prevent cardiac hypertrophy via targeting the ERK pathway
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Background: Although extracellular-regulated kinases (ERK) are a well-known central mediator in cardiac hypertrophy, no clinically available ERK antagonist has been tested for preventing cardiac hypertrophy. Selumetinib is a novel oral ERK inhibitor that is currently under Phase II and Phase III clinical investigation for advanced solid tumors. In this study, we investigated whether Selumetinib could inhibit the aberrant ERK activation of the heart in response to stress as well as prevent cardiac hypertrophy.

Methods and results: In an in vitro model of PE-induced cardiac hypertrophy, Selumetinib significantly inhibited the ERK activation and prevented enlargement...
Results: The mean age of the patients was 28.4±6.9 and the mean ejection fraction was 27.8±8.4%. Heart failure was the most common symptom (98%) and was 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 using the national database. 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%) while arrhythmia was the initial presentation in 5 patients (12.8%). 14 patients had recovery of ejection fraction in 6 months (39%) with a mean EF of 55.5±6.3. While arrhythmia was the initial presentation in 5 patients (12.8%). 14 patients had recovery of ejection fraction in 6 months (39%) with a mean EF of 55.5±6.3. Heart failure was the most common symptom (98%) while arrhythmia was the initial presentation in 5 patients (12.8%). 14 patients had recovery of ejection fraction in 6 months (39%) with a mean EF of 55.5±6.3.

Acknowledgement/Funding: none

P2635 | BEDSIDE
Clinical profile and outcomes of peripartum cardiomyopathy in a southeast Asian tertiary centre: the PERIPHIL study
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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 using the national database. 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%) while arrhythmia was the initial presentation in 5 patients (12.8%). 14 patients had recovery of ejection fraction in 6 months (39%) with a mean EF of 55.5±6.3. Heart failure was the most common symptom (98%) while arrhythmia was the initial presentation in 5 patients (12.8%). 14 patients had recovery of ejection fraction in 6 months (39%) with a mean EF of 55.5±6.3.

Conclusion: These results suggest that treatment with tafamidis may have stabi-

P2637 | BENCH
Circulating microRNAs as biomarkers for diffuse myocardial fibrosis in patients with hypertrophic cardiomyopathy
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Background: Myocardial fibrosis is a hallmark of various cardiovascular diseases, but it is difficult to be diagnosed non-invasively. Circulating microRNAs may represent novel markers for cardiovascular diseases.

Methods: In the present study, we evaluate whether circulating miRNAs serve as biomarkers for diffuse myocardial fibrosis in patients with hypertrophic cardiomyopathy (HCM).

Methods: Cardiac magnetic resonance imaging with postcontrast T1 mapping was performed to non-invasively quantify diffuse myocardial fibrosis in HCM patients and these patients were classified into 2 groups (T1<470 ms or T1>470 ms, as likely or unlikely to have diffuse fibrosis, respectively). First, we screened 84 miRNAs using human serum/plasma miRNA array on plasma of 8 HCM patients (4/group based on T1 time) and 4 healthy controls. From the results of this initial screen, 16 miRNAs were selected based on their fold changes and relevance to myocardial fibrosis for further validation by Taqman real-time PCR in 55 HCM patients.

Results: Among the 16 miRNAs, 14 (miR-18a, miR-146a, miR-30d, miR-17, miR-200a, miR-19b, miR-21, miR-193–5p, miR-10b, miR-15a, miR-199b–5p, miR-29a, and miR-133a) were upregulated in HCM patients with T1<470 ms compared with those with T1>470 ms, and 11 (except miR-192, miR-296–5p and miR-133a) were significantly inversely correlated with postcontrast T1 values. Individual miRNA had moderate diagnostic value for diffuse myocardial fibrosis (AUC: 0.663–0.742), but the diagnostic value was greatly improved (AUC: 0.87) for a combination of 8 miRNAs. In comparison, circulating markers of collagen turnover did not have predictive values for diffuse myocardial fibrosis.

Conclusions: These findings suggest that circulating miRNAs provide attractive candidates as putative biomarkers for diffuse myocardial fibrosis in HCM.

P2639 | BEDSIDE
Gradient reduction after percutaneous septal ablation modifies the risk profile in hypertrophic obstructive cardiomyopathy
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Introduction and methods: In 513 patients (pts., mean age: 55.5±14.3 years) treated with percutaneous septal ablation (PTSA) for symptomatic hypertrophic obstructive cardiomyopathy (HCM) we analyzed predictors of long-term outcome.

Results: Hospital mortality was 1% (5 pts.). Mean CK rise was 513±249 U/l (ref: 0–100 U/l). A DDD-pacemaker (DD-DPM) was to be implanted in 45 pts. (9%) for PTSA-induced AV conduction problems. During follow-up (66±54 months [range: 0.1–207.0] 2820 pt-years), 56 pts. (11%) died, of these 22 (4%) from non-cardiac, and 34 (7%) from cardiovascular diseases. Overall survival was 93% at 5 years, and 90% at 10 years.

Conclusions: The cumulative risk of post-PTSA arrhythmias for several univariate analysis at 5 years of follow-up (hazard ratio/p value) were predictive for overall mortality: Baseline LV end-diastolic diameter (1.06/0.03), baseline age (1.07/0.0001), baseline septal thickness (1.12/0.004), ethanol dose (1.37/0.00), and syncope during follow-up after PTSA (2.73/0.02). The cumulative risk of post-PTSA arrhythmias for several univariate analysis at 5 years of follow-up (hazard ratio/p value) were predictive for overall mortality: Baseline LV end-diastolic diameter (1.06/0.03), baseline age (1.07/0.0001), baseline septal thickness (1.12/0.004), ethanol dose (1.37/0.00), and syncope during follow-up after PTSA (2.73/0.02).
Medicine I, Comprehensive Heart Failure Center, Wuerzburg, Germany; Five out of 42 patients underwent 99mTc-DPD scintigraphy that showed atrial septum or right ventricular free wall, pericardial effusion, granular sparkling of LV wall thickness mismatch, echocardiographic findings suggestive of myo-paean paradoxical low flow-low gradient severe AS, QRS voltage-left ventricular wall thickness and one or more of the following: Methods: propanodicarboxylic acid (99mTc-DPD) scintigraphy.

Five out of 42 patients underwent 99mTc-DPD scintigraphy that showed atrial septum or right ventricular free wall, pericardial effusion, granular sparkling of LV wall thickness mismatch, echocardiographic findings suggestive of myo-paean paradoxical low flow-low gradient severe AS, QRS voltage-left ventricular wall thickness and one or more of the following: Methods: propanodicarboxylic acid (99mTc-DPD) scintigraphy.

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 echocardiography in 60 consecutive CA patients (age 64±10 years, 55% male) and 30 normal controls (age 61±8 years, 60% male). All patients were enrolled in prospective clinical follow-up (median 274, quartiles 90–900 days). The endpoint was all-cause. 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 rates. Furthermore, Tei index tended to be positively associated with E/e'. 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.

Coexistence of degenerative aortic stenosis and wild type transthyretin-related cardiac amyloidosis: a potentially dangerous association that can be non-invasively identified

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Diagnostic and Specialty Medicine – DIMES, Bologna, Italy; 2 University Hospital Policlinico S. Orsola-Malpighi, Cardiology, Department of Experimental, Diagnostic and Specialty Medicine – DIMITES, 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 could negatively influence the outcome of elderly patients with aortic stenosis undergoing transcatheter aortic valve replacement (TAVR), TTR-related cardiac amyloidosis can be accurately identified by tecknetium-99m-diphosphono-1,2-propanodicarboxylic acid (99mTc-DPD) scintigraphy.

Purpose: To investigate the coexistence of cardiac amyloidosis in elderly patients with aortic stenosis referred for aortic valve replacement (TAVR) or more of the following: paradoxical low flow-low gradient severe AS, QRS voltage-left ventricular (LV) wall thickness mismatch, echocardiographic findings suggestive of myocardial fibrosis (increased thickness of LV-ventricular free wall, inter- atrial septum or right ventricular free wall, pericardial effusion, granular sparkling of ventricular myocardium). Cases with intense myocardial tracer uptake underwent endomyocardial biopsy (EMB).

Results: Five out of 42 patients underwent 99mTc-DPD scintigraphy that showed severe aortic regurgitation in all. EMB demonstrated TTR-related amyloid infiltration in all cases. Genetic analysis excluded TTR gene mutations; so wt-ATTR was diagnosed. Median age was 88 (range 86–91). 3/5 were males. Two had a history of cardiac tunnel syndrome and all were symptomatic (exertional dyspnoea, NYHA class III–IV). At echocardiography mean LV wall thickness was 18±2 mm, LV ejection fraction was 54±10% (38%–64%). Functional aortic valve area was between 0.4 and 0.9 cm²; one case had a low flow-low gradient and reduced LV ejection fraction (38%); maximum aortic gradient in the other 4 cases was 59±30 mmHg. At TAVR, 4 patients had severe AS and mild pericardial effusion was present in 3 cases. Tissue Doppler S wave was reduced in all cases. QRS voltage was normal in one and increased in 4 patients.

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.

First arrhythmic event-associated clinical disease profile in arrhythmogenic cardiomyopathy associated desmosomal mutation carriers

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Purpose: Arrhythmogenic Cardiomyopathy (ACM) is a genetically determined disorder, mostly caused by mutations in genes encoding desmosomal proteins. Progressive nature of disease results in dynamic changes of the electrocardiographic and structural/functional characteristics during follow-up. We evaluated phenotypic characteristics to be associated with the first major arrhythmic event in desmosomal mutation associated ARVC families.

Methods: A cohort of 105 desmosomal mutation carriers belonging to 39 consecutive ACM families was studied. The families were 13 of PKP2, 14 of JUP, 0.63

(0.63)

Methods: Serum C-terminal propeptide of collagen type-I (CICP), C-terminal telopeptide of collagen type-I (CITP), matrix metalloproteinase (MMP)-1, and tissue inhibitor of matrix metalloproteinases (TIMP)-1 were measured.

Purpose: We investigated prospectively whether serum markers of collagen turnover could be used as predictors for the occurrence of malignant ventricular arrhythmias in patients with NIDC implanted with an implantable cardioverter defibrillator (ICD) for primary prevention.

Results: Forty-three (41%) participants experienced the primary arrhythmic outcome at median age of 29 (21–46) years. The first event was sustained ventricular tachycardia in 31 and sudden cardiac death in 12. Definite diagnosis according to 2010 Task Force criteria showed 57% positive and 100% negative predictive value for the occurrence of arrhythmic outcome. Repolarization abnormalities (mean odds ratio range 6.94–9.09) and left ventricular dysfunction (mean odds ratio range 7.07–8.19) independently associated with clinical disease profile at the time of event.

Conclusions: Repolarization abnormalities and left ventricular dysfunction are important components of the first event-associated clinical disease profile independently of gender and genotype. Clinicians should be alerted in the appearance of such abnormalities during follow-up.

The ability of serum markers of fibrosis to predict future shocks in ICD recipients with dilated cardiomyopathy

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Background: Extracellular matrix (ECM) alterations in non-ischemic dilated cardiomyopathy (NIDC) may provide electrical heterogeneity, thus potentially contributing to the occurrence of ventricular arrhythmia and subsequent SCD.

Methods: Serum C-terminal propeptide of collagen type-I (CICP), C-terminal telopeptide of collagen type-I (CITP), matrix metalloproteinase (MMP)-1, and tissue inhibitor of matrix metalloproteinases (TIMP)-1 were measured.

Purpose: We investigated prospectively whether serum markers of collagen turnover could be used as predictors for the occurrence of malignant ventricular arrhythmias in patients with NIDC implanted with an implantable cardioverter defibrillator (ICD) for primary prevention of SCD. Patients were evaluated for any appropriate ICD delivered therapy, whether shock or antitachycardia pacing, during a 1-year follow-up period.

Results: Appropriate device therapies were delivered in 14 of the 70 patients during the follow-up period, with antitachycardia pacing in 2, antitachycardia pacing with shocks in 4, and shocks in 8. Preimplantation MMP-1 levels were significantly higher in patients who had appropriate ICD-delivered therapy than in those who did not (8.9±14 ng/ml vs. 58±18 ng/ml, p=0.008 and 0.46±0.19 ng/ml vs. 0.19±0.07 ng/ml, p=0.001).

The same was true for baseline serum concentrations of TIMP-1 and CITP (89±14 ng/ml vs. 58±18 ng/ml, p=0.008 and 0.46±0.19 ng/ml vs. 0.19±0.07 ng/ml, p=0.001).
Conclusions: Undoubtedly, ECM alterations play a crucial role in the constitution of an arrhythmicogenic substrate in NIDC and, given the availability of therapies to prevent fatal ventricular tachyarrhythmias, the quest for factors that have a very good correlation with appropriate ICD discharges in these patients is logical. Our results confirm the role of serum markers of collagen turnover as predictors of arrhythmic events in ICD recipients and could provide an auxiliary tool in this context.

P2643 | BEDSIDE
Novel epsilon wave characteristics in arrhythmogenic cardiomyopathy
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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 as 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 two-dimensional echocardiography. Epsilon waves 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 T wave onset and measured with an automated software. 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 septal segment of the left ventricle (p=0.94). Patients with epsilon waves exhibited increased RVOT diameter (p=0.0001). 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=0.0001). 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
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Background: We investigated the efficacy of macitentan in combination with sildenafil on hemodynamic and morphological parameters in rats with monocrotaline-induced PAH.

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, i.p.); group 3 [MCT-macitentan (10 mg/kg/day)]; group 4 [MCT-macitentan + sildenafil (10 mg/kg/day + 50X2 mg/kg/day)]; RV afterload was assessed by measurement of PASP from TR velocity and right atrial pressure. For quantification of RV performance, FAC was measured. Differences from baseline were investigated and the effects of sildenafil and macitentan were compared with control and sildenafil-alone 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.

P2645 | BEDSIDE
Lack of pharmacokinetic interaction between the dual endothelin receptor antagonist macitentan and the combined oral contraceptive, estrogen and ethinyl estradiol
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Background: Macitentan is a dual endothelin receptor antagonist (ERA) approved for the long-term treatment of pulmonary arterial hypertension. ERAs have been associated with teratogenicity 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 women 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 (AUC∞) 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 AUC∞ of the HC were within the bioequivalence criteria. For EE, geometric mean ratios (90% CIs) of Cmax and AUC∞ were 0.92 (0.85, 0.99) 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 co-administered with macitentan were well tolerated. The most frequently reported AE was headache (69%). One serious AE (asthma bronchiale), assessed as the AEs related to macitentan, 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 | BEDSIDE
Audit of prostanoid use in a nationally designated PH centre
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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, treprostil and iloprost, subcutaneous treprostil and nebulised iprost. Prostanoid 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 non operable (CTEPH-NO) 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 PAH and CTEPH-NO 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 yrs).

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 58ng/kg/min for those on treprostinil.

P2647 | BENCH
Comparison of caveolin-1 isoforms expression in the right ventricle and lungs of monocrotaline induced pulmonary hypertension
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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 hypertenion.

Methods: Wistar rats was injected with monocrotaline (MCT; 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 after stopping treprostinil, leynapha, and significant weight loss.

Results: MON-treated rats had lower body weight when compared to controls (MON: 242±46 g vs. CON: 236±44 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 weight was significantly increased (MON: 0.28±0.02 g vs. CON: 0.17±0.01 g, P<0.05), as well as the weight of lungs (MON: 247±12.0 g vs. CON: 172±0.04 g, P<0.01). Caveolin-1 expression in the right ventricle was diminished (MON: 66±14 vs. CON: 100±29) and in lungs was significantly decreased (MON: 30±11 vs. CON: 100±27, P<0.01). The expression of phosphorylated isoform pTyr14CAV-1 when calculated as pTyr14C_AV-1/CAV-1 ratio was not changed in the right ventricle (MON: 98±35 vs. CON: 100±26), while in lungs was significantly increased (MON: 135±64 vs. CON: 100±24, P<0.05). Further the mRNA level of CAV-1 alpha isoform was significantly reduced in the right ventricle (MON: 0.5±0.04 vs. CON: 1±0.10, P<0.01) and so was in lungs (MON: 0.57±0.07 vs. CON: 1±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±0.19, P<0.01), as well as in lungs (MON: 0.43±0.06 vs. CON: 1±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 pTyr14C_AV-1 in lungs and its unchanged amount in the right ventricle can point to a different progressing processes in these organs.

Acknowledgement/Funding: APVV-0887-11, VEGA 1/0981/12, VEGA 1/0564/13

P2648 | BEDSIDE
Evaluating hemodynamics at rest and exercise capacity by echocardiographic parameters in patients with pulmonary hypertension
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Introduction: Cardiac index (CI) at rest and peak VO2 during exercise are prognostic factors of long-term survival in pulmonary hypertension (PH). Echocardiography is widely used for assessing severity of PH as a non-invasive and useful method. The relationship of these prognostic factors and echocardiographic parameters are not studied in detail.

Purpose: We have investigated the relationship between hemodynamics at rest or exercise capacity and echocardiographic parameters routinely measured in patients with PH.

Methods: From April, 1, 2012 to August, 31, 2014, we examined transthoracic echocardiography, right heart catheterization and cardiopulmonary exercise testing (CPET) in 36 patients who were admitted to our institution. Patients with left heart disease, adult congenital heart disease and those with obstructive or restrictive lung disease were excluded.

Results: Mean age was 53±14.8 yrs, 28% were males and 33% of the patients were in WHO functional class III/IV. Mean values of the hemodynamics were: pulmonary vascular resistance (PVR) 13.1±7.4 Wood Units, mean pulmonary arterial pressure 47.4±11.0 mmHg, CI 2.1±0.7 L/min/m2. Mean peak VO2 obtained by CPET was 13.9±4.5 mL/kg/min. First, the relationship between echocardiographic parameters and hemodynamics were tested. There was no correlation between the ventricular end-diastolic dimension (LVdD) and early diastolic velocity of the septal mitral annulus (E) strongly correlated with CI (LVDd: R=0.614, P<0.001; E': R=0.633, P<0.001). Right atrial pressure (RAP) was significantly correlated with CI (R=0.494, P<0.003; RAP: R=0.504, P<0.002). Multiple regression analysis incorporating clinical, laboratory findings, hemodynamics and echocardiographic parameters, revealed that LVDd and E' were significantly associated with CI at rest (LVDd: β=−0.477, P<0.001; E': β=−0.599, <0.001). Second, the purpose was to evaluate the role of ACE and ACE2 in pulmonary hypertension capacity were analyzed. TRP; TAPSE and LVdD significantly correlated with peak VO2 (TRPG: R=−0.595, P<0.001; RAP: R=0.548, P=0.001; LVDd: R=0.478, P=0.004). Multiple regression analysis showed that TAPSE and TRP were significantly associated with peak VO2 (TAPSE: β=−0.146, P=0.018; TRPG: β=−0.365, P=0.035). Conclusion: In patients with PH, LVDd and E' were significantly associated with CI, while TAPSE and TRPG were significantly associated with peak VO2. Echocardiography is useful in predicting prognostic factors of PH both at rest and during exercise.

P2649 | BENCH
Involvement of angiotensin converting enzyme 2 in pulmonary hypertension
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Introduction: Pulmonary hypertension (PH) is a rare disease characterized by hypertrophy 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 measured.

Results: Patients with PH had a significantly higher ACE2 activity (40±4±6 U/l) compared with the control group (22.6±2±1 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 plane systolic excision (TAPSE) also significantly correlated with right ventricular ejection fraction (p=0.05). Similarly, the activity of ACE positively correlated with the inversely measured mean pulmonary arterial pressure (mPAP) values (p=0.01, n=13). In contrast, a significant, negative correlation was identified between circulating ACE activities and mPAP (p<0.05, n=9). There was no significant connection in the concentration and activity of ACE in the PH and control groups. There was no correlation between the echocardiographic parameters (diameters of left atrium and left ventricle, wall thickening, calculated right ventricular pressure) and the activity of ACE, ACE2 and amount of ACE.

Conclusion: ACE shedding increases in parallel with the progression of pulmonary hypertension, suggesting a role for ACE2 in the pathomechanism of the disease. Moreover, ACE2 was identified as a serum biomarker of PH, which can be used to screen patients with potential PH and to follow the progression of disease.

P2650 | BEDSIDE
Comparison of the effects of bosentan on endothelial function in patients with pulmonary arterial hypertension or chronic thromboembolic pulmonary hypertension
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Background: Although bosentan, a dual endothelin receptor antagonist, is effective for the treatment of pulmonary arterial hypertension (PAH), it is often contraindicated 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 the FMD between the two groups at baseline. There was 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 (6.0±2.37% vs. 8.0±7.18%; p<0.0001). FMD was also significantly improved after bosentan treatment in patients with PAH associated with collagen tissue disease (6.4±8.17% vs. 8.3±3.16%; p=0.023) and in those with PAH associated with other comorbidities and idiopathic PAH (5.7±6.09% vs. 7.6±8.08%; p=0.001). However, in patients with CTEPH, there was no significant difference in FMD after bosentan treatment (5.3±5.37% vs. 8.16±2.98%; 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 of peripheral endothelial function in patients with PAH.

P2651 | BESIDE

**Baseline characteristics and outcome of adult patients with pulmonary hypertension in Africa: results from the Pan-African Pulmonary Hypertension Cohort (PAPUCO) study**

<table>
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<tr>
<th>PE (n=80)</th>
<th>MT (n=198)</th>
<th>P-value</th>
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<tr>
<td>Survival 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% (p&lt;0.009).</td>
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<td>Conclusion: In CTEPH, these data confirm better outcomes due to PE compared to MT. Mortality of Spanish CTEPH patients undergoing PE, which seems to be due to a low referral rate for operability assessment.</td>
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**Acknowledgement/Funding:** Bayer Schering Pharma for supporting this Registry (REHAP)

P2653 | BESIDE

**Sleep-disordered breathing in pulmonary arterial hypertension PAH and in pulmonary hypertension due to left ventricular dysfunction - comparison of clinical characteristics**

<table>
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**Acknowledgement/Funding:** Bayer Schering Pharma for supporting this Registry (REHAP)
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 1st January 1970 and 31st December 1993 with a diagnosis of congenital heart disease according to the International Classification of Diseases (8th, 9th and 10th edition). Follow-up data collected for all patients until 31st 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. 13.7 times higher (95%, p < 0.001, CI 1.16–16.33) 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, the age of diagnosis or the complications of heart malformations (according to the same 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 66% 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 patients with congenital heart disease 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

GROW-UP CONGENITAL HEART DISEASE AND SURGERY

P2654 | BEDSIDE Survival into adulthood of patients with congenital heart disease in Sweden

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Background: The aim of the present study was to investigate the survival trends in children with congenital heart disease who reaching adulthood in Sweden.

Purpose: The aim of this study was to clarify the incidence of endocarditis in adults with congenital heart disease.

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.

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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 High incidence of endocarditis in adults with congenital ventricular septal defect

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Background: Ventricular septal defects (VSD), if hemodynamically important, are usually 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

P2656 | BEDSIDE The unnatural history of valvular pulmonary stenosis: outcome up to 40 years after surgical repair

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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±3.4 years after surgical correction of PS during childhood between 1968–1980.

Results: 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 was 90% at 30 years (Fig. 1a) and 69% at 35 years (Fig. 1b) and 35% in 13%, LVEF by biplane Simpson method was abnormal 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, re-intervention 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-B-073

P2657 | 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 may be at increased risk of hemorrhagic stroke potentially due to concomitant intracranial vascular malformations reported to be associated with certain diagnoses.

Purpose: We sought 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 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,
coarctation of aorta and Ebstein’s anomaly); The risk of hemorrhagic stroke was
associated with the second Marelli group, HR 4.28 (95% CI 2.03–6.60, p < 0.001)
compared to controls. Furthermore, patients with a complex congenital heart dis-
ease 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. Fur-
ther studies are needed to understand the mechanisms of hemorrhagic stroke in young
patients with congenital heart disease.

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Medical Research Council, and partly by grants from Stroke Centre West in Swe-
den.

P2658 | BEDSIDE
Macitentan superior to bosentan in pulmonary arterial hypertension
due to congenital heart disease?
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A.P.J. Van Dijk2, A.H. Zwijnder1, B.J.M. Mulder1, B.J. Bouma1,
1Academic Medical Center of Amsterdam, Cardiology, Amsterdam, Netherlands;
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Background: Recently macitentan, a new oral endothelin receptor antagonist
(ERA), has shown to improve mortality and morbidity of patients with 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, cur-
rently on bosentan treatment, were evaluated with a standardized treatment pro-
tocol, 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
Wilcoxon signed-rank analyses to investigate changes in 6-MWD, WHO functional
class, and biomarkers.

Results: Currently 35 PAH-CHD patients were switched to macitentan (mean
age 45 years, 43% male, 34% Down syndrome, 74% Eisenmenger syndrome).
No serious adverse events were reported. After three months macitentan treat-
ment, WHO classification improved in 8 (28%) and worsened in 2 (7%) patients
(mean difference – 0.42, 95% CI – 1.03–0.20, p=0.031). No change in 6-MWD (391±128 to 402±127 meters, p=0.196) was de-
noted. NT-pro-BNP was significantly reduced (723 to 496 ng/L, p=0.031), while
K. Wadell4, B. Johansson1.

Conclusion: Our preliminary data suggests that a switch from bosentan to maci-
tentan is nowadays incorporated in clinical practice. We compared the predictive
abilities of biomarkers cystatin C and NT-pro-BNP outperformed the functional
parameters in predicting mortality and clinical events in PAH-CHD patients. There
is no evidence to support whether PAH-CHD patients are at increased risk of mortality
and clinical events.

P2659 | BEDSIDE
Comparative outcomes after acute aortic dissection in genetic
toapthopathy syndromes
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Aims: Aortic dissection at a young age is often the first manifestation of a genetic
aortopathy, including non-syndromal thoracic aortic aneurysms and dissections
(TAAD), Marfan syndrome (MFS) and bicuspid aortic valves (BAV). Outcomes
after dissection for TAAD are less well known than for MFS. Risk factors for dis-
section and subsequent outcomes are less well known for BAV and TAAD.

Methods: Probands presenting with acute dissection between 1988 and 2014
were evaluated for an underlying genetic aortopathy, enrolled in a surveillance
program and family members were screened. Outcomes were compared with adult
patients without dissection using Kaplan-Meier, logistic and Cox regression
models.

Results: A total of 144 probands (age 43.7±10.1 years, 76% male; 76% TAAD,
19% MFS, 4% BAV) were compared with 623 patients without dissection (age
35.4±13.9 years, 72% male; 33% TAAD, 31% MFS, 36% BAV), of whom 102
were first-degree relatives. Median follow-up was 7 years (interquartile range 3–
15 years). Independent predictors for presentation with dissection included TAAD
(odds ratio (OR) 12.6 (95% confidence interval (CI) 5.3–29.9)), MFS (OR 6.9
(95% CI 2.6–17.2)), family history of aortic dissection (OR 3.3 (95% CI 2.2–5.1))
and age (OR 1.05 (95% CI 1.03–1.07); all p<0.001). Aortic diameter at time of
dissection was <50 mm in 45% and did not predict presentation with dissection
(p=0.104). Survival after dissection was comparable between TAAD, MFS and
BAV patients (p=0.899), but lower than in patients without dissection (p<0.001).
Recurrent dissections occurred in 15 (19%) probands (TAAD n=11, MFS n=3,
BAV n=1; p=0.091), with family history of aortic dissection as the only indepen-
dent risk factor (hazard ratio 3.6 (95% CI 1.1–11.8); p=0.032).

Conclusions: Risk of aortic dissection is greater with TAAD than with MFS or
BAV and is independent of aortic diameter. Recurrent dissection may be more
likely in TAAD, although long term survival was similar for MFS and TAAD. Family
history of aortic dissections is a strong predictor for both presenting with acute
dissection and re-dissection.

P2660 | BEDSIDE
Functional parameters or biomarkers: which best predicts prognosis
in adults with pulmonary arterial hypertension due to congenital heart
disease?
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Background: Adults with pulmonary arterial hypertension due to congenital heart
disease (PAH-CHD) have a poor prognosis. Current guidelines emphasize to fo-
cus on functional parameters, including six-minute walk distance (6-MWD) and
WHO functional class, while in acquired left sided heart failure the use of biomark-
ers is nowadays incorporated in clinical practice. We compared the predictive
value on both functional parameters and biomarkers for mortality and clinical
events.

Methods: In this prospective observational study clinical variables, including
functional parameters and biomarkers, were determined in 91 consecutive PAH-
but not controls (mean age 41 years, 40% female) between 2010 and 2014. Clin-
sical events comprised worsening functional classification, worsening heart failure,
symptomatic hyperviscosity, haemoptysis and arrhythmia. We used Cox regres-
sion to determine predictors for mortality and clinical events.

Results: Median follow-up was 4.8 years (range 0.1 to 9.3 years), during which
28 (31%) patients died. Age (HR 1.3, 95% CI 1.1–1.5), TAPSE <15 mm (HR 3.2,
95% CI 1.4–7.3), cystatin C (HR 1.2, 95% CI 1.1–1.4), estimated glomerular fil-
tration rate (HR 0.8, 95% CI 0.7–0.9) and NT-pro-BNP (HR 1.7, 95% CI 1.2–2.4)
predicted mortality. WHO class and 6-MWD were not predictive for mortality. Simi-
lar results were found for the prediction of clinical events.

Conclusion: Biomarkers cystatin C and NT-pro-BNP outperformed the functional
parameters in predicting mortality and clinical events in PAH-CHD patients. There

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seems to be a more prominent role for biomarkers in decision-making for treatment in PAH-CHD patients.

P2663 | BEDSIDE

Evaluation of transition services for adolescents with congenital heart disease: attendance at first adult congenital cardiac appointment
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Background: Transition to adult services for young adults with chronic conditions is a contemporary and challenging issue. Most congenital heart disease (CHD) patients require lifelong specialist care and follow-up. At our institution CHD patients are cared for by a paediatric cardiologist and then transfer to the adult congenital heart disease service (ACHD) within the same campus. There has been a developing transition programme over the last five years which has included information leaflets about the move to adult services, transition information days for patients and families and joint transfer clinics led by a patient’s paediatric cardiologist together with an ACHD consultant and clinical nurse specialist (CNS).

Purpose: To evaluate the effectiveness of our transition process and transfer clinics in ensuring CHD patients are not lost to follow-up in the transfer of care from paediatric to adult congenital cardiac services.

Methods: We retrospectively identified those CHD patients who had attended a transfer clinic and transitioned from paediatric to adult congenital services between 2011–2013. Appointments for, and attendance at, their first ACHD clinic review were identified with the use of the electronic patient record (EPR), patient information system (PIMS) and medical notes as needed.

Results: We identified 112 CHD patients who had attended a transfer clinic. 100% of patients had at least one ACHD clinic appointment on file: 23 (20%) had their first ACHD appointment booked for a future date to the time of data analysis. Of the remaining 89 patients, 78 (87.5%) had attended their first scheduled ACHD clinic. Patients who did not attend (DNA) their first appointment were then phoned and sent subsequent dates: 5 (5.6%) attended their 2nd clinic appointment and 2 (2.2%) attended on their 3rd or 4th appointment. 2 patients (2.2%) failed to attend any appointments and were identified as having left the country and 2 patients (2.2%) are not traceable.

Conclusion: This audit highlights the effectiveness of a transfer clinic and transition process in ensuring the seamless transfer of care to the ACHD service within our institution. However, although the 87.5% attendance rate at the first scheduled appointment is high, further work from our ACHD cardiac catheter and transfusion clinic and CNS specialists and clinic administration staff was required to ensure 96% of patients were eventually seen in an ACHD clinic. Further work is planned to explore the reasons behind the DNA rate.

P2664 | BEDSIDE

Chronological changes in mitral regurgitation after atrial septal defect closure in adults; predictors of aggravation of mitral regurgitation
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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. MR of ASD 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, and after 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
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Background: Quantification of ventricular kinetic energy (KE) in patients with single ventricle and Fontan circulation has not been investigated. A normal LV KE may be linked with improved cardiovascular outcomes. The purpose of our study was to measure LV KE in patients with a Fontan circulation and determine if the KE was decreased compared to controls.

Methods: Eleven patients (3 females, median age 12, range 3–29) with functional single ventricle and Fontan circulation underwent CMR with a 1.5-T Philips scanner including a four-dimensional phase-contrast flow sequence. Eight healthy volunteers (2 females, median age 26, range 23–36) were used as a reference. Ventricular segmentation was performed in 30 time frames per cardiac cycle and imported to the 4D flow dataset. Ventricular KE was calculated as KE=1/2mv^2 and was normalised over all voxels inside the ventricle and calculated as KE=1/2mv^2/ρv^4. A significant reduction in KE was defined as a decrease of KE/ρm>0.85. The mean follow-up period was 25±5 (range 3–31) months.

Results: The mean KE indexed for LV end-diastolic volume (EDV) and peak KE indexed for EDV in group F was significantly lower than in controls (12.1±4.8% vs –25.9±4.1%, respectively, P<0.06) and LV torsion (12.1±5.4% vs –25.9±6.1%, respectively, P=0.03) were similar to those measured in controls. At multivariate analysis global LV longitudinal strain was significantly correlated only with age at surgery (P<0.005; Coeff. =–0.046; Std.Error=0.016).

Conclusions: To the best of our knowledge this is the largest study on ASO patients by using STE. We demonstrated that in asymptomatic ASO patients despite a normal LV EF there is a significant reduction in longitudinal myocardial deformation significantly correlated with the age at surgical repair. Thus our findings suggest to early operate d-TGA patients and to continue monitoring ventricular function in such patients assessing also global longitudinal deformation.
in patients compared to controls (p < 0.001). Patients with a short outflow tract and the aortic valve situated more proximal in the ventricle had similar systolic and diastolic KE peaks resembling the controls left ventricular pattern. Patients with a more prolonged outflow tract had higher systolic KE peak than diastolic resembling the right ventricular pattern of controls.

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.

EXERCISE IS THERAPY IN HEART DISEASE

P2666 | BEDSIDE
Effects of functional electrical stimulation of lower limb muscles on circulating endothelial progenitor cells, CD34+ monocytes and VEGF-A in heart failure with reduced ejection fraction

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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 endothelium-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 (HFRHF).

Methods: Fontan patients with lower diastolic E/E’ (p < 0.002) and a marginally significant increase in EPC (p = 0.003). FES induced a significantly higher increase in VEGF-A [Δ-VEGF-A/Δ-6MWD (rho=0.549, p = 0.003) and Δ=MHC/Δ-E/E’ (rho=−0.597, p=0.001)]. Δ-VEGF-A and Δ-EPC correlated significantly with Δ-6MWD (r=0.549, p=0.003 and r=0.684, p=0.001, respectively) and Δ-CD34 both with Δ-6MWD (r=0.648, p<0.001) and with Δ-E/E’ (r=0.597, p=0.001).

Conclusions: FES induces similar changes in VEGF-A and EPC and CD34+ cell mobilization in parallel to improving exercise capacity and central hemodynamics in HFRHF.

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 measure essential in vivo LV 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. There was no gender difference in LV thickness. The diastolic fraction of mice was similar to the males (+24.5% female vs. +31.3% male, p = 0.05) and it was more pronounced in females. The myocardial fibrosis was more pronounced in females (+27.7% female vs. +14.5% male, p = 0.05) but gender differences in LV hypertrophy were not significant between males and females.

Conclusions: Gender differences in LV hypertrophy were not significant. Gender differences in exercise-induced LV hypertrophy were more pronounced in females. The diastolic fraction of mice was similar to the males (+24.5% female vs. +31.3% male, p = 0.05) and it was more pronounced in females. The myocardial fibrosis was more pronounced in females (+27.7% female vs. +14.5% male, p = 0.05). Despite the more significant hypertrophy in females, characteristic functional parameters of athletes’ heart did not differ in males, but increased markedly in females (+14.0% 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 properties and improved LV stiffness in both males and females.

Conclusions: In conclusion, we report that exercise training improves LV systolic function in both males and females, while increasing LV diastolic stiffness in females. The gender-specific response of the LV to exercise is modulated by characteristic molecular pathways.

P2668 | BENCH
Exaggerated exercise blood pressure response is related to increased arterial stiffness, asymmetric dimethylarginine and osteoprotegerin in essential hypertension

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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 atherosclerosis 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 I 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 >210 mmHg 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 (pNS). 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<0.0001), OPG (5.4±0.1 vs 4.1±0.5 pmol/l, p<0.0001) and PWV (8.9±1.7 vs 7.5±0.9 m/sec, p<0.0001), independendty 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<0.0001), ADMA (r=0.284, p<0.05) and PWV (r=0.424, p<0.0001).

Multiple regression analysis showed that 24-h systolic BP (β=0.210, p<0.003), male sex (β=0.270, p<0.05), ADMA (β=0.225, p<0.006) and OPG (β=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 sympathetic activity. We measured serum high-sensitivity C-reactive protein (hs-CRP) and thrombomodulin as parameters of vascular endothelial damage in a cohort of 100 consecutive HF patients (p), 68.8±10.8, 71% male, class IIIb/IV, mean ejection fraction=31%, who underwent exercise testing using standard Bruce protocol and were submitted to cardiac resynchronization therapy (CRT). Lately, in small groups of patients, exercise modalities like high intensity interval training (HIIT), seem to have beneficial central and peripheral effects.

Methods: Study of 100 consecutive HF patients (p), 68.8±10.8, 71% male, class

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 (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 (p<0.05).}

Conclusion: 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

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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 amlopidine (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 ∆SBP ≥210mmHg in men and ∆SBP ≥190 mmHg in women) and those without HRE (n=170).

Conclusion: Increased activity of RAAS induced vascular endothelial damage resulting in the excessive BP elevation during exercise even at moderate intensity in HT patients.

P2673 | BENCH

High intensity interval training effects in patients with heart failure submitted to cardiac resynchronization therapy

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It is well known that not all patients submitted to cardiac resynchronization for heart failure (HF) positively respond to this therapy. On the other hand, exercise has been demonstrated to have additional benefits to cardiac resynchronization therapy (CRT). Lately, in small groups of patients, exercise modalities like high intensity interval training (HIIT), seem to have beneficial central and peripheral effects.

Aim: To evaluate the effects of high intensity interval training in patients with HF and CRT.

Methods: Study of 100 consecutive HF patients (p), 68.8±10.8, 71% male, class

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 (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 (p<0.05). (Figure).
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 HITT 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 3 months after CRT by: clinical functional class (NYHA) evaluation, echocardiography, for left ventricular ejection fraction (LVEF) and left ventricular end systolic (LVESS) and end diastolic (LVEDV) volumes: cardiopulmonary test, for peak oxygen consumption (VO2p) and duration; 123-MIBG scintigraphy, for early heart-mediastinum rate (HMRR), late heart-mediastinum rate (HRMR) and wash-out (WO).

Results: Comparing the 2 randomized study groups (A and B), clinical functional class variation (Δp) [p=0.01], ΔVO2 (-18.970±29.565 vs 13.21±18.774±p=0.012) and HMRR/045±0.1 vs -0.137±0.202; 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 (Δp=0.004), and ΔVO2 (-18.970±29.565 vs 8.289±18.492; p=0.003) were significantly better in the exercise group. HRMR 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 B and C together, variation of LVEF, LVEDV, LVESS, VO2p and exercise test duration, had no significant difference (p>ns).

Conclusion: Exercise training in heart failure 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 volume or variation of peak oxygen consumption and exercise test duration.

Adequate cardiopulmonary exercise test (HHH1).

Heart rate recovery, measured as the difference between peak HR and HR 1 minute later (HRRR1, bpm).

Results: The results are shown in Table. There were significant improvement in exercise capacity in both groups. Exercise training resulted in significant improvement of HRR1 reflecting parasympathetic nerve activation in LVAD pts without significant effect on HR. On the contrary, exercise training allowed higher levels of physical activities with significant improvement of HR in CT pts but not HRR1, consistent with underlying pathophysiology of denervated transplanted heart.

Comparison of HT and LVAD gpts

<table>
<thead>
<tr>
<th>Heart rate profile</th>
<th>LVAD group</th>
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<tbody>
<tr>
<td>HT baseline</td>
<td>LVAD group</td>
</tr>
<tr>
<td>MET level</td>
<td>5.3±1.6</td>
</tr>
<tr>
<td>Resting HR (bpm)</td>
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<tr>
<td>Peak HR (bpm)</td>
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<td>HRRR1 (%)</td>
<td>2.7±3.4</td>
</tr>
<tr>
<td>CR (%)</td>
<td>35±15</td>
</tr>
</tbody>
</table>

Conclusions: The opposite divergent relationship of HRR1 and CR among post heart failure pts and LVAD pts reflected different pathophysiologic 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 French multicenter study on the combination of exercise training + electrical myostimulation treatment in chronic heart failure (HF-CREMS study)

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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 quadricipital 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 mass and 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/IV: 52/48%; LVEF: 29.75±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) quadricipital EMS sessions (20”on/20”off, 1 hour/session). Before and at the end of the protocol, all the patients performed a cardiopulmonary stress test, a 6 min walking test, evaluation of muscular circumference, strength and biological assays (CPK, LDH, Aldiole, 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 consistent for sub maximal parameters (gain of VO2 max: +17 ± 11 %, anaerobic threshold: + 8 ± 10%) and for muscular circumference and strength and 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

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1 University 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 normotenstive men.

Methods: Participants from the Kuopio Ischemic Heart Disease Study underwent symptom-limited maximal exercise testing using a cycle ergometer at baseline and 10 year follow-up. This prospective study included 431 participants (mean aged 50±6.7 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 32.7 ml/kg/min), conducted at the 11-year follow-up. The change in CRF (%) was classified on the basis of quartiles as percentages.

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 (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.

Conclusions: This 21-year follow-up study demonstrated that more marked decreases in CRF were independently associated with the risk of hypertention.

**P2677 | BEDSIDE**

Physical inactivity increases endostatin and osteopontin in patients with coronary artery disease


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Background: The balance between the angiostatic factor endostatin (ES) and...
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

ExerciseTraining prevents diastolic dysfunction induced by fructose overload in old female ovariectomized rats

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In the present study we investigated whether exercise training can prevent the MS and cardiac structural and functional changes in presence of a high fructose diet in aging animals. Aged female Wistar rats (24 months) were ovariectomized and treated with an overload of D-fructose for induction of SM. The animals were divided into 5 groups: Control (C) Ovariectomized (O), Fructose (F), Trained (T) and Trained Fructose (TF). Animals from T and TF groups were submitted to exercise training (ET) 1 h/day, 5 days/wk for 8 wk on a treadmill. Training decreased the adipose tissue (T: 4.3±0.5 g vs. 5.3±0.7 g). ES and OPN concentration decreased significantly with increasing activity level (F=5.5; p<0.001 and F=3.6; p<0.01). ES/OPN dependent on physical activity

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.
Results: The prevalence of VE was similar in athletic 0.6% (n=34) and non-athletic 0.6% (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 diameters. On the contrary, athletes with VE had significantly greater maximal LV wall thickness and larger right ventricular diameters (RV1D, RV2D, RV3D) 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-recification analysis shows rate-dependent intranodal conduction facilitation related to physical conditioning status
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Introduction: Dynamic coupling between atrio-ventricular duration (AVD) and RR-interval relates to AV conduction facilitation and susceptibility to supraventricular arrhythmias. Phase-recification 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-recification-driven RR-interval coupling.

Methods: Heart-ludenary (HS, n=10, 8±7.9 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 100ms-width classes, from 700ms to 1200ms. For each class, mean of normal RR-intervals (MRR) and mean of the peak-to-peak P-R wave interval (MRP) 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. (p <0.05)

Results: No overall intergroup differences regarding MPR vs. MRR 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-recification-dependent behavior, with steepest PR/RR slopes observed during parasymptomatic driven AC phases, reflecting sympathetic and parasympathetic influence on heart rate.

P2683 | BEDSIDE
Right precordial T-wave inversion in healthy endurance athletes can be explained by lateral displacement of the cardiac apex
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Background: T-wave inversion in the right precordial leads (TWIV2–3) on ECG is more frequently observed amongst endurance athletes (EAs) than the general population, the underlying mechanisms for which remain poorly understood.

Purpose: The purpose of this study was to test the hypothesis that TWIV2–3 reflects lateral displacement of the heart such that the surface ECG leads overly a greater proportion of the right ventricle (RV).

Methods: 68 EAs and 41 non-athletic control subjects (C) underwent ECG and cardiac magnetic resonance imaging (CMRI). As well as standard measures of biventricular function and volume, novel measures of cardiac displacement and orientation were analyzed from horizontal long axis images. These included RV wall thickness in diastole (RVD), ratio of cardiac to hemithorax area (C/HTx%), the percentage of the circumferential displacement of the RV apex toward the axilla (%LatD) and the angle of interventricular septum with respect to the thoracic mideplane (%septal).

Results: All cardiac volumes, RVD, C/HTx%, %LatD and %septal were greater in EA than in C. As compared to EAs without TWIV2–3, EAs with TWIV2–3 (n=26) did not have greater RV wall thickness or cardiac volumes (RVD 4.9 vs 4.8 mm, P=0.695, LVEDV 231 vs 229mls, P=0.836, RVEDV 257 vs 254mls, P=0.748) but all measures of cardiac displacement towards the axilla were greater (%LatD 45.6% vs 37.9%, P<0.001, %septal 54.29% vs 46.83%, P<0.001, and C/HTx% 48.3% vs 41.9%, P<0.048).

Conclusions: In healthy EAs, TWIV2–3 is associated with displacement of the RV towards the left axilla rather than RV dilation or hypertrophy. TWIV2–3 inversion may be explained by the position of the RV relative to the surface ECG leads.

P2684 | BEDSIDE
Circulatory power and exercise ventilatory power during exercise over time during sequential combination therapy in pulmonary arterial hypertension
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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-5) was the preferred combination partner, followed by the addition of intra-venous 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<0.001). After further increase in LA size after training, this percentage remained unchanged. Chiari stenosis was normal in athletes both before and after training.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls</th>
<th>Competitive athletes</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA volume index, mL/m²</td>
<td>20.7±4.7</td>
<td>27.1±6.6</td>
</tr>
<tr>
<td>RA volume index, mL/m²</td>
<td>17.3±3.8</td>
<td>23.4±6.3</td>
</tr>
<tr>
<td>LA enlargement criteria</td>
<td>0%</td>
<td>6%</td>
</tr>
<tr>
<td>RA enlargement criteria</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

1Athletes vs. controls; pre-training vs. post-training.
P2685 | BEDSIDE

Influence of cardiorespiratory fitness, body composition and blood pressure on retinal vessel diameters in Swiss primary school children - the sportcheck study

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Background: Cardiovascular risk is associated with retinal arteriolar narrowing and venular widening. The study examined the association of physical fitness, body composition and blood pressure with retinal vessel diameters in young children.

Methods: In the cross-sectional study, 391 primary school children (6–8 years) of the Swiss canton Basel Stadt were screened for body mass index, waist circumference, percentage body fat and blood pressure. Primary outcome was the influence of the 20m shuttle run test with an additional battery test of 20m sprint, jumping sideways and balancing backwards. Retinal microcirculation was examined using a Static Retinal Vessel Analyzer.

Results: The 20m shuttle run test was associated with narrower retinal venular diameters (−0.9 (95% CI: −1.8; −0.1) μm/unit shuttle run, p=0.04). The 20m sprint performance was associated with narrower retinal arteries (4.7 (0.8; 6.6) μm/unit sprint, p<0.002). For the anthropometric parameters, only diastolic blood pressure and not body composition was independently associated with narrower retinal arteries (p=0.003).

Discussion: Endurance but not explosive strength performance has a beneficial influence on retinal vessel diameters. Exercise-based prevention strategies may need to focus more on aerobic endurance games and reduction of diastolic blood pressure in order to promote vascular health in young children.

Acknowledgement/Funding: Department of Education of Basel-Stadt

P2686 | BEDSIDE

Watching television and mortality from pulmonary embolism among middle-aged Japanese men and women: the JACC study


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Background: Several papers have reported that pulmonary embolism was predisposed by prolonged television watching. However, no prospective study has examined the relationship between television watching and the occurrence of pulmonary embolism.

Purpose: To examine the association between prolonged television watching and risk of pulmonary embolism mortality among middle-aged Japanese men and women.

Methods: A total of 86,024 participants (36,007 men and 50,017 women), aged 40 to 79 years, who completed a self-administered questionnaire including information about average television watching time per day at the baseline survey be-sealed between 1980 and 1983, and were followed up for a median duration of 18.4 years. Mortality from pulmonary embolism was identified on the death certificate. Hazard ratios of mortality from pulmonary embolism according to television watching was estimated using Cox proportional hazard model with adjustment for age at baseline, sex, history of hypertension, history of diabetes mellitus, smoking status, drinking status, body mass index, walking and sports habit, and menopausal status.

Results: During the follow-up period, 59 deaths from pulmonary embolism were observed. The multivariate hazard ratios were 1.61 (0.89–2.91) for those watching television 2.5 to 4.9 hours average per day, and 2.38 (1.15–4.93) for ≥5.0 hours with reference to <2.5 hours. Two more hours of watching television were associated with increased risk of pulmonary embolism mortality with multivariable hazard ratio of 1.31 (0.99–1.75, P=0.06). The association was more apparent among the younger ages of <60 years at baseline with multivariate hazard ratios of 3.14 (1.10–8.96) for 2.5 to 4.9 hours and 6.49 (1.93–21.88) for ≥5.0 hours with reference to <2.5 hours.

Conclusion: Prolonged television watching was associated with increased risk of mortality from pulmonary embolism among middle-aged Japanese men and women.

Acknowledgement/Funding: Grants-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan

P2687 | BEDSIDE

Changes in cardiac troponin, natriuretic peptides, D-dimer, and cardiac hemodynamics after strenuous exercise: a meta-analysis

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Background: Acute coronary syndrome (ACS) and pulmonary embolism (PE) are among the most common cardiovascular emergent events. Both 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 the utility of several biomarkers as well as alterations in cardiac function after strenuous sports.

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 in this study.

Methods: We performed a meta-analysis of biomarker changes (cTnT, hsTnT, cTnI, NT-proBNP, BNP, 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 morbidity directly after endurance exercise. Altogether, 45 studies could be included: 33 ones met the inclusion criteria for cTnT, 4 for hsTnT, 12 for cTnI, 17 for BNP, 17 for NT-proBNP, 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 (LVEF).

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/ml (95% CI: 4.26; 16.57), for NT-proBNP +67.30ng/ml (95% CI: 49.93; 84.68), and for D-dimer +262.27ng/ml (95% CI: 165.86; 358.69). RV-EDD increased and RV-EF decreased after exercise, while no significant changes were observed in LVEF.

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 changes can mimic PE, ACS, heart failure or cardiac injury. An accurate interpretation of elevated cardiac biomarkers after strenuous exercise is thus mandatory.

P2688 | BEDSIDE

Physical activity and the incidence of major cardiovascular diseases: Evidence from the China Kadoorie Biobank Study

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Purpose: Higher physical activity is associated with decreased risk of major cardiovascular disease (CVD) in Western populations, but evidence from Chinese populations is limited. Moreover, most previous studies have assessed mainly recreational related physical activity rather than total activity from different domains.

Methods: We analysed prospective data of over 0.5 million people aged 30–79 years who were recruited into the China Kadoorie Biobank Study from 10 areas in China. Information about the frequency, duration and type of activity was used to derive an estimate of intensity in metabolic equivalent of task (MET) of each activity. Physical activity was calculated as MET hours per day (MET-h/d) spent on work, transport, housework, and non-sedentary recreation. After excluding individuals with a prior history of cardiovascular disease at baseline Cox regression models were used to yield hazard ratios (HRs) relating physical activity to disease risk adjusting for age, sex, study area, and other potential confounders. The HRs were corrected for “regression dilution bias” using a self-correlation (−0.52) for MET-h/d ascertained from a re-survey of about 20,000 individuals conducted on average 3 years later to ascertain the association with “usual” physical activity. Results: There was a strong positive association of “usual” physical activity with risk of major CVD with a log-linear dose-response relationship. Comparing the highest (<40 MET-h/d) with the lowest (<8 MET-h/d) physical activity group, there was a 49% lower (95% CI: 44%, 54%) in the risk of MVE, and between 34% and 42% lower risk of stroke, ICH, and ischaemic stroke, respectively. The results did not change materially after exclusions of individuals with other prior chronic diseases and varied little across different subgroups of participants.

Conclusions: In Chinese adults, higher usual physical activity was associated with lower incidence of major cardiovascular diseases. These findings suggest that targeted strategies should be employed to increase levels of physical activity in China.
**P2690 | SPOTLIGHT**

**Suppressed middle-acidity by oral bicarbonate ingestion affected stroke volume responses during an all-out long sprint cycling event**


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**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 VO2AT, which may affect cardiorespiratory effects of exercise on cardiorespiratory progression. Interestingly, 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**

**P2692 | BEDSIDE**

**Exertional oscillatory ventilation as a long-term prognostic factor for patients with post-acute coronary syndrome**


Urasoe General Hospital, Cardiovascular Medicine, Okinawa, Japan

**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 299 post-ACS patients (median age = 59.3 years; 89.0% male; LVEF 59.1±11.8%) who underwent cardiological 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±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) of patients 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

**P2689 | BEDSIDE**

**Usefulness of chest pain units as fast-track screening for ACS in low-intermediate risk patients**


Hospital Universitario Ramón y Cajal, Madrid, Spain

**Purpose:** The potential advantages of chest pain units (CPU) for rapid exclusion of ACS are many, including an appropriate risk stratification, unnecessary hospital admission, 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 with low intermediate risk.

**Methods:** A total of 105 patients presenting chest pain of low-intermediate risk for the ED were included over a two and a half year period. After negative cardiac biomarker determination and normal or incomplete ECG, a stress test was performed the day after admission in the ED; either an exercise treadmill test (ETT) or stress myocardial perfusion imaging (MPI) based upon patient characteristics. Data was analysed using SSSS statistical system.

**Results:** The median age was 58 (13SD) years, 59 (56.2%) were males, with 51 (48%) 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 71.71 (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 revaluated as outpatients. 20 patients presented a non-diagnostic test, thus requiring early follow-up consults in less than 30 days with further 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. CONCLUSIONS: Patients managed in a CPU 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 revaluated 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.

**P2691 | BEDSIDE**

**Cardiovascular adaptation to exercise / Exercise, physical activity and sport in health**


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**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 yr) 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 dilatation (FMD) in the brachial artery. Carotid femoral pulse wave velocity (cPWV) 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, cPWV and ftPWV (p=NS for all). Importantly, both CAE (8.57±2.53% vs. 6.37±1.48%, p <0.05) and hIAE (5.85±1.71% vs. 5.83±1.77%, p <0.001) caused a significant improvement in FMD compared to baseline measurements. Moreover, CAE and hIAE had no impact in cPWV, compared to baseline measurements (p=NS for both). Interestingly, compared to baseline measurements, CAE (8.17±1.48m/sec vs. 9.28±2.0m/sec vs. 9.14±1.07m/sec vs. p <0.002) significantly improved ftPWV.

**Conclusion:** Endothelial function is favourably affected by both continuous moderate-intensity aerobic exercise and high intensity interval aerobic exercise which may exert beneficial cardiorespiratory effects of exercise on atherosclerosis progression. Interestingly, 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.
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 (3942.5 vs. 1866.0 pg/ml, p=0.03) and lower LVEF (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

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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. The main purpose of these scenarios is to elicit individual stress response to RTT and are still lacking. This study aimed at evaluating the predictive accuracy (PA) of heart rate variability analysis (HRVAs) to assess the amount of ATS induced in POs by RTT training including use of force skills.

Methods: Performance monitoring and physical activity were continuously monitored with a seamless garments sensor electrode and a miniaturized telemetric wireless device in 24 POs during RTT. The RWS consisted of different phases providing alternation of low- (LS) and high-stress (HS) challenges. Baseline State-Trait Anxiety and Anger were assessed with the STAI Y1-Y2 and STAXI2 questionnaires. Rating Scale Mental Effort and NASA Raw Task Load Index measured stress and workload. State Anxiety and Anger were reassessed after each RWS. Performance monitored with video cameras was scored by instructors. HRV parameters were computed in the time- and frequency-domain and with non-linear methods, from standard (300-seconds) and very-short (60-seconds) intervals. Discriminant Analysis (DA) was used to identify which parameters were more efficient to assess ATS providing separation between LS and HS.

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 efficient in differentiating between LS and HS. At univariate analysis several HRV features were significantly different (p<0.01) between LS and HS situations. At DA the two stress conditions were screened, and were assessed with the STAI Y1-Y2 and STAXI2 questionnaires. Rating Scale Mental Effort and NASA Raw Task Load Index measured stress and workload. State Anxiety and Anger were reassessed after each RWS. Performance monitored with video cameras was scored by instructors. HRV parameters were computed in the time- and frequency-domain and with non-linear methods, from standard (300-seconds) and very-short (60-seconds) intervals. Discriminant Analysis (DA) was used to identify which parameters were more efficient to assess ATS providing separation between LS and HS.

Conclusions: ATS induced by police RTT determines changes of cardiac autonomic nervous system which are different in LS and HS situations. DA may provide accurate assessment of stress response useful to study the relationship between stress and performance on individual basis and to design more personalized coping training.

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 are defined using the Youden-index. Myocardial ischemia as assessed by MPI was defined as a summed difference score (SDS) of ≥ 2 or presence of a transient ischemic 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 59%, specificity 90%) and lead I was the best second 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 69%, specificity 57%).

P2696 | BEDSIDE
Impaired beta cell function attenuates training effects by reducing the increase in heart rate reserve and heart rate recovery in patients with myocardial infarction

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Background: We had previously reported that maximum oxygen uptake (peak VO2) was reduced in patients with acute myocardial infarction (MI) compared with diabetes mellitus (DM). We also reported that exercise tolerance in DM patients remained low after 3-months of exercise training, and we speculated that blunted heart rate (HR) response to sympathetic nerve stimulation may be the cause of reduced peak VO2 and blunted training effects. This study investigated exercise training effects on the exercise tolerance and heart rate dynamics in patients with insulin resistance (IR) or pancreatic β-cell dysfunction.

Methods: Seventy patients (60.1 years) with MI participating in a phase 2 cardiac rehabilitation program were studied. Patients diagnosed with DM were excluded. Homeostasis model-assessment (HOMA) indices were used to divide patients into 3 groups. HOMA indices were calculated by using immunoreactive insulin (IRI) and fasting blood sugar (FBS) as follows: HOMA-IR = IRI (µU/mL) x FBS (mg/dL)/405 and HOMA-β = IRI × 360/(FBS − 63). We defined IR as a HOMA-IR ≥ 2.0 and impaired β-cell function as a HOMA-β < 0.5. Patients in this study were divided into 3 groups: A, insulin resistance group with HOMA-IR ≥ 2.0 and HOMA-β < 0.5; B, normal group with HOMA-IR < 2.0 and HOMA-β ≥ 0.5; C, impaired β-cell function group with HOMA-IR < 2.0 and HOMA-β < 0.5. A car-diopulmonary exercise test (CPX) was performed and peak VO2 was measured.

Results: The peak VO2 at baseline was comparable between Groups A, B, and C (24.5, 26.1 and 25.7 mL/min/kg, respectively). After training, they improved to 29.4, 29.4 and 28.2 mL/min/kg, respectively (p<0.01). However, both the increase and percentage increase in peak VO2 were lower in Group C than Group A (p<0.05). HR reserve (peak HR – rest HR), and HR recovery immediately 1 min after exercise during CPX were calculated in 45 patients who were not taking negative chronotropic agents. Although the HR recovery in Groups A and B significantly increased after training (baseline vs. after training: 73.4 vs. 85.5, 74.6 vs. 85.3, respectively, p<0.01), it was unchanged in Group C (76.7 vs. 80.4). HR reserve at both baseline and after training had significant positive correlations with peak VO2. HR recovery was 1.9 beats/min lower in group C than group A. HR recovery in group C did not increase after cardiac rehabilitation.

Conclusion: Comprehensive treatment including vigorous exercise training as well as diet therapy will be needed in such prediabetic patients to improve both exercise capacity and β-cell dysfunction.

Exercise, physical activity and sport in health

P2699 | BEDSIDE
Stage 3 or 4 chronic kidney disease disrupts the improvement in exercise capacity after hospital discharge in patients with ischemic heart disease

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Background: Poor exercise capacity is well known to increase mortality after hos-
pital discharge in ischemic heart disease (IHD) patients, which is often detected in them complicated with chronic kidney disease (CKD). Although CKD potentially disrupts the improvement in exercise capacity, it remains unclear in IHD patients. This study aimed to investigate whether CKD disrupted the improvement in exercise capacity after hospital discharge in IHD patients.

Methods: We studied 182 IHD patients (64±11 years, 155 males) who were admitted to our hospital due to unstable angina pectoris or acute myocardial infarction. We assessed patients’ characteristics including estimated glomerular filtration rate (eGFR), left ventricular ejection fraction, duration of hospital stay and quadriceps isometric muscle strength during the hospitalization. Patients with eGFR > 60 mL/min/1.73m² and 15 < eGFR ≤ 60 mL/min/1.73m² were diagnosed with stage 1 or 2 CKD and stage 3 or 4 CKD, respectively. We measured 6-minute walk distance (6MWD) as a parameter of exercise capacity at discharge and 3 months after discharge. We defined the increase of > 33 meters in 6MWD during the follow-up period as a significant improvement of exercise capacity. Multivariate logistic analysis was used to confirm the effect of CKD on the improvement of exercise capacity.

Results: The prevalence rate of patients who showed no improvement in exercise capacity was significantly higher in patients with stage 3 or 4 CKD than with stage 1 or 2 CKD (p<0.002). In the multivariate logistic regression analysis, stage 3 or 4 CKD significantly contributed to no improvement in exercise capacity (odds ratio, 2.16; 95% CI, 1.06–4.39; P<0.03).

Conclusions: Stage 3 or 4 CKD disrupted the improvement in exercise capacity after hospital discharge In IHD 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

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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 to evaluate the impact of regular trainings in pts with advanced heart failure after ICD and CRT implants on quality of life (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 62.1±9.8 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, ns. 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, and 1.5±2.1 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 vs. 1.0±0.6, 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.

**P2698 | SPOTLIGHT**

Carotid intima-media thickness and arterial functional properties in young patients with advanced heart failure and recreational long distance runners and weight lifters - A pilot study

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Purpose: Exercise-induced arterial adaptations hold important implications for cardiovascular health. The aim of the study was the investigation of carotid intima-media thickness and arterial elastic properties of young high level and recreational athletes of dynamic and static sport disciplines.

Methods: 76 healthy male volunteers took part in the project and comprised five groups. Group A consisted of 17 high level long distance runners, aged 30±6.5 years old and group B of 14 recreational ones, aged 28±6.6 years old. 15 high level and 24 recreational athletes comprised group C and 28 elite and 12 recreational ones, aged 25±9±4 years old, comprised group D. Control group E consisted of 14 sedentary men, aged 29±9±3 years old. All athletes denied having taken any illegal performance enhancing substances.

All participants underwent echocardiographic evaluation for the calculation of left ventricular mass index (LVMI) and body surface area adjusted left ventricular end diastolic volume (LVEDV/BSA). Carotid intima-media thickness of right (CIMTR) and left (CIMTL) common carotid arteries was also measured by echo, according to guidelines. Finally, applanation tonometry was applied for carotid-temoral pulse wave velocity (cfPWV) calculation, as the gold standard index of arterial stiffness.

Total arterial compliance (Ct) was derived from cfPWV, with the use of published formula. All tonometrically acquired parameters were evaluated both at rest and in the third minute of a handgrip strength test protocol (index (H)).

Results: LVMI obtained higher values in group A by 23.7% (p<0.05) compared to E. LVEDV/BSA was higher in group A than groups C, D and E by 15.3% (p<0.05), 15.8% (p<0.05) and 14.5% (p=0.07) respectively. No statistically significant differences of CIMTR or CIMTL were reported among groups, but recreational athletes of both sport disciplines obtained lower values than high level ones and non-athletes. At rest, cfPWV was higher in groups C and E by 10.8% (p<0.05) and 20.1% (p<0.01) respectively compared to B. The latter presented higher values of Ct by 25% (p<0.05) than C and by 29.1% (p<0.01) than E. During the handgrip tests groups B and D presented the lowest values of PWV(H) and Ct, respectively.

Conclusion: Recreational level of systematic exercise results in more favorable arterial functional adaptations compared to high level, even in young athletes. Dynamic type of exercise enhances arterial elastic properties to a higher extent compared to the static type.

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Neighbourhood environmental attributes associated with walking in South Australian adults: differences between urban and rural areas

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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; RW: 3.22±0.77 vs 2.61±1.00 and OW: 3.29±0.61 vs 2.77±1.02. 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, 1.78, 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?

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Background: The influence of exercise ‘training’ on baroreceptor function during pregnancy is largely unknown. A recent report suggested that diminished baroreceptor sensitivity (BRS) and reduced cardiac parasympathetic tone in late pregnancy is largely unknown. A previous report suggested that diminished BRS. These presumably advantageous influences of exercise could enhance maternal preparedness for labour via a relative cardiac sympathetic dominance.

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). Multivariate 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. 7.4%, p<0.001). Using multivariate 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

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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. (PWC 170). 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 (MPVA: 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).

Table 1. Exercise BP, screen time and MPVA

<table>
<thead>
<tr>
<th>Subgroups</th>
<th>Mean systolic exercise BP</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>148.7 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>143.3 mmHg</td>
<td>140.1–146.6 mmHg</td>
</tr>
</tbody>
</table>

Discussion: Even with high MPVA, high screen time was associated with a higher exercise BP. In the present study, sitting (or totally inactive) time was associated with a higher exercise BP independent of the amount of physical activity.
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 (6MWLT) 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. We used the 65–75% of maximum heart rate training range, controlled by frequency heart counter FS2 Polar. 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)</td>
<td>50±6±16.95</td>
<td>-</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>24.7±5.64</td>
<td>25.7±5.56</td>
</tr>
<tr>
<td>VO2max (mL/kg/min)</td>
<td>28±2.916</td>
<td>31.8±8.36</td>
</tr>
<tr>
<td>6MWLT (m)</td>
<td>523.7±7.10</td>
<td>608.1±71.78</td>
</tr>
<tr>
<td>Cognitive function (MMSE’s point)</td>
<td>24±0.00</td>
<td>26.4±0.92</td>
</tr>
<tr>
<td>Glycemia (mmol/L)</td>
<td>11±1.57</td>
<td>190.6±23.7</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11±1.32</td>
<td>12.6±1.33</td>
</tr>
</tbody>
</table>
| VO2max, maximum volume of oxygen consumption; 6MWLT; six minutes walk test; MMSE, Mini Mental State Examination.

Conclusion: We found that intradialytic aerobic training has a beneficial effect on functional capacity and cognitive function in CKD patients on HD.

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P2705 | BEDSIDE
Endothelium-dependent relaxation in patients referred for cardiac rehabilitation
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Actual guidelines do not consider flow-mediated dilation as a first line diagnostic test in cardiovascular rehabilitation. However, the endothelium-dependent relaxation of the brachial artery (EDDBA) has been demonstrated to correlate with peak VO2 and to be an independent predictor of outcome in patients with coronary artery disease (CAD) as well as peripheral arterial disease. Aim of the present study was to assess whether EDDBA can predict the response to exercise training (ET) and the outcome of patients referred for an outpatient cardiac rehabilitation program. We prospectively enrolled 467 patients (mean age 64±8) with documented CAD who underwent primary PTCA/stenting (n=229) or CABG (n=238). Patients underwent EDDBA before and after a 24-endurance ET program (each session lasting 40 min) at the hospital gym at 70% of peak VO2 (time from the acute event, 97±65 days from the acute event, despite standard medications. Exercise training improved the EDD response in 80% of pts with an abnormal response at baseline. The results emphasize the importance of EDD in identifying pts with abnormal endothelial reactivity after revascularization which may benefit the most from cardiac rehabilitation.

Acknowledgement/Funding: AOR Lancisi Ancona

P2706 | BEDSIDE
Inspiratory muscle weakness is associated with exercise intolerance in patients with heart failure with preserved ejection fraction
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Background: Inspiratory muscle weakness (IMW) is associated with exercise intolerance in patients with heart failure with reduced ejection fraction. However, such relationship remains unestablished in patients with heart failure with preserved ejection fraction (HPF EF).

Purpose: To evaluate the effect of IMW on exercise intolerance in patients with HPF EF.

Methods: The present study enrolled 40 patients with HPF EF (EF ≤50%). IMW was defined as the percentage of maximum inspiratory pressure to normal predicted values <70%. The function of the diaphragm was assessed by ultrasound measurement of muscle thickening of the diaphragm.

Results: IMW was prevalent in 27.5% of patients. Patients with IMW had significantly lower peak vital capacity to normal predicted values (%VC), lower percent knee extensor muscle strength to body weight (%KEMS), poorer nutritional status as assessed by the geriatric nutritional risk index, and shorter 6-minute walk distance (6-MWD) compared with patients without IMW (all p<0.05). Further, patients with IMW had a lower decrease in end-inspiration (median value: <3.9 mm) was significantly associated with a high prevalence of IMW and reduced 6-MWD (all p<0.05). Subgroup analysis showed that IMW was accompanied by a further decrease in 6-MWD in patients with restrictive pulmonary dysfunction (i.e. >90% of predicted) or lower-limb muscle weakness (median value: %KEMS <30%) (all p<0.05).

Conclusions: In patients with HPF EF, IMW is associated with exercise intolerance, regardless of comorbid pulmonary dysfunction and peripheral skeletal muscle impairment.

Acknowledgement/Funding: JSPS KAKENHI Grants (nos. 60598944 and 25461058).

P2707 | 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, as well as E/e' and pVO2 in patients with both preserved EF (r=−0.33, p=0.007, r=−0.35, p=0.006, r=−0.35, p=0.002, r=0.42, p<0.0001 and r=−0.41, p<0.0001, respectively) and reduced EF (r=−0.65, p<0.0001, r=−0.53, p=0.0008, 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<0.51, p<0.0001, 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=0.0002) In multivariate regression analysis, Vp (r=0.41, p=0.0002), e' (r=0.16, p=0.02) and A (r=0.22, p=0.03) were selected as significant determinants for pVO2 (r<0.59, p<0.0001) in patients with preserved EF, and age (r=−0.45, p=0.002), Hb (r=−0.30, p=0.03) and BNP (r=−0.28, p=0.03) were selected as significant determinants for pVO2 (r<0.76, p<0.0001) in patients with reduced EF.

Conclusions: 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.
P2709 | BEDSIDE
Usefulness of exercise testing in prediction of short-term outcome among patients with stable coronary artery disease
A.M. Kiviniemi¹, T.V. Kentta¹, M.J. Juntilla¹, J.S. Perkoniemi¹, O.P. Piira¹, S. Lepojarvi¹, O. Ukkola¹, A.J. Hautala², M.P. Tulppo², H.V. Hukulä¹ on behalf of The ARTEMIS investigators. ¹University of Oulu, Oulu University Hospital, Medical Research Center Oulu, Oulu, Finland; ²Verve 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 changes to exercise and recovery, indicating abnormal cardiac autonomic function, predict outcome of patients with 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 (p=0.001). The highest quartile of SCORE_Exe (≥2.1) was derived from these HRs, involved 15.8-fold risk (95% CI: 7.3–34.3, p=0.001) for the primary composite endpoint and remained as potent predictor when adjusted for demographic and clinical variables and ejection fraction (HR: 9.9, 95% CI: 4.2–23.3, p=0.001).

Results: Twenty percent patients (1.3%) and 16% cardiac deaths (1.1%) occurred during the follow-up. All EC <95% CI: 2.1–10.0, CRI 55%: 4.2–13.6 and HRR 95% CI: 3.4–95% CI: 1.7–6.8 predicted the primary endpoint independently from each other (p<0.01 for all). The combination of simple exercise test variables, including measured HR, and continuous net reclassification index (0.036, 95% CI: 0.019–0.053, p<0.001) predicted the primary endpoint independently from each other (p<0.01). Reclassification also improved, as documented by categorical (0.264, 95% CI: 0.060–0.467, p=0.011) and net reclassification index (1.197, 95% CI: 0.941–1.453, p<0.001).

Conclusions: The combination of exercise test variables, including measures of fitness and autonomic responses to exercise and recovery, is a powerful predictor of short-term outcome in patients with stable CAD and provides prognostic information beyond established risk markers.

Acknowledgement/Funding: The Finnish Technology Development Centre, the Academy of Finland and the Finnish Foundation for Cardiovascular Research

Exercise training and physical activity 471

P2710 | BEDSIDE
Prognostic value of double product reserve during cardiopulmonary exercise test in patient with idiopathic dilated cardiomyopathy
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Background: The double product reserve (DPR) is as indirect indicator of myocardial oxygen uptake and it has been known to be related with 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±14.5 years, mean ejection fraction 29.5±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/VO2 slope (r=0.61, 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 idiopathic 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 measurements 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.
Exercise training and physical activity / Decreasing cardiovascular risk in vulnerable populations

P2714 | BENCHMARK
Aerobic exercise improves vascular insulin sensitivity by upregulating cholinergic anti-inflammatory pathway in spontaneously hypertensive rats
X.Z. Hou1, Y. Zhang1, C.J. Mi1, W.X. Jing1, L. Yang2, L. Tao3, F. Gao4 on behalf of Insulin. 1Fourth Military Medical University, Department of Physiology, Xi’an, China, People’s Republic of China; 2Fourth Military Medical University, Department of Cardiology, Xi’an, China, People’s Republic of China

Background: Exercise has been recommended as a part of lifestyle modification 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: To demonstrate that aerobic exercise training could upregulate cholinergic anti-inflammatory pathway of 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).

Methods: Venous insulin resistance contributes to elevated peripheral vascular resistance and subsequent hypertrophy. 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.

Results: Young (8-wk-old) hypertensive 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).

Conclusion: The beneficial role of physical activity was proved important only for subjects with normal Body Mass Index, but not for overweight/obese subjects. Thus, clinicians should educate overweight and obese that losing weight is the first target for reducing CVD risk.

P2714 | BEDSIDE
A community pharmacy-based cardiovascular risk screening service implemented in a resource-limited community
Z. Jahangard-Rafsanjani1, N. Hakimzadeh1, K.H. Gholami1, A. Sarayani2, Tehran University of Medical Sciences, Tehran, Iran (Islamic Republic of Iran); 1Institute of Cardiovascular Diseases, Nihon University, Tokyo, Japan

Purpose: To assess the feasibility and effect of a pharmacy-based cardiovascular risk screening service in an urban referral community pharmacy in Iran.

Methods: A community pharmacy-based cardiovascular risk screening service was established in a pharmacy in the central part of Tehran, Iran. A total of 287 clients aged between 30–75 years with or without cardiovascular risk factors were screened.

Results: Seventy-two percent of clients were women, and 48% were obese. One hundred and sixty-three clients (56.8%) had at least one cardiovascular risk factor. The mean age of the clients was 58.8 years. The prevalence of diabetes mellitus was 0.3%.

Conclusion: The findings of our study were (1) the prevalence of diabetes mellitus was 0.3%; (2) the prevalence of obesity was 56.8%; (3) the prevalence of hypertension was 48.1%; and (4) the prevalence of dyslipidemia was 42.2%.

P2715 | BENCHMARK
Aerobic exercise improves vascular insulin sensitivity by upregulating cholinergic anti-inflammatory pathway in spontaneously hypertensive rats
X.Z. Hou1, Y. Zhang1, C.J. Mi1, W.X. Jing1, L. Yang2, L. Tao3, F. Gao4 on behalf of Insulin. 1Fourth Military Medical University, Department of Physiology, Xi’an, China, People’s Republic of China; 2Fourth Military Medical University, Department of Cardiology, Xi’an, China, People’s Republic of China

Background: Exercise has been recommended as a part of lifestyle modification 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.

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P2716 | BEDSIDE
Aerobic exercise improves vascular insulin sensitivity by upregulating cholinergic anti-inflammatory pathway in spontaneously hypertensive rats
X.Z. Hou1, Y. Zhang1, C.J. Mi1, W.X. Jing1, L. Yang2, L. Tao3, F. Gao4 on behalf of Insulin. 1Fourth Military Medical University, Department of Physiology, Xi’an, China, People’s Republic of China; 2Fourth Military Medical University, Department of Cardiology, Xi’an, China, People’s Republic of China

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P2717 | BENCHMARK
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X.Z. Hou1, Y. Zhang1, C.J. Mi1, W.X. Jing1, L. Yang2, L. Tao3, F. Gao4 on behalf of Insulin. 1Fourth Military Medical University, Department of Physiology, Xi’an, China, People’s Republic of China; 2Fourth Military Medical University, Department of Cardiology, Xi’an, China, People’s Republic of China

Background: Exercise has been recommended as a part of lifestyle modification 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.

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Results: Young (8-wk-old) hypertensive 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).

Conclusion: The beneficial role of physical activity was proved important only for subjects with normal Body Mass Index, but not for overweight/obese subjects. Thus, clinicians should educate overweight and obese that losing weight is the first target for reducing CVD risk.
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 little or no regular exercise, 201 (70%) were overweight or obese, and 140 (49%) had raised waist circumference. Of them, 146 (50%) of the participants were referred for due to high Framingham score or at least one abnormal test; 26 (9%) CVD risk greater than 20%, 32 (11%) high systolic blood pressure (140 mmHg), 50 (17.4%) high total cholesterol level, 108 (37%) low HDL-C level, 22 (7.5%) with abnormal blood glucose level. The mean of calculated 10-year risk of cardiovascular disease was 8.5±9.7. Approximately half of the the individuals who received the follow-up recommendation had made an appointment with their physician (54%). Overall, 15.9% of the individuals had received medications and 15.9% received appropriate advice for modifying their risk factors from their physician. Moreover, 7.5% were under work-up by the physician.

Conclusion: 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 wide spread utilization. A plan to increase the awareness of clients to follow up recommendations is required.

Acknowledgement/Funding: Tehran University of Medical Sciences

P2716 | BEDSIDE

Liraglutide is more effective than lifestyle changes in modulating subclinical and visceral fat distribution, liver steatosis, insulin sensitivity and beta-cell function after comparable weight loss

F. Santilli1, M.T. Guagnano1, A. Tartaro 2, E. Angelucci 3, P. G. Simeone1, A. Consoli 1.

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.

Purpose: To evaluate the concurrent effects of liraglutide on body weight, fat mass, insulin resistance and beta cell preservation, we hypothesized that this class of drugs may exert additional cardiometabolic actions on top of those anticipated for lifestyle intervention-mediated weight loss.

Methods: Twenty-two metformin-treated obese subjects with impaired glucose tolerance (IGT), impaired fasting glucose (IFG) or newly diagnosed T2DM, were randomized to liraglutide treatment (1.8 mg/d) or lifestyle counselling to assess the efficacy of liraglutide in T2DM.

Results: Liraglutide use led to a significantly greater weight loss compared to lifestyle changes, and a significant reduction in visceral fat mass and liver steatosis. Moreover, liraglutide demonstrated a beneficial effect on insulin sensitivity (Matsuda Index) and β-cell performance (by Insulin Secretion-Sensitivity Index-2 (ISSI-2)) during multiple sampling oral glucose tolerance test.

Conclusion: This pilot study may help establishing a cause-and-effect relationship between T2DM pathogenesis and natural history. Liraglutide may favourably impact T2DM pathogenesis and natural history.

Acknowledgement/Funding: Grant from the Ministry of University and Research

P2717 | BEDSIDE

Adherence to evidence-based therapies and incidence of clinical outcomes among high cardiovascular risk patients: the react registry

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Background: The aim of this registry was to test the association of adherence to evidence-based therapies with the incidence of major cardiovascular events (MACE) in high risk patients from Brazil, a middle income country.

Methods and results: REACT is a multicenter registry that aims to document current clinical practice of patients at high cardiovascular risk in Brazil. Patients were eligible if they were over 45 years with or at risk for atherothrombotic disease. From May 2015 to May 2016, 1885 consecutive (mean age 65.9 years, 51.4% male) subjects were enrolled in this study. Combined use of aspirin, statin and angiotensin converting enzyme inhibitor (ACEI) had lower rates in baseline 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 within 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: Brazilian society of Cardiology

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

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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 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 Metabolic Equivalent (MMax), an established CRF test, 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 higher an individual’s CRF, the lower prevalence of depression (p=0.051). Results demonstrate a small significant negative correlation at IA (r=−0.13, p=0.0098) and EOP (r=−0.10, p=0.0507), however, no significant correlation was found between change of MMax and HADS-D at EOP (r=0.11, p=0.557, 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 MMax</td>
<td>1.63 (0.02)</td>
<td>1.49, 1.77</td>
</tr>
<tr>
<td>Mean changes in HADS depression score</td>
<td>−1.68 (0.15)</td>
<td>−1.80, −1.59</td>
</tr>
<tr>
<td>Mean change in HADS anxiety score</td>
<td>−1.05 (0.14)</td>
<td>−1.18, −0.92</td>
</tr>
<tr>
<td>Mean change in Dartmouth Co-op</td>
<td>−2.99 (0.22)</td>
<td>−3.49, −2.49</td>
</tr>
<tr>
<td>Mean change in EQ-VAS</td>
<td>−11.22 (1.79)</td>
<td>−9.91, 13.52</td>
</tr>
<tr>
<td>Mean change in BMI</td>
<td>−1.70 (0.07)</td>
<td>−1.45, −1.15</td>
</tr>
</tbody>
</table>

Conclusion: Small negative correlations between MMax and HADS-D were demonstrated at IA and EOP, indicating that CRF increases, depression reduces. 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 MMax or HADS-D at EOP was not great enough to show significant correlations. Analysis over a longer time period is recommended to investigate this association further.
vation 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 ≤140/90 mmHg. In crossover method, all patients were administrated 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 < 0.001, 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 (r = 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

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**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 LLM 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.

**P2721 | BEDSIDE**

Adherence to Mediterranean diet protects against cardiovascular disease independently of creatinine clearance rate: the 10-year (2002-12) Follow-up of Attica study


**Background:** Decreased creatinine clearance rate is of utmost importance for increased CVD risk, whereas higher level of adherence to Mediterranean dietary pattern is associated with decreased CVD risk. Adherence to Mediterranean diet has been usually considered protective by managing CVD risk factors and its role in prevention of cardiovascular outcomes has rarely been studied. The aim of our work was to explore role between Mediterranean and 10-year incidence of CVD, after taking into account creatinine clearance rate.

**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). Creatinine clearance rate was calculated using formula that takes into account gender, age, weight and creatinine of subjects. Adherence to Mediterranean diet was assessed using the MedDietScore. During 2011–2012, 2583 out of the 3042 baseline participants attended the 10-year follow-up of the ATTICA study.

**Results:** Having creatinine clearance rate greater than 60 ml/min was associated with decreased 10-year CVD risk (Relative Risk (RR) = 0.246, 95% CI: 0.137–0.440). After adjusting adherence to Mediterranean diet, smoking, family history of CVD, diabetes mellitus, hypertension, hypercholesterolemia and C-reactive protein levels, both creatinine clearance rate and MedDietScore remained independently and inversely associated with 10-year CVD risk (all p-values < 0.05). The analysis was stratified according to the tertiles of MedDietScore, where no trend was observed.

**Conclusion:** Adherence to Mediterranean diet is protective against CVD risk, independently of the creatinine clearance rate of the subjects, suggesting that dietary evaluation and advice is needed for CVD prevention, even for subjects with established CVD risk factors.

**P2722 | BEDSIDE**

Obese hypogonadal men with a history of cardiovascular diseases (CVD) benefit from long-term treatment with testosterone undecanoate (TU): observational, real-life data from a registry study

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**Introduction and objectives:** Hypogonadism is associated with cardiometabolic risk. Studies suggest that hypogonadism increases the risk of all-cause and cardiovascular mortality. While some short-term studies have been performed in men with CVD, there are no data on long-term effects of testosterone (T) therapy in men with CVD.

**Methods:** In a prospective, cumulative, observational registry study from a single urologist’s office, 340 men with T<12.1 nmol/L received TU injections for up to 87 months. In this subgroup analysis, 68 men with a previous diagnosis of CAD (n=40) and/or history of myocardial infarction (n=40) and/or stroke (n=6) were analysed. These patients are considered high-risk patients by any definition. Mean age was 67.2 months. All men except four were obese. 68 men were included for 3 years, 54 for 4 years, 54 for 5 years, and 28 for 7 years. Declining numbers reflect the nature of the registry but not drop-out rates.

**Weight** (kg) decreased from 105.0±13.71 to 90.79±8.92. Waist circumference (cm) decreased from 112.07±9.97 to 99.14±5.63. BMI decreased from 37.27±4.45 to 29.58±3 kg/m² (p<0.0001 for both). Mean weight loss was 18.75±0.71%

**Fasting glucose** decreased from 108.74±17.06 to 96.14±2.0 mg/dl, HBAlc from 7.8±1.3 to 5.86±0.49% (p<0.0001 for both).

Total cholesterol decreased from 304.66±34.09 to 187.75±7.6, LDL from 184.28±37.51 to 120.64±29.29, triglycerides from 308.38±56.3 to 187.04±7.65 mg/dl. HDL increased slightly from 63.79±17.79 to 67.14±16.71 (p<0.0001 for all). The total cholesterol/HDL ratio decreased from 5.16±1.55 to 2.97±0.77 (p<0.0001).

**Liver enzymes:** aspartate transaminase (AST) decreased from 42.16±13.17 to 19.71±2.17, alanine transaminase (ALT) from 42.56±5.55 to 19.39±3.25 U/L (p<0.0001 for both).

Systolic blood pressure (BP) decreased from 167.82±11.01 to 147.85±9.6, diastolic BP from 102.28±8.23 to 80.07±7.13 mmHg (p<0.0001 for both). Pulse pressure declined from 65.54±5.24 to 62.32±1.5 (p<0.0001).

C-reactive protein decreased from 3.97±1.73 to 0.32±0.44 mg/dl. Haemoglobin increased from 14.45±0.68 to 15.03±0.45 g/dl, haematocrit from 47.27±4.45 to 50.38±4.45% (p=0.0001 for both).

**Conclusion:** CR can improve the reverse cholesterol transport, independent of LLM, resulting in the secondary prevention.

**Acknowledgement/Funding:** Bayer Pharma AG partially funded entry data and statistical analyses.
Adherence to Mediterranean diet reduces the risk for 10-year type 2 diabetes development. The role of TNF-α and homocysteine as possible mediators

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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 to examine inflammatory and oxidative stress biomarkers as candidate mediators of this relationship.

Methods: At baseline (2001–2), a random sample of 1514 men and 1528 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 MedDietScore (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-α and homocysteine 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 partially explained by TNF-α and homocysteine levels.

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, LVEF, stent number and length, stent type was a 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**

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**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 Cardiovascular Registry (n=17,746). We analyzed mortality and target vessel revascularization (TVR) at 2 years. Cox multivariable 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=0.86, 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 2-year mortality (HR=0.59, 95% CI: 0.49–0.71, 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: −7.5, −2.5, p<0.001).

**Conclusion:** Comparative outcomes of zotarolimus-eluting stents in British Columbia: a real world analysis of 17,747 patients using propensity score and instrumental variable methods

**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 (Kajander et al. 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.
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 OCT. 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 Evaluating 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

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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 nanosize pores surface eluting sirolimus.

Methods: In this prospective, multicentre, open-label study, patients were enrolled with documented stable angina or silent ischemia and planned intervention when requiring stent implantation (without overlapping) in at least two separate lesions of similar morphologic characteristics. Each lesion was randomised to be treated with a BVS or a MBP-DES. After the procedure patients were scheduled alternatively for 6 or 12 months evaluation with optical coherence tomography. Primary endpoint is % of uncovered struts at 6 months. Secondary endpoints include % of uncovered struts at 12 months and decrease in % of uncovered struts from 6 to 12 months, among others.

Results: Up to date 82 patients have been included (37 with BVS+everolimus MBP-DES and 18 with BVS+sirolimus MBP-DES). Among these, 14 patients (28 stents) have been so far examined with OCT at 6 months. In 9 patients examined stents were everolimus MBP-DES+BVS, in 3 BVS+sirolimus MBP-DES and in 3 BVS+biolimus MBP-DES. Up to date 82 patients have been included (37 with BVS+everolimus MBP-DES and 18 with BVS+sirolimus MBP-DES). Among these, 14 patients (28 stents) have been so far examined with OCT at 6 months. In 9 patients examined stents were everolimus MBP-DES+BVS, in 3 sirolimus MBP-DES+BVS and in 2 biolimus MBP-DES+BVS. The % of uncovered struts was 3.9% with MBP-DES and 4.7% with BVS (p=0.4). Pending of final follow up and analysis of the whole cohort, at 6 months the proportion of uncovered struts is low and comparable between biodegradable polymers.

Conclusions: Pending of final follow up and analysis of the whole cohort, at 6 months the proportion of uncovered struts is low and comparable between biodegradable everolimus-eluting scaffolds and metallic drug-eluting stents with biodegradable polymers.

Acknowledgement/Funding: Unrestricted grants from Boston sci, Abbott vascular, St Jude, Biotronik and Biosensors

P2731 | BEDSIDE The paradigm shift of peri-contrast staining (PSS) in first generation DES era to second generation DES era

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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 group 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 angiographical 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 first generation DES group (25.3%). Baseline 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-local.
PSS was highest of second generation DES group. (smooth contour PSS: 37.9% vs 16.7%, p<0.002, and monotonic PSS: 34.5% vs 61.1%, p<0.003) There was no significant difference in target lesion revascularization (TLR) and stent thrombosis (ST) between the two groups. (N.S.) Cumulative incidence of TLR and ST in smooth contour PSS was higher than in non-smooth contour PSS group. (TLR: 57.1% versus 21.2%, p<0.018, and ST: 14.3% versus 0%, p=0.025).

Conclusions: The occurrence of PSS decreases in second generation DES era and smooth contour PSS appeared to be significantly associated with TLR and ST.

P2734 | BEDSIDE
Long-term outcomes in NANOM-FIM trial: 5-year analysis
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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 (0 vs 4 in 5 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 DES 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±0.6. 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 of 1-year MACE (hazard ratio (HR)= 1.063; 95% confidence interval (CI): 1.007–1.10, HR=2.676; 95% CI: 1.366–5.663). Subgroup analyses showed no significant differences in the incidence of MACE between patients with and without diabetes (4.1% vs. 4.0%, p=0.963), between those presented with and without acute MI (4.7% vs. 3.4%, p=0.275) and between those with and without diabetes (4.1% vs. 4.0%, p=0.963), between those presented with and without diabetes (4.1% vs. 4.0%, p=0.275) and between those with and without diabetes (4.1% vs. 4.0%, p=0.963).

Conclusions: Our study demonstrates excellent 1-year clinical outcomes of DES in Korean patients with ACS. These efficacy and safety of DES were consistent for ACS patients, regardless of diabetes status, presented with acute MI or multi-vessel disease.

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P2737 | BEDSIDE
Simple versus complex drug-eluting stenting for coronary bifurcation lesions: an updated meta-analysis of randomized controlled trials

Background: Pecunature 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.

P2740 | BEDSIDE
Impact of a dedicated chronic 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 (PCIs). 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 and non-specialist operators.

Methods: We prospectively evaluated 206 consecutive CTO interventions performed over a 2 year period by 2 dedicated CTO operators. The designated CTO 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 straffly 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 O–1), 93% vs 20% (J-CTO 2), 89% vs 17% (J-CTO 3) respectively (p < 0.001).
BFS cohort. (6.3% vs. 2.5%, p<0.001). 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.

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 acute 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 pre-dilatation correlated with percent recoil, and so optimal lesion preparation seems to be mandatory in order to maximise the mechanical properties of the scaffold.

Background: In vivo acute recoil of the ABSORB bioabsorbable vascular scaffold (BVS) was evaluated in selected patients.

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<0.001), more often female (37.1 vs. 24.7%, p=0.01) or diabetic (22.7 vs. 12.9%, p<0.01), 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 by concerns regarding 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. 32.0±13.5mm, p<0.001) and average stent length (19±7.8 vs. 21±7.7mm, 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<0.001). At mean follow up of 258 days clinically driven restenosis PCI (2.8% for BFS vs. 2.5% for BES, p=0.41) and target lesion revascularization 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 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.

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. The primary endpoint was in-hospital major adverse cardiac events. The secondary endpoint was defined as a final residual stenosis of less than 20% by visual estimation and Thrombolysis in Myocardial Infarction (TIMI) 3 flow on the final angiogram. OCT was performed 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 11 (44%) patients, non-STEMI in 1, non-CAD 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 2.74±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=0.003). 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 strut malapposition directly after STENTYS placement is low. Balloon post-dilatation could further improve stent strut apposition in SES.

Methods: Simplified vascular closure device deployment without an arteriogram: single center experience in over 2000 consecutive patients

Aim: To prospectively assess the effectiveness and safety of Angio-Seal in patients undergoing coronary angiography and/or percutaneous coronary intervention (PCI) without use of local anesthetic.

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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 hematoma (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 Anglo-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 study
K.K.W. Olsen1, M. Maeng1, L.O. Jensen2, M. Nobuyoshi.
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/abscence of diabetes mellitus. Clinical endpoints included MACE, 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=1,239 patients, n=189 diabetic patients). MACE 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 MACE rates were similar for the 2 stent types (13 [7.9%] vs. 14 [8.0%]; HR 1.00, 95% CI: 0.47–2.12, p=0.96). Among non-diabetic patients, however, the landmark analyses showed that BES had fewer MACE (46 [4.7%] 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.

Conclusions: 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 biabsorbable polymer had lower MACE and TVR rates beyond 1-year follow-up, which may suggest longer-term benefit in this subgroup.

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P2746 | BEDSIDE
Serial observation of everolimus-eluting stent incomplete stent apposition by frequency domain optical coherence tomography
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Background: Previous clinical studies revealed the capability of optical coherence tomography (OCT) for the detection of uncovered struts and late incomplete stent apposition (ISA) which are associated with very late drug-eluting stent thrombosis.

Aims: The purpose of this study was to investigate the incidence and predictors of ISA of everolimus-eluting stent (EES) by frequency-domain OCT (FD-OCT).

Methods: OPUS-CLASS Cohort B was a randomized, multi-center study to test the efficacy of FD-OCT-guided percutaneous coronary intervention (PCI), and enrolled totally 60 patients. Of these 36 patients received EES and underwent serial (post and follow-up) FD-OCT analysis. Quantitative OCT analysis was performed every 1 mm.

Results: ISA at follow-up phase were detected in 10 (28%) patients. Among qualitative angiographic findings, moderate or severe calcification was more frequently observed in patients with ISA (50% vs. 7%, p=0.0092). In cross-section level OCT analysis, mean ISA area at post-PCI phase was greater in patients with follow-up ISA (0.52±0.37 mm² vs. 0.24±0.13 mm², p=0.043). In struts-level OCT analysis, number of cross-section with ISA (by every 1-mm analysis), was greater in patients with ISA of follow-up phase (8.5±7.9 frames vs. 2.2±1.1 frames, p=0.032). In the results of receiver operating characteristics (ROC) analysis for predicting follow-up ISA, area under the curve for the number of cross-section with ISA was 0.88. The sensitivity and specificity for ISA at follow-up phase was 80% and 81% (cut off: 4), respectively (Figure).

Conclusions: When the ISA is observed at equal to or over 4 cross-sections (1 cross-section/mm), additional balloon dilatation may be required.

P2747 | BEDSIDE
Incidence and clinical impact of longitudinal stent deformation after the PROMUS element platinum chromium-everolimus eluting stent implantation
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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).

Results: Of 803 patients with 1050 lesions, we performed an intravascular ultrasound (IVUS) and post-dilatation 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-dilatation 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-dilatation 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%, p=0.14, p=0.88; 9.1% vs. 2.8%, p=0.019). Of 803 patients with 1050 lesions, we performed an intravascular ultrasound (IVUS) and post-dilatation 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-dilatation 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-dilatation 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%, p=0.14, p=0.88; 9.1% vs. 2.8%, p=0.019).

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, 1230 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.
Clinical outcome of aorto-ostial lesions treated with first or second generation drug-eluting stents

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Background: Aorto-ostial lesion is still a challenge for coronary intervention even in the drug-eluting stent (DES) era. However, the impact of drug-eluting stent with second-generation DES on clinical outcomes has not yet been fully evaluated. Our aim was to assess the relationship between stent overlap and clinical outcomes after the Nobori biolimus-eluting stent (BES) and the Xience/Promus cobalt chromium everolimus-eluting stent (CoCr-EES) implantation.

Methods: Between February 2010 and July 2012, a total of 2528 patients with 3409 lesions undergoing BES (1464 patients with 1973 lesions) and CoCr-EES (1064 patients with 1436 lesions) implantation were analyzed. Based on the presence of stent overlap and number of DES per vessel, patients were divided into the 3 groups: (1) those with stent overlap; (2) those with single DES per vessel; and (3) those with multiple DES per vessel without stent overlap. We assessed the cumulative incidence of clinically driven target lesion revascularization (CDTLR) and definite stent thrombosis within 2-year.

Results: Of 2528 patients with 3409 lesions, 856 patients had 917 lesions with stent overlap (505 BES and 351 CoCr-EES), 1071 patients had 1105 lesions with multiple DES without stent overlap (44 BES and 63 CoCr-EES), and 1565 patients had 1237 lesions with single DES (915 BES and 650 CoCr-EES). At 2-year, the cumulative incidence of CDTLR and definite stent thrombosis were higher in patients with stent overlap than in those with multiple DES without stent overlap and with single DES (12.0% vs. 10.9% vs. 5.1%, p<0.001 and 1.6% vs. 0.4%, p=0.002, respectively). There were no significant differences in the rates of CDTLR and definite stent thrombosis between stent overlap and with multiple DES without stent overlap (12.0% vs. 10.9%, p=0.7 and 1.6% vs. 0.0%, p=0.2, respectively). However, the cumulative incidences of CDTLR and definite stent thrombosis were higher in patients with stent overlap than with single DES (12.0% vs. 5.1%, p<0.001 and 1.6% vs. 0.4%, p=0.001, respectively). There were no significant differences in the rates of CDTLR and definite stent thrombosis between the BES and CoCr-EES.

Conclusions: Stent overlap with BES and CoCr-EES showed higher incidence of CDTLR and definite stent thrombosis compared with single DES. Conversely, no significant differences in CDTLR and definite stent thrombosis were found in patients with stent overlap and multiple DES.

P2750 | BEDSIDE

Bioabsorbable vascular scaffold radial expansion and conformation compared to a metallic platform

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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

SF was observed in 363 lesions after first-generation DES implantation (de novo, 306; ISR, 57) and in 131 lesions after second-generation DES implantation (de novo, 97; ISR, 34). The figure shows the incidences of SF.

Conclusion: The incidence of SF in de novo lesions has decreased with the advent of second-generation DES; however, that in ISR lesions has not improved and still remains a critical issue.

P2749 | BEDSIDE

Impact of stent overlap on 2-year clinical outcomes in patients treated with biolimus-eluting stent and cobalt chromium everolimus-eluting stent

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Background: Stent overlap was associated with impaired long-term clinical outcomes in the first-generation drug-eluting stent (DES) era. However, the impact of stent overlap with second-generation DES on clinical outcomes has not yet been fully evaluated. Our aim was to assess the relationship between stent overlap and clinical outcomes after the Nobori biolimus-eluting stent (BES) and the Xience/Promus cobalt chromium everolimus-eluting stent (CoCr-EES) implantation.

Methods: Between February 2010 and July 2012, a total of 2528 patients with 3409 lesions undergoing BES (1464 patients with 1973 lesions) and CoCr-EES (1064 patients with 1436 lesions) implantation were analyzed. Based on the presence of stent overlap and number of DES per vessel, patients were divided into the 3 groups: (1) those with stent overlap; (2) those with single DES per vessel; and (3) those with multiple DES per vessel without stent overlap. We assessed the cumulative incidence of clinically driven target lesion revascularization (CDTLR) and definite stent thrombosis within 2-year.

Results: Of 2528 patients with 3409 lesions, 856 patients had 917 lesions with stent overlap (505 BES and 351 CoCr-EES), 1071 patients had 1105 lesions with multiple DES without stent overlap (44 BES and 63 CoCr-EES), and 1565 patients had 1237 lesions with single DES (915 BES and 650 CoCr-EES). At 2-year, the cumulative incidence of CDTLR and definite stent thrombosis were higher in patients with stent overlap than with single DES (12.0% vs. 10.9% vs. 5.1%, p<0.001 and 1.6% vs. 0.4%, p=0.002, respectively). There were no significant differences in the rates of CDTLR and definite stent thrombosis between stent overlap and with multiple DES without stent overlap (12.0% vs. 10.9%, p=0.7 and 1.6% vs. 0.0%, p=0.2, respectively). However, the cumulative incidences of CDTLR and definite stent thrombosis were higher in patients with stent overlap than with single DES (12.0% vs. 5.1%, p<0.001 and 1.6% vs. 0.4%, p=0.001, respectively). There were no significant differences in the rates of CDTLR and definite stent thrombosis between the BES and CoCr-EES.

Conclusions: Stent overlap with BES and CoCr-EES showed higher incidence of CDTLR and definite stent thrombosis compared with single DES. Conversely, no significant differences in CDTLR and definite stent thrombosis were found in patients with stent overlap and multiple DES.

P2751 | BEDSIDE

Transradial versus transfemoral approach for chronic total occlusions of coronary arteries: feasibility and predictors of success

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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, TFA 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, 82.8% (269) were performed by TFA 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. 46.6%), mean lesion length (30.8 vs. 28.2mm), calcified lesions (51.5% vs. 40%) and mean contrast volume (251±112 vs 251±122ml). Compared to TFA, TRA patients had shorter fluoroscopy time (25±14 vs 35±22 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 TFA group (78.5% vs 63.6%, p=0.02). Logistic regression analysis demonstrated as 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 1.308–5.820]). 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 TFA in PCI, this vascular approach use in first attempt of PCI for CTO showed a comparable success rate and a lower adverse events rate with 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.
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 4.92±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 metal 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 trame stent method in treatment of coronary bifurcation lesions**

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**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 search of 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 observed stresses 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**

**Fracture of a stent reserve assessed by pressure wire could predict proper stent deployment**

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**Background:** There are different methods for assessing the results of coronary intervention, some are morphological and the others are physiological. Myocardial fractional flow reserve (FFMffy) 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 dilatation by measuring myocardial fractional flow reserve using intracoronary pressure wire.

**Methods:** FFMffy and quantitative coronary angiography (QCA) were obtained before PCI, after stent placement and after post-stenting balloon dilatation in 120 patients (LAD in 76 patients, RCA in 36 patients and LCX in 8 patients). FFMffy was calculated as the ratio of PD/PA during intracoronary adenosine (50 mcg and 20 mcg in the left and right coronary artery 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 dilatation produced non-significant more reduction in the percent diameter stenosis (6±24% with P value =0.05). FFMffy after PCI was significantly higher than that at baseline conditions before intervention (0.48±0.18 at baseline versus 0.89±0.09 after stenting, p<0.05). There was significant increase in FFMffy after post-stenting balloon dilatation (0.94±0.05 versus 0.89±0.09).

**Conclusions:** Post-stenting Balloon dilatation 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**

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**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 ACS patients at high risk of bleeding who are treated with GP IIb/IIIa inhibitors (GP) due to “bail-out” situations or thrombotic complication (Ila C recommandation by ESC guideline 2014).

**Methods:** The Clotinab application in high risk Acute Coronary Syndrome under transradial PCI (CAP) registry, retrospectively, 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 hematoma, intracranial hemorrhage and other bleeding complications.

**Results:** After propensity score matching, there were no differences in baseline characteristics between the 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=2.795; 95% CI, 1.085 to 7.198; p=0.033).

**Conclusion:** TRI in patient with high risk ACS treated with GPI is associated with better clinical outcomes and lower bleeding tendency at 30 days.
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 abliminal bioabsorbable polymer at 3, 6 and 12 months after implantation

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Background: The everolimus-eluting stent with abliminal bioabsorbable polymer (EES-BP) is a new generation drug-eluting stent with features potentially favouring an early healing process which could promote shorter periods of dual antiplatelet therapy.

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 alternatively in two different centers. Lesions should have the same characteristics in the two groups. Each patient was examined with OCT at 3, 6 and 12 months. The proportion of uncovered struts was 6.5% at 3 months and 3.7% at 12 months.

Results: A total of 55 patients have been included. Among these, 29 have been evaluated in clinic OCT up to 3 months and 14 patients (18 struts) at 6 months. The mean stent diameter was 3.02±0.4 and 3±0.4 mm respectively (p=0.8) and stent length 17.9±5.6 and 17.1±5.3 mm respectively (p=0.7). The proportion of uncovered struts was 6.5% at 3 months and 3.7% at 6 months (p=0.3).

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

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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 side-branch predilation (TF) technique.

Methods: Patients with lesions treated with EES-BP stents were scheduled for follow-up OCT at 3, 6, 12 months. The proportion of uncovered struts was 6.5% at 3 months and 3.7% at 12 months.

Results: Among these, 29 have been evaluated including OCT up to 3 months and 14 patients (18 struts) at 6 months. The mean stent diameter was 3.02±0.4 and 3±0.4 mm respectively (p=0.8) and stent length 17.9±5.6 and 17.1±5.3 mm respectively (p=0.7). The proportion of uncovered struts was 6.5% at 3 months and 3.7% at 6 months (p=0.3).

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

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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 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), 64% treated by TF in 52%, CX in 16% and RCA in 30% and left main in 2%. Lesion length was 34.5±11.17 mm and vessel size 2.93±0.41 mm. Stented length was 39.8±14.08 mm (1.4 stents per lesion). Postdilatation was used in 75% of cases and IVUS in 15%. Radial access accounted for 70% of cases

Results: There were 14 in-hospital MACE at 30 days and only one case of stent thrombosis (0.2%). At 12 months, the total MACE rate was extremely low (1.3%). There were 2 cardiac deaths (0.3%), 6 cases of MI of the treated vessel (1%) and 3 TLR (0.5%), with 4 cases of stent thrombosis (0.6%).

Conclusions: In this real-world, prospective registry, 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.

P2760 | BEDSIDE
Rotational atherectomy through the radial artery: procedural success and long term clinical outcomes

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Background: Complex percutaneous coronary intervention (PCI) through the transradial approach (TR) is increasingly being preferred over the femoral access (TF). Nevertheless, rotational atherectomy (RA) is still being performed using the TF in selected cases.

Purpose: To assess if RA performed through the TR is associated with the same procedural success as the TF and evaluate long term clinical outcomes.

Methods: From January 2009 to December 2014, 176 consecutive patients (pts) underwent RA and were retrospectively analyzed (183 procedures). Choice of access was according to the target vessel, need for >7 Fr guidewires/catheters/bigger burrs and operator experience. TR was used in 98 procedures (53.6%, TR group (gp)) and TF in 85 (46.4%, TF gp). Mean follow-up was 26±14 months. Procedural success and major adverse cardiovascular events (MACE) were evaluated.

Results: Procedural success was 100% in both gps. Baseline characteristics were similar except for the presence of hypertension (74.5% in TR gp vs 87%, p=0.02), family history of coronary artery disease (1.1% in TR gp vs 6.5%, p=0.01) and prior coronary artery bypass graft (4.3% in TR gp vs 14.5%, p=0.01). In TR gp, smaller guide catheters were used (mean 6.3 vs 6.6 Fr, p=0.001 CI 0.2–0.5), with a mean of 1.2±0.4 vs 1.3±0.5 burrs per pt (p=NS) and a mean maximum burr size of 1.4±0.17 vs 1.5±0.2mm (p=0.008, CI 0.02–0.13); DES were implanted in 85.4% pts vs 77.5% (p=NS). TF was preferred for the treatment of the right coronary artery (25.9% vs 15.3%, p=0.07) while TR was the choice for the left (64.7% vs 74.1%, p=0.07). In TR, mean maximum stent diameter was 3.3 vs 3.1mm (p=NS) and mean total stent length was 32.9±15.5 vs 35±17.7mm (p=NS). Minor peri-procedural complications were similar in both gps. Crossover from TR to TF was observed in 7.1% of the overall group. In 2009, RA PCI through TR was the main operator preference at our centre; then, inverted three years later: 0.8 in 2012, 0.2 in 2013 and 0.8 in 2014, showing an increasing confidence of the operators in TR. No differences were detected regarding in-hospital/long term all-cause mortality or MACE but a trend was observed showing more TLR in the TF gp (13.2% vs 5.5%, p=0.08).

Conclusions: Our data suggest that despite the use of smaller guiding catheters and burrs in equally complex patients, TR was able to achieve a similar procedural success as TF, without increasing peri-procedural complications and with a trend to less TLR, with operator experience being decisive. RA via the TR approach is feasible and safe and associated with good long term clinical outcome.
**P2761 | BEDSIDE**

Provisional versus planned double-stenting strategy in coronary bifurcation lesions treated with bioresorbable scaffold

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**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 ≤ 2.25 mm were identified [PS strategy 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 17.1±8.0 vs. DS 21.2±8.8, p=0.04) and a greater number of true bifurcation lesions (PS 52.5% vs. DS 91.3%, p<0.001). Intracoronary vascular 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 significant 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=0.91). Definite scaffold thrombosis was observed in 1 patient in the PS group but the thrombosis occurred in a BRS implanted distal 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

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**Background:** Stent length may be an important variable to consider when selecting the optimal PCI strategy for target lesions. While longer stents are associated with lower risk of restenosis, they are also associated with increased risk of binary restenosis and stent thrombosis. The importance of Optical Coherence Tomography intracoronary pull-back in complex coronary lesions is becoming increasingly evident. The use of Optical Coherence Tomography (OCT) guidance during PCI has been demonstrated to provide real-time information on the extent and nature of the coronary lesion, the distribution and depth of the plaque, and the stent apposition. In this study, we aimed to evaluate the role of OCT pull-backs in the management of lesions with long stent length (>40 mm).

**Purpose:** To investigate the influence of Optical Coherence Tomography (OCT) guidance during PCI on clinical outcomes in patients with long stent length (>40 mm). Specifically, we aimed to assess the impact of OCT pull-backs on the occurrence of binary restenosis and stent thrombosis, as well as to analyze clinical outcomes and patency of BVS by computed tomography scan at mid-term follow-up.

**Methods:** We evaluated patients treated with BVS for bifurcation lesions in complex coronary lesions. The use of bioresorbable scaffolds (BRS) in percutaneous coronary intervention (PCI) could provide additional clinical benefits as compared with metallic drug-eluting stents (DES). The Japanese-CETO score of complexity, 21 (46%) were considered to be routine PCI, and the remaining 7 (15%) were considered for further post-dilation with DES. There were no significant differences in major adverse cardiac events (MACE) between the two groups (PS 9.5% vs. DS 11.2%, p=0.91). Definite scaffold thrombosis was observed in 1 patient in the PS group but the thrombosis occurred in a BRS implanted distal 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.

**P2763 | BEDSIDE**

Computed tomography scan assessment at follow-up in patients with chronic total occlusion treated with bioresorbable vascular scaffolding

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**Background:** Everolimus-eluting bioresorbable vascular scaffold (BVS) implantation in chronic total occlusion (CTO) could provide improved clinical outcomes compared to long-term follow-up as compared with metallic drug-eluting stents (DES).

**Objectives:** To assess the feasibility of BVS for the CTO percutaneous treatment as well as to analyse clinical outcomes and patency of BVS by computed tomography scan at mid-term follow-up.

**Methods:** From February 2013 to June 2014, 121 CTO in 116 patients were revascularized and treated percutaneously in our center. From them, 42 patients with 46 CTO were successfully treated with BVS implantation and they constitute the study group. All occluded segment were predilated with balloons of increasing diameter testing the uniform expansion of them. After BVS implantation, post-dilation using non compliant balloons with a maximum diameter 0.5 mm more than BVS diameter was performed. A computed tomographic (CT) scan was scheduled for all patients at least 6 months after treatment.

**Results:** The mean age was 66.9 (19.1%) and 89.5% were male. Diabetes mellitus was present in 14 (33%) and 15 (36%) had a previous PCI. The target vessel was predominantly the left anterior descending artery (22, 48%). According to the Japanese-CETO score of complexity, 21 (46%) CTO were difficult or very difficult. This study aimed to investigate clinical outcomes of patients treated with a bioresorbable scaffold (BVS) for bifurcation lesions between May 2012 and November 2014. A total of 122 consecutive bifurcation lesions with side branch (SB) diameter ≤ 2.25 mm were identified [PS strategy 99 lesions (89 patients) and DS strategy 23 lesions (22 patients)].

**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 lesions
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Background and introduction: Percutaneous treatment of coronary bifurcation lesions (CBL) is associated with a low procedural success rate and high incidence of target lesion revascularization (TLR), and stent thrombosis. The procedural outcome is accepted as the default technique, but stent implantation on both branches of the bifurcation is still controversial. The “mini-crush” 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. 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 2010 in all consecutive patients who were treated with implantation of DES with mini-crush technique for the treatment of true CBL. Clinical follow-up at our out-patient 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 revascularization (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/STEMI) in 52.3% of the cases and acute myocardial infarction (STEMI) in 18.3%. 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 definitive 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 documented. The cumulative incidence of clinical events was documented in 4% (450 patients) and was localized at the ostium of the side branch in all of the cases.

Conclusions: Our results suggest that the treatment of bifurcation lesions by means of mini-crush stenting technique is associated with excellent immediate success and provides good angiographic and clinical outcomes at 1-year in a 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
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2Department of Cardiology, Naples, Italy

Background: The only difference between the first and second generation zotarolimus-eluting stent (ZES) is the coated polymer, which controls drug-eluting delivery. The only difference between the first and second generation zotarolimus-eluting stent (ZES) is the coated polymer, which controls drug-eluting delivery. The purpose of this study was to evaluate the acute performance of systematic BRS use in CTO lesions.

Methods: A total of 714 patients (pts) receiving FR-ZES or SR-ZES were pooled from 2 groups. Secondary endpoints were: periprocedural changes in the index of microvascular resistance (IMR post-PICI – IMR pre-PICI), 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-PICI 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.

P2767 | BEDSIDE
Acute performance of second generation everolimus-eluting bioresorbable vascular scaffolds for percutaneous treatment of chronic total occlusions
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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.

Results: Clinical and angiographic characteristics of the patients were not different between the two groups; however, the incidence of target lesion revascularization (TLR) and target vessel revascularization (TVR) were lower in pts receiving SR-ZES up to 3 years (TLR: HR: 0.342, 95% CI: 0.129–0.916, p=0.035; TVR: 0.413, 95% CI: 0.177–0.962, p=0.041). There was a trend toward lower procedural outcomes overtime.

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.

P2768 | BEDSIDE
Device and procedural success rate of bioresorbable vascular scaffolds for percutaneous treatment of chronic total occlusions performed at a single center were prospective evaluated. Patients with reference vessel diameter (RVD) ≥ 2.25 mm and ≥ 3.8 mm, heavy calcification within the CTO segment and target lesion in bifurcation.
The Sakakibara Heart Institute of Okayama, Okayama, Japan

Background: Despite striking reduction of restenosis, treatment strategy is still challenging for patients with in-stent restenosis (ISR) after second generation drug-eluting stent (DES). Although Paclitaxel-coated balloon (PCB) is standard treatment for DES-ISR, excimer laser coronary angioplasty (ELCA)+PCB strategy may provide potential benefit with adjunctive neointima scaffolding (vaporizing).

Methods: Consecutive 57 ISR patients with second generation DES were randomly assigned to PCB (n=28) or ELCA+PCB treatment group (n=29). Consecutive 57 ISR patients with second generation DES were randomly assigned to PCB (n=28) or ELCA+PCB treatment group (n=29).

In ELCA group, coronary athereectomy by 1.4 to 2.0mm ELCA catheter was performed prior to PCB dilation. Patient groups were compared with 12 month clinical outcomes, angiographic, and OCT quantitative indices. In addition, percent residual neointima (%RN) after procedure, defined as average neointimal area (+2.5±2.8 mm2, p<0.03), OCT analysis showed average lumen area was larger and %RN was significantly lower in the ELCA+PCB than in the PCB group (8.7±1.6 vs 8.0±1.9mm2, p=0.03, and 27±16 vs 34±16%, p=0.03, respectively). Follow-up showed no adverse cardiac events in either group, %DS 23±11% and 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 DES fracture were observed in 2 cases (3% respectively). Mean scaffold area was 8.25±2.92 and 9.52±5.54 in overlapping and non-overlapping segments respectively. No case of incomplete scaffold apposition was detected.

Conclusions: BRs use for CTOs 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 routinary use of BRs in the CTO setting.
**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 of 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>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 (0.74–3.20)</td>
<td>0.25</td>
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<tr>
<td>Age ≥ 70 years old</td>
<td>1.49 (0.71–3.17)</td>
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**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

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**Background:** Previous studies reported drug-eluting stent (DES) induced significant impairment of the coronary epicardial endothelium-dependent vasomotor function in the distal portion of the treated vessel.

**Purpose:** This study evaluated whether DES also provokes coronary microvascular endothelial dysfunction at the late phase after stent implantation.

**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 \( \frac{\pi}{2} \) (coronary diameter/2) × (APV/2). The percentage change of CBF in response to the endothelium-dependent and independent vasodilators (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.

**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).
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 Promus Element (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 in vivo stent length divided by nominal stent length. Longitudinal stent deformation was defined as %SS > 10%.

**Results:** Patients' and procedural characteristics were similar between 2 EESs. Mean %SS showed a trend toward smaller in the Promus Premier than Promus Element (13.7±8.0% vs. 14.7±7.5%) although the difference did not reach statistical significance. Incidence of the longitudinal stent deformation was significantly lower in Promus Premier than the Promus Element (0% vs 13.8%).

**Conclusions:** Modified stent platform favorably affect the longitudinal strength of the Promus Element EES. Longitudinal stent deformation may not be an issue anymore for the modified version of the Promus EES.

P2777 | BENCH
A rabbit iliac model for testing the acute thrombogenicity and long-term biocompatibility of novel coronary stents and scaffolds.

**Introduction:** The rabbit iliac model is the most widely used for in vivo thrombogenicity studies. The rabbit iliac model has proven to be a reproducible method for assessing both the acute thrombogenicity and long-term biocompatibility of novel coronary stents and scaffolds.

**Methods:** 10 novel prototype RGD-peptide coated stents versus bare metal stents. Differences in thrombus formation were assessed using immunofluorescence staining, platelet deposition, and platelet impedance aggregometry studies, which showed a moderate antiplatelet action of coronary stents with the vessel wall and circulating blood. A recovery period of 2–4 weeks was used to compare the thrombotic formation bilaterally. Following euthanasia, the stented vessels were flushed, removed and fixed in formalin. Platelet deposition on both stents was compared using immunofluorescence staining. The expelled vessels were also imaged using OCT.

**Results and conclusions:** We performed 15 acute procedures, including 6 bio-absorbable vascular scaffolds versus durable polymer drug eluting and 13 recovery procedures, including 10 novel prototype RGD-peptide coated stents versus bare metal stents. Differences in cyclical flow variation, platelet deposition and OCT will be presented for the acute model and histopathological findings for the recovery model.

**Conclusions:** The rabbit iliac model has proven to be a reproducible method for assessing both the acute thrombogenicity and long-term biocompatibility of novel coronary stents and scaffolds.

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 included 25 rabbits carried out in the New Zealand White rabbit. The rabbit iliac model is the most widely used for in vivo thrombogenicity studies. The rabbit iliac model has proven to be a reproducible method for assessing both the acute thrombogenicity and long-term biocompatibility of novel coronary stents and scaffolds.

**Results:** We performed 15 acute procedures, including 6 bio-absorbable vascular scaffolds versus durable polymer drug eluting and 13 recovery procedures, including 10 novel prototype RGD-peptide coated stents versus bare metal stents. Differences in cyclical flow variation, platelet deposition and OCT will be presented for the acute model and histopathological findings for the recovery model.

**Conclusions:** The rabbit iliac model has proven to be a reproducible method for assessing both 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
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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 DES implantation in our institution, were included in 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 (proximal or distal) and the segment of NIT of 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 treatment of true coronary bifurcation. The procedural outcome
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Background and Introduction: True coronary bifurcation lesions (CBL) defined as Medina classification 1, 1, 1; 1, 0, 1; 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 side branch stent techniques and devices have been developed to improve clinical outcomes in this setting.

Purpose: 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” technique (MCT) for the treatment of CBL.

Methods: 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 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, periprocedural 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±7.3 (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.

P2784 | BEDSIDE
Takotsubo cardiomyopathy in regional Australia
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Background: Takotsubo cardiomyopathy (TCM) is prevalent, under recognized and often miss diagnosed. Detection rates reflect index of suspicion over a broad range of clinical 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 demographics; population 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 HL/or 23 (26%) had DM. 4/23 (17%) had a FH of CAD. Depression was present in 12/23 (52%), anxiety 4/23 (18%), concomitant psychiatric diagnoses were present in 12/23 (52%). Of these 6/23 (26%) had suggested TCM. Of these 6/23 (26%) had suggested TCM.

Conclusion: In regional Australia in line with urban reports there is a major prevalence of TCM. While tighter 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 in-hospital post myocardial infarction screens have focused on the susceptibilities to injury, future work should target mediators of re-

P2786 | BEDSIDE

Determinants and temporal trends of in-hospital and late onset heart failure (HF) after acute myocardial infarction (AMI): a study of 230,408 AMI patients between 1996-2010

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 Aim: To study predictors and characteristics of patients with in-hospital and late onset post-AMI HF.

Background: Few data are available on determinants of in-hospital and late-onset HF after AMI.

Methods: SWEDHEART 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 claus, use of diuretics or use of iv inotropic drugs. Late-onset HF was defined as readmission within 2 years of hospitalization in patients with 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-

Table 1. Changes in baseline characteristics of patients with in-hospital and late-onset HF after an index AMI

<table>
<thead>
<tr>
<th>In-hospital HF</th>
<th>Late-onset HF (at 2 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996-97</td>
<td>2005-09</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>73.8</td>
</tr>
<tr>
<td>Female (%)</td>
<td>39.5</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>35.4</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>34.6</td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>23.1</td>
</tr>
<tr>
<td>Prior Stroke (%)</td>
<td>17.6</td>
</tr>
<tr>
<td>Rad (%)</td>
<td>7.4</td>
</tr>
<tr>
<td>Renal failure (%)</td>
<td>5.1</td>
</tr>
<tr>
<td>STEMI/LBBB (%)</td>
<td>35.9</td>
</tr>
</tbody>
</table>

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.
Background: Heart failure (HF) is a major public health problem, especially in industrialized nations. Population-based studies have shown that, over time, the incidence of heart failure remained overall stable, while survival improved. Other studies also demonstrated that mortality rate increased by increasing patients’ age. Moreover, several studies showed that mortality was different in male vs. female patients with HF.

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 due to cardiovascular disease (23% of all hospital discharges for cardiovascular disease). The progress in treatment of HF has achieved to lengthen the life 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.

P2790 | BEDSIDE

Outpatient consultation supporting post-discharge heart failure patients reduces 30-day re-hospitalization rate

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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 discharge with the diagnosis of HF is 20–30%, which accounts for a significant fraction of health care 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: 1) 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: A retrospective analysis of all HF hospitalizations was performed. All patients were referred to a specific 30-day consultation. Risk of re-admission was calculated using the CORE HF risk re-admission score (Yale) at first visit. Patients were attended by specialized HF nurses and physicians, both GPs and geriatricians, within 3–5 days after discharge. An educational intervention was performed by nurses and a visually friendly drug prescription sheet was supplied. During the 30 day period patients were visited as many times as necessary, and then were referred for the GP for a close visit via a notification together with a written medical report and the drug prescription sheet. IV diuretic treatment was administered if required.

Results: During the first 9 months of the consult 141 patients were attended (mean age 81.5[9.6] years, 25% were >88 years old; 52.2% 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). Time setting of Internal Medicine or Geriatric Unit wards or other non-Cardiology wards were referred to a specific 30-day consultation. Risk of readmission was calculated with the CORE HF risk re-admission score (Yale) at first visit. Patients were attended by specialized HF nurses and physicians, both GPs and geriatricians, within 3–5 days after discharge. An educational intervention was performed by nurses and a visually friendly drug prescription sheet was supplied. During the 30 day period patients were visited as many times as necessary, and then were referred for the GP for a close visit via a notification together with a written medical report and the drug prescription sheet. IV diuretic treatment was administered if required.

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)

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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. Besides, emotional triggers such as grief/loss 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±11.4 vs. 66.5±13.1; p=0.40), female gender (40.7% vs. 39.4%; p=0.32) and heart rate (normal sinus rhythm: 92.9% vs. 90.4%; p=0.73), patients with ARD triggers 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), cardiogenic shock (17.1% vs. 4.1%; p=0.009) and invasive mechanical ventilation (27.5% vs. 14.8%; 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 (98.2±22.2 vs. 86.7±21.6; p<0.001). A five year survival analysis revealed increased MACCE
(25.0% vs. 14.8%; p<0.002) and mortality rates (18.8% vs. 9.0%; p<0.001) in ARD patients.

Conclusion: Acute respiratory distress related to COPD, asthma or other pulmonary conditions is a relevant trigger for TTC. Patients with such triggers require acute cardiac and intensive care more frequently than other TTC patients, which is associated with higher long-term MACCE and mortality rates.

P2729 | BEDSIDE
Telephone access to a heart failure unit: a useful health resource to prevent clinical decompensation and hospital readmissions in high-risk heart failure outpatients

Background and introduction: Heart failure (HF) programmes/units (HFU) are recommended in the latest European guidelines on HF. Increased access to healthcare by telephone contact and facilitated access to care during episodes of decompensation are recommended for patients (pts) with HF. However, there’s not much evidence on the use of telephone access (TA) and its benefits for high-risk HF outpatients followed-up in a HFU.

Purpose: To assess the use and clinical/benefit costs of TA for high-risk HF-outpatients followed-up in a HFU.

Methods: From February 2014 to October 2014 we analyzed received telephone call (TC) from family members and patients followed-up in our HFU. TC were received and answered by a HF-specialized nurse supported by a HF-Cardiologist. Patient clinical characteristics, telephone use, reasons for calling, medical & nurse interventions due to TC and clinical outputs were registered and analyzed.

Results: From 64 pts (pts) visited in our HFU during this time, 110 pts (33,1%) did use the telephone access. 73% of them were men, mean age was 70.5±13 years, 89% were on NYHA class II–III, Mean Left Ventricle Ejecction Fraction: 31±2%, 46% were on beta-blockers, 96% on Bblockers. Their Charlson comorbidities index was 4.36±2.3. We received 177 TC (mean TC/patient:1.6) and more than half of them (53%) could be independently resolved over the telephone by the nurse. From the 177 received TC, 25 (14%) were due to bureaucratic issues and 152 (86%) because of clinical reasons: nurse control of clinical parameters (16%), clinical worsening (38%), symptomatic drug side effects (e.g. hypotension:12%;12%) etc. From these symptomatic TC, 76 pts (69%) required an intervention: 5 pts (6%) were referred to Primary care physician and 71 pts resulted in an unscheduled visit to our HFU because of worsening HF (94%). 4 pts (5%) were directly sent to the emergency room and 3 more pts (4%) were directly referred to Primary care physician and 71 pts resulted in an unscheduled visit to our HFU because of worsening HF (94%). 4 pts (5%) were directly sent to the emergency room and 3 more pts (4%) were directly sent to the emergency room and 3 more pts (4%) required hospital admission from our HFU. In the rest of them (64 pts) clinical improvement was achieved by an increase in oral medication and/or intravenous (iv) diuretic administration (25 pts) and/or iv intermittent levosimendan administration (1 pt). Treatment of early decompensation in these 64 pts in a HFU prevented 59 visits to the emergency department and 5 HF-rehospitalizations with its consequent cost-reduction

Conclusions: Telephone access to a HFU for high-risk heart failure outpatients is a useful tool to treat early clinical decompensation and prevent visits to the emergency department and hospital readmissions. TA can be a cost-saving in a HFU.

P2729 | BENCH
Pathological monitoring after heart transplantation: 10-year-experience from single heart transplantation center
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Purpose: To evaluate the consecutive patients underwent HTX from our center from 2004 to 2014 and to analyze the pathological characteristics of heart transplant recipients during the third polysomnographic evaluation with CPAP titration.

Methods: From August 2004 to June 2014, 253 patients underwent HTX during this 10-year study period, a total of 706 EMBS were performed in 240 patients. Among 703 biopsies with myocardium tissues, 354 (50.4%, 354/703) showed no evidence of acute cellular rejection (ACR, grade 0). Among the remaining biopsies, acute cellular rejection was seen in 289 ACR (41.1%, 289/703) including mild rejection (grade 1R) in 286 (38.1%, 286/703) and moderate rejection in 21 (3.0%, 21/703) EMBS. No severe rejection (3R) was found in this group. Antibody-mediated rejection (AMR) was found in 5 EMBS and 2 of these 5 EMBS had the pathological diagnosis of moderate rejection (grade 2R). Immunohistochemical analysis of these 5 EMBS with AMR showed intravascular CD68 positive macrophages aggregation in 5 biopsies and linear C4d deposit only in 3 biopsies. Recurrence of giant cell myocarditis was found in the first EMB after HTX.

Conclusions: EMB is still the gold standard for routine surveillance of cardiac allograft rejection and other lesions. The prevalence and severity of both ACR and AMR are lower in this case series. The cause of C4d negative AMR should be explored and other factors related to endothelium injury might help us to identify some AMR after heart transplantation.

P2729 | BEDSIDE
Is noninvasive ventilation effective and safe in cardiogenic pulmonary edema in very old patients?
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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 face mask NIV.

The average duration of NPPV was 30±12 h. After 12 hours of the NIV in these patients has determined an improvement of the cardiac frequency from 121±18 to 73±9 (p<0.001), respiratory frequency from 39±7 to 19±2 (p<0.002). Arterial blood saturation increased from 72±5 to 95±5% (p<0.0001), pH from 7.20±0.11 to 7.40±0.09 (p<0.001), pO2 from 50±14 to 99±4 (p<0.001) as well, while pCO2 decreased from 72±12 to 42±14 (p<0.02). Significant variations of systolic 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 mortality. The choice of NIV aims to avoid complications, particularly in fragile patients as “very old patients”.

P2729 | BENCH
Effect of sleep position on cardiac arrhythmias in patients with heart failure and obstructive sleep apnea syndrome
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Background: Cardiac arrhythmias is the most common leading cause of death in congestive heart failure (CHF) patients. Overnight rostral leg fluid displacement in CHF patients is known to be related to the high prevalence and severity of obstructive sleep apnea syndrome (OSAS).

Purpose: We prospectively evaluated the effect of lying in semi-recumbent position on sleep duration and frequency of cardiac arrhythmias in CHF patients with OSAS.

Methods: The study group consisted of 30 CHF patients (26 men, mean age 54.7±10.2) who were admitted to outpatient clinics of heart failure. All patients had chronic heart failure with low left ventricular ejection fraction (mean LVEF: 28.7±6.6%) and were receiving optimal guideline recommended medical treatment. These patients underwent polysomnography conventional in lying flat position first and were diagnosed as OSAS. After OSAS diagnosis, polysomnography was repeated within one week in a semi-recumbent position for evaluating the position effect. Among the study patients CPAP was applied to available 22 of them during the third polysomnographic evaluation with CPAP titration. The ECG records during these interventions were evaluated after completing all of the procedures.

Results: Mean apeana-hypopnea index was 30.8±5.2 events/h while lying flat and decreased to 17.6±12.1 events/h in semi-recumbent position (p=0.001). Significant decrease in oxygen saturation index decreased from 22.1±19.8 to 12.7±11.5 events/h (p<0.0001) and mean nocturnal oxygen saturation (SpO2) (p=0.050) and lowest (SpO2) (p=0.004) were improved in semi-recumbent position. The most common arrhythmias were ventricular premature contractions (63%), supraventricular tachycardias (28%), atrial premature contractions (26%), atrial fibrillation (23%), ventricular tachycardias (13%), respectively. Total number of arrhythmias was 46 while lying flat and decreased to 36 in semi-recumbent position (p=0.025). The most striking decrease in the total number of arrhythmias was evident during CPAP treatment from the patient position. The total number of arrhythmias was 30 in flat position and 23 in semi-recumbent position whereas decreased to 16 with the effect of CPAP (p=0.001 and p=0.035 respectively).

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Conclusions: This study showed that the severity of OSAS and the total number of arrhythmias decreased significantly in semi-recumbent sleep position in patients with CHF. The maximal decrease in arrhythmias were achieved during the CPAP treatment.

P2796 Ferric carboxymaltose in iron deficient heart failure patients: a meta-analysis on individual patient data


Background and aim: Despite recent developments in heart failure (HF) management, the morbidity and mortality in this clinical syndrome remain unacceptable high and trials patients 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 chronic cardiac (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 is performed using all available completed trials conducted in systolic CHF patients with ID (FER-CARS-01 and FER-CARS-02, EFFICACY-HF and EFFICACY-HF) comparing 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/IV) with LVEF <45% and with presence of ID (defined as ferritin <100 ng/dl, or ferritin 100–300 ng/dl if transferrin saturation (TSAT) <20%). FER-CARS-01 and FAIR-HF were randomized 2:1, EFFICACY-HF and CONFIRM-HF 1:1 to treatment with FCM or placebo. CONFIRM-HF lasted 52 weeks and during the correction phase, FCM-treated patients received a cumulative dose of 1 500–2 000 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-CARS-01 12 weeks, respectively. During the correction phase of these trials, iv injections of 200 mg until the individually required cumulative dose calculated by the Ganzoni formula. Patients received a 200 mg maintenance iv FCM dose every four weeks until the end of the trial. The primary efficacy endpoints are the rate of and time to first hospitalisation(s) or death for any cardiovascular reason. The key secondary endpoints include time to and time to first hospitalisation(s) due to worsening HF or death for any cardiovascular reason, hospitalisation(s) for any cardiovascular reason, hospitalisation(s) due to worsening HF and all-cause hospitalisation(s) as well as all-cause hospitalisation(s) or all-cause death, all-cause death and death for any cardiovascular reason. An independent and independent, blinded Clinical Endpoint Committee adjudicated all hospitalisations and deaths. Additional secondary efficacy endpoints are change from baseline in PGA, 6MWT distance, NYHA, EQSD and Hb and iron parameters (TSAT, ferritin, transferrin) as well as days lost and length of hospitalisation (days). The safety endpoints include all adverse event and laboratory parameters.

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 important 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

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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 use. 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 apnea (OSA) and central sleep apnea (CSA) were included. Data were collected before and during the first night of therapy (AHI: 33.3±15.9 to 7.9±7.4/h, p<0.001). More important, markers of hypoxemic burden like time spent with oxygen saturation below 90% (T90-), as well as lowest or mean oxygen saturation (SaO2) and number of oxygen desaturation of at least 3% were reduced by either therapy (table: *p<0.05). Further, moderate to severe SDB (AHI >15/h) was treated by adaptive servoventilation (ASV).

Results: A total of 323 patients (25 female, 68±10 years, BMI 29.7±5.1, NYHA 2±1, NT-proBNP 2774±1761 pg/mL, LVEF 34±13%) 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 hypoxemic burden like time spent with oxygen saturation below 90% (T90-), as well as lowest or mean oxygen saturation (SaO2) and number of oxygen desaturation 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


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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/mmHg, 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/mmHg, highest quartile) after adjusting for age and examination year. Median ECP was associated 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 (hazards 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.

P2799 | BEDSIDE Impact of sleep-disordered breathing and its treatment on post-discharge outcomes in hospitalized patients with left ventricular systolic dysfunction following acute decompensated heart failure

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Introduction: Hospitalizations for acute decompensated heart failure (ADHF) are associated with worse post-discharge clinical outcomes. Stratifying hospitalized patients at a high risk for worse post-discharge clinical outcomes after ADHF is important. Limited data regarding impact of sleep-disordered breathing (SDB) and its treatment by positive airway pressure (PAP) on post-discharge clinical outcomes in hospitalized patients following ADHF are available. Purpose: To investigate relationship between SDB and its treatment by PAP and post-discharge clinical outcomes.
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 analysis. Results: Overall, 114 patients including 76 patients 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, renin-angiotensin-aldosterone system blockers, hemoglobin, serum sodium, estimated glomerular filtration rate (eGFR), plasma B-type natriuretic peptide (BNP) level, percentages 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, prevalence of SDB was associated with increased risk of poor outcome and rehospitalization, which may be reversible by PAP therapy. Thus, following ADHF, hospitalized patients with LV systolic dysfunction should be evaluated for PAP treatment.

P2800 | BEDSIDE
The impact of compensated heart failure requiring hospitalization on pulmonary diffusing capacity for carbon monoxide
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Background: The reduction in pulmonary diffusing capacity for carbon monoxide (DLCO) is well documented in heart failure (HF). DLCO decreases gradually as the lung ages and structural changes. The reduced DLCO may predict all-cause mortality in chronic heart failure. However, there are no reports regarding the impact of compensated HF requiring hospitalization on DLCO.

Methods and results: We retrospectively studied 56 patients (65±15 years, LVEF 40±18%) who underwent pulmonary function tests (PFT) twice. Patients with pulmonary artery disease, congenital heart disease or cardiac surgery were excluded. Our subjects were divided into two groups: 30 patients who hospitalized for HF between the two PFT and 26 patients who did not. DLCO was expressed as a percentage of the predicted values (%DLCO). The change in DLCO was calculated as a percent change in %DLCO between the PFT. There were no significant differences between the two groups in age (61.1±15 years vs. 69.4±15 years), male gender (67% vs. 58%), BNP (213.8 (50.1–441.2) vs. 133.2 (73.9–149.9) pg/ml), estimated GFR (56±24 vs 58±16 ml/min/1.73m²), %DLCO (90.5±19.6% vs. 93.6±22.0%), the period between the two PFT (44.3±39.8 vs. 50.7±38.9 months), estimated glomerular filtration rate (eGFR), plasma B-type natriuretic peptide (BNP) level and % VC (1.06 (0.99–1.14) vs. 1.02 (0.93–1.11), P = 0.06).

Conclusion: The decrease in DLCO was associated with HF admission (P = 0.03, Table 1).

Table 1. A analysis of % change in characteristics between the two points of PFT for HF admission

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>odds ratio</td>
<td>P</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.97 (0.94–1.01)</td>
<td>0.1</td>
</tr>
<tr>
<td>Estimated GFR</td>
<td>0.99 (0.97–1.01)</td>
<td>0.6</td>
</tr>
<tr>
<td>Log BNP</td>
<td>1.03 (1.00–1.06)</td>
<td>0.02*</td>
</tr>
<tr>
<td>% VC</td>
<td>0.98 (0.94–1.02)</td>
<td>0.4</td>
</tr>
<tr>
<td>FEV1%</td>
<td>1.06 (0.99–1.14)</td>
<td>0.06</td>
</tr>
<tr>
<td>% DLCO</td>
<td>0.96 (0.92–0.99)</td>
<td>0.03*</td>
</tr>
</tbody>
</table>
| VC, vital capacity; FEV1, forced expiratory volume in one second; DLCO, diffusing capacity for carbon monoxide.

Conclusion: DLCO is decreased following compensated HF. Pulmonary congestion requiring hospitalization may cause irreversible reduction of DLCO.
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=18), and ASV cessation group (n=19). 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, apnea hypopnea 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=0.046) (Figure 1).

**Conclusion:** These results suggest that ASV is effective in not only good response group but also poor response group.

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**Keywords:** Adaptive servo-ventilation (ASV), chronic heart failure, exercise, ventilation

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**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

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**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 ACPE 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 oxygen saturation was insufficient. Exclusion criteria included cardiogenic shock, disturbance of consciousness, fatal arrhythmia, right-sided heart failure, infection, past history of noninsulin positive pressure ventilation and DNAR.

**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 significantly lower in the ASV group than the control group (19.3±11.0 vs 26.3±16.6 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.

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**Keywords:** ASV, acute cardiogenic pulmonary edema, exercise, ventilation

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**P2805 | BEDSIDE**

Is 3D interchangeable with 2D echocardiography for the initiation of device therapy in patients with heart failure with reduced ejection fraction?

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**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 (HFrEF). 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 HFrEF, when used by trainees with different levels of expertise.

**Methods:** 51 patients with symptomatic HFrEF and sinus rhythm (46 males, age 58±17 years) underwent standard transthoracic 2D and 3D full-volumes 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 reclassify 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:** 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.

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**Keywords:** 3D, 2D, echocardiography, LVEF, HFrEF, device therapy.
lower average HR ($M-VTI (cm) 21.9±4 17.2±3.9 0.000$
$SPAP (mmHg) 40±10 48±12.9 0.022$

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (HR&lt;75 bpm)</th>
<th>Group 2 (HR&gt;75 bpm)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean NYHA class</td>
<td>2.1±0.7</td>
<td>2.7±0.7</td>
<td>0.013</td>
</tr>
<tr>
<td>SPAP (mmHg)</td>
<td>40±10</td>
<td>48±12.9</td>
<td>0.022</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>40.9±4</td>
<td>34.5±3.9</td>
<td>0.026</td>
</tr>
<tr>
<td>M VTI (cm)</td>
<td>21.9±4</td>
<td>17.2±3.9</td>
<td>0.000</td>
</tr>
<tr>
<td>FT (ms)</td>
<td>480±100</td>
<td>342±96</td>
<td>0.000</td>
</tr>
<tr>
<td>Ao-VTI (cm)</td>
<td>29±1.3</td>
<td>23.1±7.2</td>
<td>0.005</td>
</tr>
<tr>
<td>ET (ms)</td>
<td>270±12</td>
<td>244±26</td>
<td>0.004</td>
</tr>
<tr>
<td>TS-SD (ms)</td>
<td>17.4±8.1</td>
<td>19.4±11.6</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusion: Lower average HR (<75 bpm) is associated with better clinical and hemodynamic response to CRT

BASIC MECHANISMS IN HEART FAILURE

P2809 | BENCH

Endoglin is required to maintain normal cardiac function in adult life

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Introduction: Endoglin, a co-receptor for ligands of the transforming growth factor-β (TGFβ) superfamily, may promote signalling through the ACVRL1 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 characterised by localised arteriovenous malformations (AVMs), fragile vessels and bleeding.

Purpose: Given the central role of the TGFβ superfamily in cardiovascular conditions, we used mouse models to determine endoglin’s role during adult life and assess its effect on cardiac function.

Methods: Depleted in adult Rosa26-Cre-ERT2,Enh1/1flox mice to generate ubiquitous 'endoglin knockout' mice.

These mice show a similar increase in heart mass and ventricular volumes to the Rosa26-Cre-ERT2 to generate endothelial specific depletion of endoglin (Eng-iKoE mice). Cardiac magnetic resonance imaging, myography, vascular casting, immunohistology and qPCR were used to evaluate cardiovascular changes after endoglin knockdown.

Results: Ubiquitous loss of endoglin leads to an enlarged heart and cardiomyocyte hypertrophy within 5 weeks, and cardiac ventricles continue to enlarge substantially over subsequent weeks. To address whether this cardiac remodelling is due to loss of endoglin in endothelial cells we generated Eng-iKoE mice. These mice show a similar increase in heart mass and ventricular volumes to the Eng-iKoE mice. We also found in the Eng-iKoE mice an increased cardiac output, progressing to high output heart failure (HOHF) associated with increased cardiac expression of brain natriuretic peptide, atrial natriuretic peptide and α-actinin. As HOHF in HHT may result from anaemia or AVMs, we first evaluated these phenotypes in Eng-iKoE mice. However, we have not detected AVMs in major organs or found evidence of anaemia that could account for the rapid increase in cardiac output. On the other hand, we did observe enlargement of
the pulmonary distal vasa vasorum 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-IKOe 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 endothelial endoglin in adult life for maintenance of cardiac structure and function.

P2811 | BEDSIDE
Clinical correlates of soluble neprilysin concentrations in patients with acute heart failure
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Background: Neprilysin (NEP) is a neutral endopeptidase that degrades natriuretic and other vasoactive peptides. A recent trial, the PARADIGM-HF, has showed 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: 126 AHF patients aged 71±11 years, 59% male, 44% with LVEF<35% admitted with AHF were studied. Blood samples were obtained at arrival to the emergency department and at discharge. NEP concentrations were measured using an ad hoc modified ELISA assay. Clinical data were recorded during the hospitalization.

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 (r=0.25; p=0.009). Creatinine and BUN were also significantly correlated to NEP levels at admission (r=0.28; p=0.002 and r=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=0.068), as well as those who were of a lower body mass index, age, gender, ejection fraction and risk factors. Mortality rates according to quartiles of HGF were 98, 183, 374 and 392 per 1000 patients and one-year HGF showed a significant interaction and added complementary prognostic information to NT-proBNP concentrations: mortality rates were higher than 100 patients and one year were 72% when both markers were below the median, and up to 490 when both markers were above the median (p=0.001).

Conclusion: NEP 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.

P2812 | BEDSIDE
Distribution of leukocyte populations is affected by cardiac resynchronisation therapy
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Chronic heart failure with reduced ejection fraction (CHF-REF) is characterized by enhanced inflammatory and abnormal immune response. Deeper understanding of the immune processes in CHF-REF is crucial for development of innovative treatment strategies. Cardiac resynchronisation therapy (CRT) created a promise of reversal of CHF symptoms. Investigations of changes of immune response before and after CRT implantation may improve understanding of the processes responsible for development and progression of heart failure. The aim of the study was to analyze the changes of crucial immunomodulatory subpopulations of peripheral blood leukocytes: monocytes/macrophages, Th17 and Treg lymphocytes.

The study enrolled 50 stable CHF patients: NYHA class II–III, EF 45–55%, and 45 patients without CHF but with similar comorbidities profile, matched for age and sex. All were on optimal medical therapy for at least 3 months and had indications for CRT listed in current ESC CHF guidelines. Patients underwent CRT device implantation and were controlled after 6 months later. All subjects underwent transthoracic echocardiography and venous blood tests. The frequencies of particular subpopulations of monocytes, Th17 and Treg lymphocytes were established using flow cytometry with antibodies against CD14, CD16, CD161, CD 25, CD120 and CD127 respectively.

We were able to show that initially CHF patients had more classical (CD14+CD16-) and non-classical (CD14+CD16+) subpopulations (by 26% and 23% respectively p<0.05 in both cases) increased resembling now the distribution of monocyte subpopulations in healthy controls. This phenomenon was observed only in patients with positive clinical response, whereas there was no change in monocyte subpopulations of patients whose clinical status did not improve. No significant change was observed in the frequencies of Th17 and Treg lymphocytes 6 months after CRT.

Our data indicate that CHF is associated with changed distribution of immunomodulatory subpopulations of lymphocytes and monocytes. Moreover, positive clinical response to CRT normalizes composition of monocyte subpopulations in CHF patients, while having no effect on Th17 and Treg lymphocytes.

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P2813 | BEDSIDE
Hepatocyte growth factor in patients with acute heart failure
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Background: Experimental models have showed 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 limited. The aim of this study was to investigate the impact of HGF in patients 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 (r=0.001), cystatin (r=0.006) and eGFR (KDO-EP, MDRD, cyst or Hoek-13 based, p<0.001). However, no correlations were found with echocardiographic parameters (LVEF, LV mass index, and left atrium diameter), nor with other parameters of cardiac remodeling. HGF provided significant prognostic information and added complementary information to NT-proBNP concentrations: mortality rates were higher than 100 patients and one year were 72% when both markers were below the median, and up to 490 when both markers were above the median (p<0.001).

Conclusion: 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.

P2814 | BEDSIDE
Excessive extracellular water accumulation in patients with sarcopenia with acute decompensated heart failure
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Background: Sarcopenia, the loss of skeletal muscle, is gaining increase attention because it has been proposed as a prognostic factor for various diseases. The aim of this study is to investigate the specific characteristics of patients with sarcopenia with acute decompensated heart failure (ADHF).

Methods: We analysed 135 consecutive patients admitted to our hospital with symptoms of ADHF (left ventricular ejection fraction 30±14%). We measured the volume of extracellular water (ECW) of the body on admission and before discharge by multi-frequency bio-impedance analysis. Sarcopenia was defined as a skeletal mass index <5.97m in males and <5.7m in females through dual energy X-ray absorptiometry immediately before discharge.

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 (ADHF).

Conclusions: Patients with sarcopenia with ADHF are older than those for the patients without sarcopenia (1093.6±457.2 vs. 718.2±1081.6 pg/ml, p<0.001). Further, the BNP levels in the compensated phase for both patient groups were similar (584.0±979.8 vs. 490.9±342.8 pg/ml) after decongestion treatment. The ratio of ECW-to-body weight at discharge by multi-frequency bio-impedance analysis. Sarcopenia was defined as a skeletal mass index <5.97m in males and <5.7m in females through dual energy X-ray absorptiometry immediately before discharge.

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 were higher than those for the patients without sarcopenia (1093.6±457.2 vs. 718.2±1081.6 pg/ml, p<0.001). Further, the BNP levels in the compensated phase for both patient groups were similar (584.0±979.8 vs. 490.9±342.8 pg/ml) after decongestion treatment. The ratio of ECW-to-body weight at discharge by multi-frequency bio-impedance analysis. Sarcopenia was defined as a skeletal mass index <5.97m in males and <5.7m in females through dual energy X-ray absorptiometry immediately before discharge.
state, rendering them resistant to further diuretic therapy. Thus, clinically indicated compensated status of patients with sarcopaenia is not sufficiently compensated as well as their hyponaemic 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 sarcopaenia and why the prognosis of such patients is uncertain.

P2815 | BEDSIDE
Procalcitonin is a marker of infection in patients with heart failure and a strong predictor of mortality: a systematic review and meta-analysis
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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. Nine articles were examined for further 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 (0.23±0.11 ng/mL versus 0.12±0.03 ng/mL, 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/mL to 0.25 ng/mL, and when compared to patients with low PCT concentrations, patients with the cut-off value PCT had increased mortality (RR 1.82; 95% CI [1.33–2.49], p < 0.001).

Conclusions: PCT allows short-term risk stratification in patients with CHF.

P2816 | BEDSIDE
The influence of gender on epidemiology, precipitating Factors, management and prognosis of the patients with acute decompensated heart failure: insights from KorHF Registry
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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 consented during the third trimester (28–30 weeks’ gestation) and within 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: We sequentially assessed 463 consecutive Japanese pregnant women during the third trimester (28–30 weeks’ gestation) and within 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, 33.1±4.9 years; age of delivery, 35 years; 18.2%, pregnancy-induced hypertension (PIH), 4.5%; oxygen use, 31.9%; delivery by cesarean section, 12.2%; and mean hemoglobin levels during the third trimester and after delivery, 11.1±0.9 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±23.2 pg/mL) than in women at 28–30 weeks’ gestation.

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 variously, so we emphasize the importance of the approach concerning these differences.
tion (16.8±12.5 pg/mL; p<0.0001). Moreover, BNP levels were strongly associated with anemia after delivery. In multivariate analysis, the factors affecting elevated cTnI levels were PIH (odds ratio [OR]: 5.04, 95% confidence interval [CI]: 1.23–18.5, p=0.025), malposition of the placenta (OR: 5.60, 95% CI: 1.47–19.4, p=0.012), oxytocin use (OR: 2.91, 95% CI: 1.16–7.64, p=0.021), and anemia after delivery (OR: 2.91 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?

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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 (NFP) and 38 were frail. Using mFP, 68 were NFP and 52 were frail. Frailty was independent of age, LVEF and renal function. Frailty (by FP or mFP) was associated with being female, anaemia, hypoalbuminaemia and mortality (Figure). Using Cox proportional hazards model, frailty as assessed by mFP remained an independent predictor of survival but frailty as assessed by FP did not.

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 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 vs. 3490) patient admissions 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 1303 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% (ARR 13.2%; ARR 1.7%), equating to a potential 72 lives saved in that year.

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 rates for recurrent heart failure at 0–2, 2–4, 4–6 and 6–8 months were 7.3%, 3.1%, 2.1% and 3%. 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 readmission 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>Heart failure admission per patient during 8 months after discharge by patient type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–2 months</td>
</tr>
<tr>
<td>All patients</td>
<td>92/1266</td>
</tr>
<tr>
<td>HF-pEF</td>
<td>28/410</td>
</tr>
<tr>
<td>HF-pEF</td>
<td>64/856</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time after discharge</th>
<th>Admission per patient during 8 months after discharge by admission type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–2 months</td>
</tr>
<tr>
<td>All admissions</td>
<td>293 (23%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>92 (7.2%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>50 (3.8%)</td>
</tr>
<tr>
<td>Non-cardiovascular</td>
<td>151 (12%)</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. HFrEF and HFrEF demonstrate similar readmission patterns.

P2821 | BEDSIDE

Necropsy findings in patients with heart failure

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Introduction: Heart failure is a condition associated with high mortality and understanding the mechanisms of death can contribute to the care of patients. Howw
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±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 rhabdomyotic disease in 63 (12.6%). According to the autopsy, the first post-graft rejection was 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 athroesclerosis in 169 (33.8%), diabetes mellitus in 76 (15.2%) and chronic obstructive pulmonary disease in 5 (10.6%).

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**

**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.

**Results:** Of the 270 patients examined, 108 patients were male, with a mean age 60±9.260; 260 patients presented with fever and polyarthralgia and 81 developed palpitations. And there were 3 sudden cardiac deaths. Arrhythmias occurred in 46.8% of cases; they included bradyarrhythmias (33%), atrial and ventricular ectoic 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 bradyarrhythmias suggest Chikungunya myocarditis.

**P2824 | BEDSIDE**

**Objective:** The main causes of death were acute graft rejection 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 athroesclerosis in 169 (33.8%), diabetes mellitus in 76 (15.2%) and chronic obstructive pulmonary disease in 5 (10.6%).

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. Morr 1, I. Mendoza 2, K. Gonzalez 1, I. Villalobos 1, Y . Meza1, C. Morr1, C. Morr1, J. Marques1, 1 Central University of Venezuela (UCV), Tropical Cardiology Department, Caracas, Venezuela; 2 Jackson 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.

**Results:** Of the 270 patients examined, 108 patients were male, with a mean age 60±9.260; 260 patients presented with fever and polyarthralgia and 81 developed palpitations. And there were 3 sudden cardiac deaths. Arrhythmias occurred in 46.8% of cases; they included bradyarrhythmias (33%), atrial and ventricular ectoic 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 bradyarrhythmias suggest Chikungunya myocarditis.

**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**

**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.

**Results:** Of the 270 patients examined, 108 patients were male, with a mean age 60±9.260; 260 patients presented with fever and polyarthralgia and 81 developed palpitations. And there were 3 sudden cardiac deaths. Arrhythmias occurred in 46.8% of cases; they included bradyarrhythmias (33%), atrial and ventricular ectoic 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 bradyarrhythmias suggest Chikungunya myocarditis.

**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.
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

<table>
<thead>
<tr>
<th>Predictor</th>
<th>No. of patients</th>
<th>Mean annual total contacts (CI)</th>
<th>Incidence rate ratio (CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>674</td>
<td>10.8 (10.2–11.4)</td>
<td>1.05 (1.00–1.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>299</td>
<td>12.1 (11.2–13.0)</td>
<td>1.09 (1.00–1.20)</td>
<td>0.045</td>
</tr>
<tr>
<td>Prescribed loop diuretic</td>
<td>No</td>
<td>424</td>
<td>9.9 (9.3–10.6)</td>
<td>1.00 (0.94–1.07)</td>
</tr>
<tr>
<td>Yes</td>
<td>549</td>
<td>12.1 (11.4–12.9)</td>
<td>1.17 (1.07–1.27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVSD severity</td>
<td>Mild</td>
<td>379</td>
<td>11.8 (11.0–12.7)</td>
<td>1.03 (0.98–1.09)</td>
</tr>
<tr>
<td>Moderate</td>
<td>425</td>
<td>11.0 (10.2–11.7)</td>
<td>0.93 (0.89–1.02)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severe</td>
<td>169</td>
<td>10.3 (9.4–11.3)</td>
<td>0.86 (0.80–0.93)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of LVSD (yrs)</td>
<td>0–1.99</td>
<td>282</td>
<td>12.4 (11.4–13.5)</td>
<td>1.00 (0.94–1.07)</td>
</tr>
<tr>
<td>2–3.99</td>
<td>256</td>
<td>11.2 (10.3–12.2)</td>
<td>0.88 (0.79–0.97)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥4</td>
<td>435</td>
<td>10.3 (9.7–11.0)</td>
<td>0.85 (0.78–0.94)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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

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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 and ESC 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% pr. 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 19%, abnormal blood pressure response 13% (all age groups), maximal left atrium dimension ≥ 30 mm 7% (20±4 mm (mean±SD), non-sustained VT 23%. 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 was 8.4% (23/275) (AHA/ACC 2011) and 4.5% (14/310) (ESC 2014) (ESC vs. AHA/ACC, p=0.02). 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

J. Jalalain1, A. Tammadori2, M. Iranian3, M. Saravi4, A. Mohgadamnia5, S. Khafi5, 1 Mazandaran University of Medical Sciences, Sari, Iran, 2 Department of Cardiology, Fatemeh Zahra Hospital, Sari, 3 Babol University of Medical Sciences, Department of Hematology, Babol, 4 Babol University of Medical Sciences, Student Research Committee, Babol, 5 Babol University of Medical Sciences, Department of Cardiology, Babol, Iran

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 transhoracic 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 this patients.

P2829 | BEDSIDE

Deterioration of left ventricular function in patients caused by right ventricular stimulation: can it be predicted by LV-function at the time of implant?

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Background: Right ventricular pacing (RVP) may lead to asynchronous contraction, systolic dysfunction, and heart failure (HF). Not much is known about...
the incidence in patients (PTS) treated with pacemakers (PM) for standard antibradycardic 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%) 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%). Anteriority of LV function was observed in 23% (35%) of PTS, 45% preserved their initial LV function and 24% impaired their LV function within group 3. 26/1131 (2.3%) PTS developed severe HF (NYHA:3) and were upgraded to biventricular pacing (CRT). The incidence was 12.1% (in group 1, 8.4% in group 2 and 7.8% 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 //91% (age 71 yrs) patients who have diabetes mellitus and coronary artery disease were excluded. LV layer contractility and relaxation were assessed by radial and circumferential strain (by 29 and 37%). LV stiffness increased in HTN with LVH (1.0±0.2 mmHg), especially those in endocardium, could be deteriorated by pressure overload that causes LV hypertrophy (LVH) and fibrosis, resulting in hypertensive heart failure (HHF) with reduced or preserved ejection fraction. However, discrimination between hypertensive heart disease and HHF has not been fully examined. We sought to noninvasively examine LV properties and elucidate the feature of HHF using novel one-beat three-dimensional speckle tracking echocardiography with volume rate of 60–80vps (3D-STE).

**Methods:** We examined 54 controls (age 69±9), 50 patients with HTN without LVH (age 70±9), 40 patients with HTN with LVH (age 69±6) and 24 patients with HF (age 71 yrs) patients who have diabetes mellitus 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 estimated using KT index that we reported as log (left atrial active emptying function/ left atrial minimum volume index). PCWP was calculated as 10.8−12.4x KT index. LV stress was calculated as log (left atrial active emptying function/ left atrial minimum volume index). LV stress were expressed as log (left atrial active emptying function/ left atrial minimum volume index). LV stress were expressed as log (left atrial active emptying function/ left atrial minimum volume index). LV stiffness increased in HTN with LVH (1.0±0.2 mmHg), especially those in endocardium, could be deteriorated by pressure overload that causes LV hypertrophy (LVH) and fibrosis, resulting in hypertensive heart failure (HHF) with reduced or preserved ejection fraction. However, discrimination between hypertensive heart disease and HHF has not been fully examined. We sought to noninvasively examine LV properties and elucidate the feature of HHF using novel one-beat three-dimensional speckle tracking echocardiography with volume rate of 60–80vps (3D-STE).

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**Results:** Endocardial SR-S and SR-IVR even in HTN without LVH decreased without reduction of LVEF (SR-S; control: 2.6±0.6, LVH (−): 2.3±0.6, LVH (+): 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 −0.5±0.2 s–1). LVEF, 67±6, 67±6, 69±8 and 55±12%, respectively, p<0.05 vs control. Endocardial SR-S and SR-IVR were significantly greater than the corresponding epicardial SR (by 29 and 37%). LV stiffness increased in HTN with LVH and further increased in HHF (0.27±0.13, 0.26±0.12, 0.44±0.29 and 0.71±0.30, respectively) associated with increased PCWP (14.9±2.6, 9.6±2.7, 10.3±3.8* and 14.5±2.9 mmHg, respectively) and diastolic stress (9.9±4.3, 9.0±3.8, 13.1±6.8* and 17.2±6.1 dynes/cm², respectively). On multivariate regression analysis, PCWP was an independent predictor of HF. Using 11 mmHg as a cutoff value, sensitivity and specificity of 45% to predict HHF was 100% and 81%.

**Conclusion:** Noninvasive 3D-STE examination revealed that LV endocardial contractility and relaxation decreased even in HTN without LVH and further decreased in HHF and that HHF had more reduced EF associated with increased PCWP, LV stress and LV stiffness. Elevated PCWP estimated by KT index was an independent predictor of HF.
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 (2D-LVEF) was calculated using Simpson’s biplane method. Real-time three-dimensional full volume images of the left ventricle were recorded and analyzed. Left ventricular end-diastolic volume (EDV), end-systolic volume (ESV), stroke volume (SV), ejection fraction (LVEF), and global circumferential strain (GCS), global radial strain (GRS), and global strain (GSD) (3D-SF) were calculated. Time to peak GCS (T-s), Time to peak GCS (T-cs), Time to peak GRCS (T-s), and Time to peak GS (T-3d) were analyzed. Volume parameters were standardized by body surface area (BSA) and heart rate.

**Results:** Compared with the controls, ESRF patients had significantly lower GCS, GRS, and 3D-LVEF (GCS: −18.8±3.2% vs −17.0±2.3%, p<0.05; GRS: 39.4±3.4% vs 37.0±3.5%, p<0.05); 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±14.2 mm³/m²; ESV: 16.3±3.2 vs 22.0±6.9 mm³/m²; SV: 21.3±4.3 vs 26.4±6.5 mm³/m², p<0.001). Additionally, T-s and T-cs were defined in the left ventricle (T-mv): 38.5% vs 41.6%, TS: 38.5% 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 analyses showed GCS was an independent predictor of LVEF in patients with ESRF (beta =−1.49, 95% CI (−2.02)−(−0.95), p<0.001).

**Conclusions:** Renal failure leads to subclinical LV deformation and dysfunction. 3DSTE may have potential in the evaluation and follow-up of patients with ESRF.

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**P2834 | BEDSIDE**

Adding brain natriuretic peptide, ultrasound lung comets or Doppler imaging on clinical guidance in 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 predicting hospitalization rates.

**Purpose:** Compare re-hospitalization rates with treatment guided by clinical findings and Doppler imaging to measure E/Ea targeting a mean below 8, AADist (PERvm) 0.70±0.45, 0.63±0.62, 0.44±0.30*, 0.59±0.39, 0.50±0.35* 1.38±1.28***

**AADist (PERv) 2.08±1.05 1.30±0.76*** 1.09±0.72*** 1.36±0.63*** 1.13±0.62*** 1.98±1.14

**EDV (ml) 136±29 155±53* 138±50 145±41 142±27 247±61***

**Age (ys) 48±13 64±13** 65±8 65±8 65±13 65±8

**Results:** Compared with the controls (29±4) being highly age-dependent. Both absolute and relative AAD dilatation was lower in patients with CAD (9.6±5.4 and 3.0±1.9, resp) compared to controls (12±2.0 and 6.0±2.6, resp). More detailed results are presented in Table 1.

**Conclusions:** Adding brain natriuretic peptide was higher in CAD-related groups (33±4) than in controls (29±4) being highly age-dependent. Both absolute and relative AAD dilatation was lower in patients with CAD (9.6±5.4 and 3.0±1.9, resp) compared to controls (12±2.0 and 6.0±2.6, resp). More detailed results are presented in Table 1.

**Results:** Adding aorta diameter was higher in CAD-related groups (33±4) than in controls (29±4) being highly age-dependent. Both absolute and relative AAD dilatation was lower in patients with CAD (9.6±5.4 and 3.0±1.9, resp) compared to controls (12±2.0 and 6.0±2.6, resp). More detailed results are presented in Table 1.

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P2837 | BEDSIDE
Optical coherence tomography imaging long term follow-up of renal arteries after radio-frequency catheter-based renal denervation
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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: 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±6.6 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 RDN.
Conclusion: Renal arteries present a favorable vessel healing post RND 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
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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. 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.

P2839 | BEDSIDE
Catheter based renal denervation for resistant hypertension. 24 month results of the EnligHTN I Study using a multielectrode ablation system
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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 a systolic BP >160 mmHg and LVH in 24 patients. On enrollment, the mean office BP were 160±16/96±14 mmHg, 150±11/83±13 mmHg and 158±8/90±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±4.7 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 or life-threatening adverse events related with the procedure.
Conclusion: 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.
P2841 | BEDSIDE
Effect on heart rate following renal denervation: Insights from the Global SYMPLICITY Registry
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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-comer worldwide registry evaluating the safety and effectiveness of treatment with the SymptycTM 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 (p <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 24-hour ambulatory heart rate.

Conclusion: In the Global SYMPLICITY Registry, RDN is associated with a significant reduction in office and 24-hour SBP 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.

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P2842 | BEDSIDE
Triple versus dual antiplatelet therapy in patients undergoing unprotected left main percutaneous coronary intervention
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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 DAPT for at least 1 month and 67 pts received TAPT. 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 independent predictors for MI at 3 years.

Conclusion: TAPT administration in pts undergoing uLM-PCI with DESs seems to be superior and safer 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: a 24-months follow-up study
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Background and introduction: The favorable impact of renal sympathetic denervation (RDN) on cardiac parameters such as on left ventricular (LV) morphology, geometry and function have 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±19/18 mmHg under 4.5±0.6 drugs] who underwent RDN were followed-up for 24 months. A full transthoracic 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±21/85±14 mmHg at 12 months and to 143±23/80±14 mmHg at 24 months (p<0.001 for all). In the RDN group, LV mass index was significantly reduced from 136±20.1 g/m² (56.5±8.7 g/m².7) to 121±16.6 g/m² (50.6±5.8 g/m².7) at 12 months and to 115.6±23.3 g/m² (48.8±9.3 g/m².7) at 24 months (p<0.01 for all). RDN decreased mean interventricular sep...
Agreement between automatic and manual measurement of heart rate in patients with atrial fibrillation

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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 M5-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 an 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 coefficient 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. Patients who had HR above 80 bpm via Microlife device may over-estimate HR of AF patients.

Conclusions: There is high correlation between two devices and manually counting HR, which decreased slightly in patient with HR above 80bpm via the Microlife device. Microlife device may be over-estimated HR of AF patients.

Agreement between automatic and manual measurement of blood pressure in patients undergoing hemodialysis

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Purpose: The present study, for the first time, demonstrated that lowering of dialysate sodium concentration improves ABPM parameters such as 24-hour systolic BP (SBP) and diastolic BP, and increasing of dialysate sodium concentration leads to decreased of ABPM parameters.

Methods: A total of 50 patients, who had creatinine clearance levels less than of 10 ml/min/1.73 m² and had been on chronic HD treatment for at least one year between March and December 2013, were recruited in this study. After enrolment, stage, study subjects were allocated to low sodium dialysate or placebo for six months via computer-generated randomization.

Results: Twenty four hour SBP, day time SBP, night time SBP and daytime DBP were significantly decreased in low sodium dialysate group after six months (p<0.05). There was no significant reduction in two groups in 24-hour DBP and daytime DBP (p>0.05). Moreover, the average antihypertensive drug was significantly reduced from 2.1±0.8 to 1.2±0.4 in the low sodium dialysate group (p<0.001) (Table). Furthermore, IDWG was found to be significantly decreased in the low sodium dialysate group after six months (p<0.001).

Conclusion: The present study, for the first time, demonstrated that lowering of dialysate sodium concentration improves ABPM parameters such as 24-hour SBP, daytime SBP, nighttime SBP and nighttime DBP in HD patients compared with standard dialysis. We also concluded that low sodium dialysate led to reduction in the IDWG and the number of antihypertensive medication.

Obstructive sleep apnea using watch-pat 200 is independently associated with an increase in the morning blood pressure surge in never-treated hypertensive patients

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This study aimed to examine the association between OSA and MS in never-treated subjects with essential hypertension. This prospective study included a total of 77 patients (men: 55.2% male) with never-treated essential hypertension. The patients were divided into non-OSA (n=23, 49.3±12.7 years old) and OSA (n=54, 55.1±12.2 years old). Baseline office systolic blood pressure was 140 mmHg (N=64), 140–159 mmHg (N=154), 160–179 mmHg (N=297) and ≥180 mmHg and no other comorbidities (N=131) in both groups. The average antihypertensive drug was significantly reduced from 2.1±0.8 to 1.2±0.4 in the low sodium dialysate group (p<0.001).

Results: Twenty four hour SBP, day time SBP, night time SBP and daytime DBP were significantly decreased in low sodium dialysate group after six months (p<0.05). There was no significant reduction in two groups in 24-hour DBP and daytime DBP (p>0.05). Moreover, the average antihypertensive drug was significantly reduced from 2.1±0.8 to 1.2±0.4 in the low sodium dialysate group (p<0.001) (Table). Furthermore, IDWG was found to be significantly decreased in the low sodium dialysate group after six months (p<0.001).

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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.

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