PROGNOSIS AND MANAGEMENT IN ATRIAL FIBRILLATION

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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 excessive atrial ectopy was defined as ≥30 premature atrial contractions per hour/day.

Results: At baseline 114 subjects were classified as having increased atrial ectopy (10.7%). In the follow up 107 subjects (10.1%) were diagnosed with incident atrial fibrillation (AF) and 121 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 was 2.5% per year, which is comparable to the risk observed in atrial fibrillation.

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

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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 antiarrhythmic 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 patients with a “temporary cause”, CHA2DS2-VASC score was higher than in other patients (3.6±1.7 versus 2.3±1.7, P<0.0001) and treatment with oral anticoagulation was less frequent (37% versus 52%, P<0.0001). The mean follow-up of 2.5 years (maximum 100 hours), 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 (HR) 0.94, 95% CI 0.97–1.0, p=0.11; Adjusted HR 1.02, 95% CI 0.79–1.32, p=0.65, after adjustment for CHA2DS2-VASC and OAC use). Mortality was higher in patients with a “temporary cause” compared to other AF patients (Crude HR 1.82, 95% CI 1.52–2.18, P<0.0001; Adjusted HR 1.43, 95% CI 1.18–1.75, p=0.004 for CHA2DS2-VASC and OAC use).

The findings were similar in patients in the low, moderate- and high-risk groups for stroke according to CHA2DS2-VASC risk score. In patients with a “temporary cause” of AF, prescription of oral anticoagulation was independently associated with a better prognosis for death (HR of 0.49, 95% CI 0.38–0.71, P<0.0001 after adjustment for age and CHA2DS2-VASC score).

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

951 | BEDSIDE
Incidence of atrial fibrillation in different types of cancer: a Danish nationwide cohort study

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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 (IRR) 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 year (66.5–66.5) and 47.4% were males. IRRs of AF in all cancer types were significantly increased and for overall cancer IRR was 1.50 (95% confidence interval (CI) 1.48–1.53). Stratified according to type of cancer, the strongest association was observed between AF and lung cancer (IRR of 3.59 (95% CI 3.43–3.76)). The other major types of cancer: colon cancer (IRR: 1.45 (95% CI 1.38–1.53)), urinary tract cancer (IRR: 1.41 (95% CI 1.33–1.51)), breast cancer (IRR: 1.23 (95% CI 1.18–1.29)) prostate cancer (IRR: 1.22 (95% CI 1.18–1.27)) and the remaining other types of cancer were also associated with an increased (IRR: 1.61 (95% CI 1.53–1.70)) risk of AF (P<0.0001 for all cancer types).

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

952 | BEDSIDE
Improving AF detection in patients with cryptogenic stroke. Insights from a prospective cohort with insertable cardiac monitor

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Background: Up to 30% of ischemic strokes are of undetermined etiology or cryptogenic. Subjects with paroxysmal 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 hypertensive
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 for the need for early monitoring in these patients.

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

Background: Cardiac implantable electronic devices (CIED) monitoring reveal 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 analysed prospectively a total of 19 patients with 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 demonstrated that the presence of AHRE was an independent predictor for silent IBL in patients without prior history of AF or stroke (OR 3.12 [1.06–9.20; p=0.05]).

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.04 (0.97–1.11)</td>
<td>0.18</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>2.19 (0.73–6.61)</td>
<td>0.16</td>
</tr>
<tr>
<td>CHADS score</td>
<td>1.63 (0.54±3.83)</td>
<td>0.08</td>
</tr>
<tr>
<td>CHADS2≥4</td>
<td>1.33 (0.91±9.4)</td>
<td>0.13</td>
</tr>
<tr>
<td>High blood pressure</td>
<td>2.71 (0.51±12.66)</td>
<td>0.06</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.54 (0.54±3.83)</td>
<td>0.41</td>
</tr>
<tr>
<td>Structural heart disease</td>
<td>1.62 (0.57±6.1)</td>
<td>0.35</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>1.08 (0.06±4.25)</td>
<td>0.53</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>0.87 (5.23±3.37)</td>
<td>0.14</td>
</tr>
<tr>
<td>Small vessel disease</td>
<td>2.10 (0.77±5.72)</td>
<td>0.14</td>
</tr>
<tr>
<td>AHRE &gt;5 min</td>
<td>3.28 (1.16±9.08)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

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 sec. 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 score was 3.01±1.3 and CHA2DS2-VASc score was ≥2 in 602 (69.8%) patients. Intracardiac echo showed no LAO 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 was observed 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 and thromboembolic risk underestimated.

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 available 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.

Table 1. Fluoroscopy time and radiation dose

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Fluoroscopy time (min)</th>
<th>Radiation dose (μGy/m2)</th>
<th>Radiation dose (μGy/m2) (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>401</td>
<td>7.3±4.1</td>
<td>5.4±3.0</td>
<td>-0.001</td>
</tr>
<tr>
<td>2</td>
<td>408</td>
<td>6.3±4.1</td>
<td>5.4±3.0</td>
<td>-0.001</td>
</tr>
<tr>
<td>3</td>
<td>113</td>
<td>5.6±3.7</td>
<td>5.4±3.0</td>
<td>-0.001</td>
</tr>
</tbody>
</table>

Conclusions: Radiation dose during CA for AF can be significantly reduced by general recommendations for radiation exposure reduction. Further significant dose reduction can be achieved by application of manufacturer’s low dose protocol. Application of all recommendation reduced the overall radiation dose for AF CA procedures to one third.

957 | BEDSIDE
Long-term comparison of the number of supraventricular ectopic complexes after either radiofrequency ablation or anti-arrhythmic drug therapy in patients with atrial fibrillation
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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 anti-arrhythmic medication (AAD) 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-
ure). In the RFA group, post-procedural median SVEC increased to 8.73 (2.53–32.15). After 3 months, median SVEC in the RFA group and AAD group was 2.43 (0.79–8.33) and 0.86 (0.22–2.87), respectively (p<0.0005). At 24 months, median SVEC in the RFA group and AAD group decreased to 1.82 (0.58–5.44) and 0.76 (0.24–2.12), respectively (p<0.002).

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

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

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

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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 scan. 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-adrenomedullin (MR-proADM), mid-regional pro-atrial natriuretic peptide (MR-proANP), C-terminal pro-endothelin-1 (CT-proET1), 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 after reviewing all available baseline and second day 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 statistical 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 none 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). The second step in the model showed that neither cardiovascular deaths (univariable model) nor the subsequent landmark model (independent of AHF) showed any significant association. MR-proADM and hs-cTnT were significantly higher in patients with cardio-vascular 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).

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

Acknowledgement/Funding: The Robert Bosch Foundation, Stuttgart, Germany, funded this study.

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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-derived post-exercise recovery of muscle oxygen consumption fits to a mono-exponential curve yields both a time constant (Tc) that is an index of mitochondrial capacity (i.e., oxygen use) as well as ability to measure reperfusion (T1/2 max, reflecting oxygen delivery).

Methods: To test the hypothesis that improvements in muscle oxygen use (train- ing) rather than vascular oxygen delivery (microvascular effects) accounts for improvements in functional status after exercise training, we measured post-exercise NIRS-based assessment of mitochondrial capacity (Tc) and microcirculation (T1/2 max) 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 symp-toms of pain. We randomly assigned subjects to NIRS-guided training (n=6, age 68.5±8.5, 33% female) versus traditional pain-based 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-based 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) improved in both PAD group (96.1±50.0 to 50.0±8.8 sec, 75.2±43.0 to 59±21.0 sec, respectively, 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±52.2 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.

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

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

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

Results: In elderly patients with multivessel CAD, MACE occurred in 44 patients (13.7%). It was significantly lower in the CR group than in the incomplete revascularization (ICR) group (7.4% vs. 21.1%, p=0.001). In multivariate Cox proportional hazards analysis with age, sex, and left ventricular ejection fraction (LVEF), LVEF and CR were independent predictors of MACE (hazard ratio (HR), 0.95; 95% confidence interval (CI), 0.94–0.97; P=0.011).

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

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 sever AS and to identify patients who might not benefit from intervention.

Methods: 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 (16.7±1.2 vs. 26.5±1.6 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 (26.8% vs. 19.3%, 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.

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

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

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

Results: In the multivariable analysis, hemoglobin, ferritin, D-dimer, vitamin D, NT-proBNP and cystatin-C levels were related to the Fried score (5 items) and Green scales (4 items). Their addition to the clinical predictive model improved discrimination (C-statistic from 0.79 to 0.89 at 2 years) and risk reclassification (net reclassification improvement= 0.34; integrated discrimination improvement= 0.08) more than using the complete Fried or Green scales. The same occurred with the composite endpoint of death or myocardial infarction.

Conclusions: A simple frailty index using walk time and NT-proBNP provide more prognostic information than the complex frailty scales after ACS.
years. 944 subjects had suffered a first CHD or stroke events, respectively 260, 218, 249 and 217 at 2, 4, 7 and 10 years of follow-up, and 1700 had died. After adjustment for socio-demographic variables, vascular risk factors, impairment in daily life activities and antidepressant use, the presence of DS was associated with a significant 31% increased risk of mortality (HR=1.31, 95% CI: 1.15−1.50), while the presence of a vascular event was related to a three-fold increased risk (HR=2.97, 95% CI: 2.56−3.44). There was no interaction between the presence of DS at study visits and occurrence of vascular event for the risk of mortality (p=0.50).

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

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

965 | BEDSIDE

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


Introduction: The treatment and outcomes of older ACS patients have improved over time. This study suggests that better guideline adherence increased. At the same time, 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 0.29, 95% CI 0.22–0.40, in 2001–2004; and, adjusted OR for PCI use vs. no PCI use 0.35m/s/year (95% CI: −0.26 to 0.13).

Methods: We analyzed 13,662 ACS patients ≥70 years enrolled in the Acute Myocardial Infarction in Switzerland (AMIS) cohort between 2001 and 2012. Use of guideline-recommended therapies and in-hospital outcomes were analyzed according to three 4-year periods (2001–2004, 2005–2008, 2009–2012). To determine associations between use of percutaneous coronary interventions (PCI) and in-hospital mortality, logistic regression providing odds ratios (ORs) and 95% confidence 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 as well increased. At the same time, in-hospital mortality of the overall population decreased from 11.6% in the first to 10.0% in the last 4-year period (P=0.020), and in-hospital major adverse cardiac and cerebrovascular events from 14.4% to 11.3% (P=0.001). This highest relative decrease of in-hospital mortality (22.7%) between first and last 4-year period was observed among octogenarians (P=0.005). In the overall population, PCI use was associated with lower odds of in-hospital mortality and ORs did not markedly change between first and last 4-year period (adjusted OR for PCI use vs. no PCI use 0.29, 95% CI 0.22–0.36, in 2001−2004; and, adjusted OR for PCI use vs. no PCI use 0.26, 95% CI 0.20–0.35, in 2009–2012).

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

966 | BEDSIDE

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

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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 rates for women increase with age, in contrast to a variable between men and women regarding CHD outcomes. At younger ages, incidence and mortality are markedly lower in women, whereas with increasing age this gap narrows. However, little is known regarding the contribution of cardiovascular risk factors to this sex/gender effect.

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 mediated through risk factors. Presumably, since no appropriate statistical modelling approach for survival data was available. Recently, a new approach for media-

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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 16.4 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 6.9) 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 amounting only to 0.2%. 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 vessel wall, 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 51.9±10.8 years, 94 men, 61 hypertensives) with no established cardiovascular disease were investigated in two examinations over a 2-year period (mean follow-up visit 1.84 years). Subjects were categorized in current smokers, non-smokers and ex-smokers. Ex-smokers were further categorized according to the time elapsed since smoking cessation: ≤15 years and >15 years. Subjects had at the beginning and end of the study the presence of cardiovascular disease, diabetes mellitus (DM), hypertension (HTN), atrial fibrillation (AF) and smoking cessation (≥6 months).

Results: Smoking at baseline was not associated with statistically significant differences in PWV. However, the annual change was statistically different between the groups of smokers, non-smokers and the 3 groups of ex-smokers (p=0.041) after adjustment for relevant confounders. Specifically, smokers had 0.23m/s/year (95% CI: 0.00 to 0.45), non-smokers 0.17m/s/year (95% CI: 0.08 to 0.25), quitters (<15 years) had 0.28m/s/year (95% CI: 0.07 to 0.49), quitters (≥15 years) 0.26m/s/year (95% CI: 0.20 to 0.31).

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

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

Results: 556 pts were included. The mean age was 81.9 years, mean LVEF was 21.6% (SD 7.7%). 21% of patients (25.7%) did not take BB, 29.8 (48.2%) took low doses BB and 145 (26.1%) achieved high doses. During follow 223 pts died (40.2%), 92 in the untreated group, 97 in the low dose and 34 at the high dose. After adjusting the Cox model with confounding and interaction variables, we found...
an HR estimated of mortality (for each 10% increase over the target dose) of 0.84 (95% CI 0.79–0.90). The final model included variables BB1/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/d of carvedilol or every 1 mg/d of bisoprolol) the probability of death is reduced by 10 to 21% and the probability of death or hospitalization for heart failure or ventricular arrhythmia between 3 and 11%.

NOVEL STRATEGIES FOR CARDIOPROTECTION

1080 | BENCH
The cardioprotection of miRNA-221 is due to direct targeting on DDIT4/mTORC1/p-4EBP1 pathway
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Purpose: DNA-damage-inducible transcript 4 (DDT4) is rapidly upregulated under multiple stresses including ischemia/reperfusion (I/R) and facilitates increased autophagy. DDT4/miRNA-221 is a predicted target of miR-221. Whether miR-221 could be a potential therapeutic target in cardioprotection is unknown. We hypothesized that miR-221 directly targets DDT4 thus inhibiting I/R-induced autophagy.
Methods: Myoblast H9c2 cells and neonatal rat ventricular myocyte (NRVM) underwent 16 or 6 hours 0.2% O2 hypoxia, respectively, followed by 2 hours reoxygenation (H-R). The mTORC1 inhibitor, Rapamycin (200nM), was administered to further enhance autophagy. Both cells were transfected with miRNA-221 mimic and scrambled mimic control (miR-221 and MC). Cell count/viability, WST assay, cell injury-induced LDH release, and GFP-LC3 labeled autophagosomes were measured. Finally, both H9c2 and NRVM were collected for RT-qPCR and WB analyses. Predicted miR-221 targeting of DDT4 was assessed by Luciferase-reporter assay.
Results: miRNA-221 significantly reduced I/R injury as indicated by higher cell count/viability and WST activity, and reduced LDH (miR-221 vs. MC p<0.05).
Conclusion: These results suggest that miR-221 acts via modulation of DDIT4 expression to improve cardiac function after I/R injury as a cell-free approach, Exo could streamline clinical translation of regenerative heart therapy.
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1082 | BENCH
Bnip3 drives mitochondrial damage in the early phase of myocardial ischemia/reperfusion injury
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Purpose: A high percentage of the damage in myocardial infarction results from the reperfusion of the ischemic myocardium. Mitochondria are central players in cell death during the early phase of reperfusion. The permeabilization of the mitochondrial outer membrane (MOM) is a major determinant of apoptosis and necrosis. In the mouse model that the inhibition of Bnip3 leads to a significant reduction of the infarct size by 51%. In cell culture studies, the overexpression of Bnip3 leads to Bak/Bax activation and apoptotic cell death. In Bax/Bak double knockout cells Bnip3 shows no effects. This suggests that Bnip3 acts via activation of MOMP formation. In our study we focused on the role of Bnip3 during early ischemia/reperfusion (IR) injury in vivo.
Methods and results: In the early phase of reperfusion we found a time-dependent increase of depolarized mitochondria in an in vivo mouse model.
Results: There was a significant increase of Bnip3 protein concentration by 50% (basal = 5.5±1.5% vs. 10 min of reperfusion = 20±6.3%, n=5, p=0.0001). The inhibition of Bnip3 using a TAT-Fusion protein, TAT-Bnip3.3,TM (transmembrane deletion mutant of Bnip3, acting as a dominant negative blocker) significantly reduced the depolarized mitochondria level by 67% after 10 min of reperfusion + Bnip3 inhibition = 6.7±3.2%, n=5, p=0.001). This was associated with a time-dependently increasing Bnip3 protein concentration by 70% in MOM during reperfusion (basal = 100% vs. 30 min of reperfusion =170±11%, n=3, p=0.0001). A high percentage of the damage is due to necrosis. Inhibition of Bnip3 prevented the incorporation of Bnip3 into MOM (10 min reperfusion + Bnip3 inhibition = 94±21%, n=3, p=0.0057) as well as a significant increase of Bax concentration in MOM during reperfusion (basal = 100% vs. 10 min of reperfusion = 456±345%, n=10, p<0.05). The Bax translocation into MOM was inhibited by 240% (10 min reperfusion + Bnip3 inhibition = 216±128%, n=10, p<0.05). Remarkably, during early phase of reperfusion no increase of cytochromeC level in cytoplasm was observed in vivo.
Conclusion: Bnip3 initiates mitochondrial damage and cell death in the early phase of reperfusion following ischemia by regulating Bax-concentration and depolarization of MOM in a cytochromeC independent process.

1083 | BENCH
Transvascular total left ventricular unloading in the acute phase of myocardial infarction markedly reduces infarct size and prevents heart failure in the long term
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Background: Ischemia takes place when myocardial oxygen demand (MVO2) exceeds oxygen supply. Direct and indirect myocardial injury (MI) results from oxygen imbalance. Usually, the myocardial infarction (MI) remains a major cause of chronic heart failure (CHF). Left ventricular assist device (LVAD) mechanically unloads the left ventricle (LV) and reduces MVO2. Theoretical analysis using the pressure-volume area (PVA), an index of MVO2, and the partial LVAD unloading (p-LVAD), where LV ejection rate remains, reduces LV preload while increases afterload, and thus does not effectively decrease PVA and MVO2. In contrast, the total LVAD unloading (t-LVAD) where LV no more ejects, markedly decreases LV volume and pressure, which may optimize MVO2. We hypothesized that t-LVAD in the acute phase of MI could reduce the infarct size and prevent heart failure in the long term.
Methods: We used a transvascular LVAD for LV mechanical unloading. In anesthetized dogs, we ligated the left anterior descending coronary artery for 180 min

Results: Although both Exo-CPC and Exo-MSC inhibited cardiomyocyte (CM) apoptosis after serum starvation in vitro if compared with Exo-F, Exo-CPC showed higher efficacy (21±4% Exo-CPC; 28±4% Exo-MSC; 40±5% Exo-F). IPC of Exo-producing cells further reduced numbers of apoptotic CM (17±1% Exo-CPC; 23±3% Exo-MSC). Exo-CPC, but not Exo-F, were proangiogenic in HUVEC (PDGF-BB, 100 ng/ml and Exo-MiR-146a were among the most highly enriched miRNA in Exo-CPC. CM transfected with miR-200 or miR-132 mimics showed increased tolerance to apoptosis, whereas siRNA specific for these miRNA had opposite effects. In vivo, LVF was significantly improved in hearts injected with Exo-CPC compared to those injected with miRNA and treated Exo-MSC both 8 weeks (p<0.05) and 4 weeks after MI (75.4±8.9% vs. 58.7±18.4%; p<0.05).
Conclusion: These results from patient-matched analyses show, for the first time, that Exo-CPC is superior to Exo-MSC at inhibiting CM apoptosis and improving cardiac function after MI in vivo. As a cell-free approach, Exo could streamline clinical translation of regenerative heart therapy.
Acknowledgement/Funding: Swiss Foundation for Cardiology
Germany; 2 University Medical Center of Mainz, Center of thrombosis and M. Ogasawara1, S. Muratsubaki 1, K. Ohno 1, T. Miura1.

Methods and results: phosphorylation at Thr308 by PDK1 and at Ser473 by mTORC2. we tested a hypothesis that CRF increases myocardial susceptibility to ischemia/reperfusion injury in CRF.

Purpose: Chronic renal failure (CRF) worsens the prognosis of patients with myocardial infarction, but the underlying mechanisms remain unclear. Here, we sought to determine whether CRF increases myocardial susceptibility to ischemia/reperfusion injury by disrupting protective Akt activation, which requires phosphorylation at Thr308 by PKD1 and at Ser473 by mTORC2.

Results: i-LVAD markedly reduced the infarct size by more than 80% relative to Sham. t-LVAD significantly increased LV ejection fraction, and end-systolic elastance (Ees) and decreased LV end-diastolic pressure (LVEDP), indicating that t-LVAD preserved LV function. NT-proBNP as a biomarker of CHF also reduced in t-LVAD (Sham 3409±690 vs. t-LVAD 1878±177 pg/ml, p < 0.05).

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

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 remodeling following injurious ischaemia/reperfusion, but intracellular activity increases chronic renal failure. 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).

Methods: Both 1527B16 mouse hearts were Langendorff perfused and subjected to 30 min reperfusion to determine the cardioprotective efficacy of the interventions by triphenyltetrazolium staining of viable tissue and planimetric assessment of infarct size. Cellular MMP activity was determined by in-situ zymography, intracellular visualization 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 nuclear 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 exenatide 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 exenatide (both at doses reducing infarct size in clinical trials), or C) two treatments (RIC+GIK or RIC+exenatide).

Results: A first set of experiments (n=4/group), with 5 min of reperfusion showed prominent phosphorylation of Akt and eNOS in control and reperfused myocardium only in animals receiving GIK, and mitochondria from these hearts showed increased stimulated respiration. NADH-based metabolomics disclosed a shift towards increased glycolysis in GIK and exenatide 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 ischemia (n=7–10/group), ANOVA demonstrated a significant effect of the number of treatments on infarct size (triphosphorylazetein, % 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+exenatide.

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

1089 | BENCH
Distinct mechanisms of cardioprotection by different H2S donors

Hydrogen sulfide has been shown to exert a variety of actions in the cardiovascular system; it promotes vasorelaxation and angiogenesis, reduces atherosclerosis and ameliorates heart failure. We and others have previously shown that H2S protects the heart from ischemia/reperfusion (I/R) injury. In the majority of studies evaluating cardioprotection, ultra fast H2S-releasing salts have been used. However, we investigated the ability of slow releasing and mitochondrial-targeted H2S donors to reduce infarct size and compared them to the inorganic salt Na2S. Anesthetized male mice were subjected to 30 min regional myocardial ischemia by LAD ligation, followed by 2hr of reperfusion. Animals were randomized into 5 groups as follows: 1) control, no further intervention, 2) Na2S (4.2 mol/kg), 3) thiouvaline (4 mol/kg), 4) GYY4137 (26.6 mol/kg) and 5) AP39 (250 mol/kg). All drugs were administered as i.v. bolus at the 20th min of reperfusion. None of the treatments affected blood pressure and all of the groups had similar risk/all areas. Analysis of efficacy and safety of transvenous leads extraction and cardioprotective pathways different from those of RIC, and have additive effects with RIC on infarct size reduction in pigs.

P1091 | BENCH
Transvenous removal of pacing and ICD leads: single referral center experience

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

Methods: Since January 1997 to December 2014, we managed 2250 consecutive patients (1718 men, mean age 65.3 years) with 4114 leads (mean pacing period 71.8 months, range 1–576). PL were 3328 (1582 ventricular, 1391 atrial, 355 coronary sinus leads). DL were 786 (765 ventricular, 6 atrial, 15 superior vena cava leads). Indications to TLR were infection in 83% (systemic 28%, local 55%). We performed mechanical dilatation using a single polypropylene sheath technique (Cook Vascular, USA) and if necessary, other intravascular tools (Catchers and Lassos, Osypka, Grentzig-Whylen, G); an Approach through the Internal Jugular Vein (JA) was performed in case of free-floating leads or failure of the standard approach.

Results: Removal was attempted in 4105 leads because the technique was not applicable in 9 PL. Among these, 4019 leads were completely removed (97.9%), 44 (1.1%) partially removed, 42 (1.0%) not removed. Among 4020 exposed leads, 625 were removed by mechanical dilatation (15.5%), 2998 by mechanical dilatation using the venous entry site (74.6%), 32 by femoral approach (FA) (0.8%) and 279 by JA (7.0%). All the free-floating leads were completely removed, 25.8% by FA and 74.2% by JA. Major complications occurred in 13 cases (0.6%): cardiac tamponade (12 cases, 2 deaths), hemotrax (1 death).

Conclusions: Our experience shows that in centers with wide experience, TLR using single sheath mechanical dilatation has a high success rate and a very low incidence of serious complications. TLR through the Internal Jugular Vein increases the effectiveness and safety of the procedure also in case of free-floating or challenging leads.

P1092 | BEDSIDE
Managing perioperative antiocoagulation therapy in patients undergoing cardiac electronic device surgery: survey in Austria, Germany and Switzerland

Objective: To evaluate the present practices in the area of periprocedural anticoagulation in Austria, Germany and Switzerland. A survey was sent to all institutions in these countries, that perform cardiac electronic device surgery.

Methods: A survey was sent to all institutions in Austria, Germany and Switzerland, that perform cardiac electronic device surgery.

Results: A total of 341 physicians responded to the survey. The results showed a high level of awareness of the importance of periprocedural anticoagulation therapy, but also a lack of standardization in the management of anticoagulation in these patients.

Conclusions: Despite the high level of awareness, there is a need for further education and guidelines to improve the management of anticoagulation in these patients.
Complications in devices

agulation (NOAC) agents are increasingly replacing phenprocoumon as oral anti-coagulant. However, data regarding the management of NOACs in the context of pacemaker or ICD implantation are missing. The purpose of this study was to survey clinical practice with regard to the use of phenprocoumon and NOACs in relation to device implantation in Austria, Germany and German-speaking Switzerland.

Methods and results: We conducted a web-based survey across centres in Austria, Germany, and German-speaking Switzerland using the tool SurveyMonkey. The questionnaire included 17 questions and was sent to 202 Austrian centers, 103 German centers and 145 Swiss centers. The survey was completed by 252 of the 1392 centers (18.10% response rate). In managing patients on NOACs, common practice was to stop NOACs in 95.83% (Austria), 89.52% (Germany) and 87.50% (Switzerland). NOACs were stopped in 88.18% (Austria), 51.40% (Germany) and 93.65% (Switzerland) one day before device implantation and usually 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 molecular weight heparin in therapeutic dosage. Management of patients on phenprocoumon varied significantly between each country. Anticoagulation was stopped in 66.67% of the centres in Austria, 46.60% of the centres in Germany, and 15.55% of centres in Switzerland. Warfarine was discontinued in 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 (cessation, bridging with heparin, restarting of oral anticoagulation) vary a lot among all centres. Our findings emphasize the need for further randomized controlled studies to determine the optimal strategy for managing anticoagulation in patients undergoing device surgery.

P1095 | 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 72.7±14.1); among these, 185 patients (50.5%; mean age = 69.7±12.3) had an implantable cardiac defibrillator or a cardiac resynchronization device with or without ICD (CRT-D or CRT-P); 45 patients had CRT-P. 85 patients had CRT-D and 55 patients had a ICD; among these 185 patients, 265 leads were removed. CS leads from 121 patients (mean age 72±15.8 years) and 141 ICD leads from 137 patients (mean age, years 68±13.4); device infection was the main indication to extraction (82,5% of cases); the mean implant time was 49.6±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 manual 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 procedures: 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 transvenous lead extraction, all 141 ICD leads were successfully removed (procedural and clinical success in 100%); without any major complication; while CS leads extraction procedure was more complex because of one failure procedure and one major complication.

P1096 | BEDSIDE

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

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Introduction: Because of the increasing change in age demographics, the increased 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) population. We report the safety and effectiveness of transvenous lead extraction in OCT.

Methods: From January 2002 to January 2015, we reviewed data from consecutive 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 procedure. Strategy consists in trying manual traction first, then looking stilet stylet extraction, then laser assisted extraction and in case of failure (or impossible upper access) conversion into a femoral approach.

Results: Of 428 pts undergoing lead extraction during the study period, 108 were OCT (25.2%) were OCT (mean age 84,0.7 years; range 80–98; 73% males). A significantly higher percentage of OCT presented heart disease (37.96% in OCT vs 15.2% in pts <80 years; P=0,03) chronic renal failure (38.8% in OCT vs 13.68% in pts <80 years; P=0,03).

Infection (all types) was a more common indication for extraction in OCT than in younger pts (79.62% in OCT vs 51.56% in pts <80 years; P<0.001), but malfunction 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 required 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 procedural major and minor complications were found between the 2 groups.

Conclusion: The OCT group was a sicker population, as reflected by their high rate of comorbidities, their advanced degree of heart failure and their high rate of complications associated with ICD therapy.

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 predictors of complications associated with ICD therapy.

Results: 579 patients (391 men, 188 women, mean age 67±28 years) were referred to the complete ICD extraction with sepsis and evidence of bacterial endocarditis. The average time from the first implant of the electrodes was 72±37 months (range 12–261 months; the oldest 211 months), the average number of electrodes in one person was 2.7. The group included 637 ICD electrodes (477 dual coil), 121 atrial and 137 LV leads. Average procedure time was 172±37 minutes. In 292 patients we used the combination of an 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).

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


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 predictors of complications associated with ICD therapy.
**P1097 | BEDSIDE**  
Direct comparison of the safety and efficacy of two rule-out strategies for acute myocardial infarction: 1h-algorithm versus combination of 1h-algorithm and undetectable levels at presentation


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

**Methods:** In a prospective international multicentre diagnostic study enrolling 2213 patients presenting with suspected AMI to the ED, the final diagnosis of AMI was adjudicated by two independent cardiologists using all available clinical information including serial hs-cTnT concentrations. Safety was quantified as the negative predictive value for AMI in the rule-out zone of the respective rule-out strategies. Efficacy was quantified as the negative predictive value for AMI in the rule-out zone of the respective strategy. Both strategies were applied using the two best-validated hs-cTn assays (hs-cTnT Roche: 1h-algorithm 0h–1h, LOD 0h–5ng/L OR (0h–12ng/L and Δ0–1h<3ng/L); and hs-cTn Abbott: 1h-algorithm 0h–5ng/L and Δ0–1h<2ng/L; 1h-algorithm+LOD 0h–2ng/L OR (0h–5ng/L and Δ0–1h<2ng/L)) to ensure that findings are independent from the hs-cTn assay used. Patients presenting with ST-segment elevation MI (STEMI) were excluded.

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

**Conclusion:** Both investigated rule-out strategies allow a safe and comparable rule-out of AMI, irrespective of the underlying hs-cTn assay. While the 1h-algorithm requires retesting of hs-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.

**P1098 | BEDSIDE**  
CRUSADE Risk Score for Predicting Major Bleeding based on BARC Standardized Definition in Patients with Acute Coronary Syndromes

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

**Methods:** From January 2012 to August 2014, we prospectively included consecutive patients with acute coronary syndromes. Major bleeding was defined according to BARC criteria as bleeding types 3 to 5. Predictive ability of the CRBS was assessed using the receiver operating characteristic (ROC) curve. 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 negative predictive value for AMI in the rule-out zone of the respective strategy. Both strategies were applied using the two best-validated hs-cTn assays (hs-cTnT Roche: 1h-algorithm 0h–1h, LOD 0h–5ng/L OR (0h–12ng/L and Δ0–1h<3ng/L); and hs-cTn Abbott: 1h-algorithm 0h–5ng/L and Δ0–1h<2ng/L; 1h-algorithm+LOD 0h–2ng/L OR (0h–5ng/L and Δ0–1h<2ng/L)) to ensure that findings are independent from the hs-cTn assay used.

**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). The 1h-algorithm allowed the rule-out in 53% of patients after 1h versus 53% with the 1h-algorithm+LOD (31% at presentation and 69% after 1h).

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

**P1100 | BEDSIDE**  
Direct Comparison of the Safety and Efficacy of Two Rule-out Strategies for Acute Myocardial Infarction: undetectable levels of hs-troponin versus copeptin in combination with troponin


**Purpose:** Addressing the increasingly recognized, yet unmet clinical need for rapid rule-out of acute myocardial infarction (AMI), several novel strategies have been developed. Due to the lack of direct comparisons in the same dataset, selection of the best strategy for clinical practice is challenging. We therefore aimed to directly compare the safety and efficacy of two previously defined strategies: LOD (Undetectable levels of high-sensitivity cardiac troponin (hs-cTn) at presentation) versus the combination of hs-cTn 1h-algorithm and 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 (NPV) for AMI in the rule-out zone of the respective 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-cTn assays (hs-cTnT Roche: LOD 0h–5ng/L; 1h-algorithm 0h–12ng/L and Δ0–1h<3ng/L; and hs-cTn Abbott: LOD 0h–2ng/L; 1h-algorithm 0h–5ng/L and Δ0–1h<2ng/L) to ensure that findings are independent from the hs-cTn assay used. As both strategies should only be applied once ST-elevation MI (STEMI) has been excluded 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 99.8%, 95% CI 99.0–100% versus LOD+1h-algorithm: NPV 99.9%, 95% CI 99.5–100%, p=ns). Regarding efficacy, LOD allowed rule-out in 24% of patients versus 59% with 1h-algorithm+LOD (p<0.001). Using hs-cTnI, the safety was very high and comparable with both algorithms (LOD: NPV 100%, 95% CI 98.8–100% versus LOD+1h-algorithm: NPV 99.2% (95% CI 98.4–99.6, p=ns). Regarding efficacy, LOD allowed rule-out in 16% of patients versus 53% with the 1h-algorithm+LOD (p<0.001).

**Conclusion:** Both investigated rule-out strategies allow a safe rule-out of AMI, irrespective of the underlying hs-cTn assay. While LOD has the obvious advantage of allowing rule-out already with the measurement at presentation, the combination of LOD and 1h-algorithm is much more effective and more than doubles the number of patients eligible for rule-out.
algorithms (LOD: NPV 100%, 95% CI 98.7–100% versus copeptin and hs-cTnT: NPV 96.4% 95% CI 95.0–97.5, p=0.002) but slightly better for LOD. Regarding efficacy, LOD allowed the rule-out in 14.7% of patients versus 53.9% with dual marker strategy (p<0.001).

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

PI101 | 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 FIR (FRISC-ICTUS-RITA 3) risk score. At ten year follow-up vital status and time of death were obtained for all patients from the national population registry (Dutch Central Bureau of Statistics). Adjudicated MI event rates will be available at the time of presentation. Cumulative event rates were estimated by a Kaplan-Meier model.

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

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

PI102 | 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 Ischaemia National Audit Project (MINAP). Adherence to care was measured against ESC guidelines for the management of NSTEMI. Adjusted time ratios (TRs) were obtained from hierarchical accelerated failure time models to determine impact using guideline recommended care on all-cause mortality.

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

After adjustment, survival times for those who missed ≥1 care opportunity were significantly shorter (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 to determine MR severity based on contrast echocardiography, which is not affected by the double orifice morphology following percutaneous edge-to-edge mitral valve repair.

**Methods and results:** Apical 4-chamber, low mechanical index contrast echocardiographic images using a 1.5 ml of a sulphur hexafluoride contrast agent at steady state conditions were recorded in 21 patients before and after percutaneous mitral valve repair. Echocardiographic backscatter in the left ventricle (LV) and atrium (LA) was determined using QLab quantification software. As compared to before the procedure a significant approximation of LV and LA backscatter was observed with reduction of MR after the procedure (enddiastolic difference between LA and LV backscatter: 2.7±3.3 dB vs. 3.3±2.6 dB; p<0.001). This decrease was mainly driven by a significant increase in LV backscatter after MitraClip implantation (enddiastolic LV backscatter: 25.5±5.9 dB vs. 23.5±4.7 dB; p<0.01), possibly explained by a higher degree of resonance of microbubbles remaining in the ultrasound field for several heart cycles as they travel forth and back between LA and LV in mitral regurgitation. In accordance with the above described observation, healthy individuals exhibited a significantly lower difference between LA and LV backscatter compared to individuals with severe MR (3.7±1.0 dB vs. 7.2±3.3 dB; p<0.01).

**Conclusions:** Our results and analysis 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 a valuable tool for quantification of MR especially in the setting of complex flow patterns as encountered 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 cardiac intervention structural procedures is well established and appreciated. However, the need for general anaesthesia (GA) throughout the procedure remains a controversial issue.

**Results:** The results were the following, presented as the average grade: see Table 1. Although the clarity of structure calculation with transnasalTEE was inferior to conventional TEE, the anatomy of relevant intracardiac structures was seen with medium quality despite the small sized probe. However, highly advanced op-eration flow in patients with severe AS. LVOT peak acceleration flow velocity and predictive factors for overestimation of EAVA have yet to be clarified.

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

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

**Results:** AVA and trans-aortic valve mean pressure gradient by echocardiography 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.

**Conclusions:** The size of the LA, specially the area obtained in four chambers view is a good independent predictor of the development of AF after TAVI.

**P1108 | BEDSIDE**

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

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

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

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

**Results:** AVA and trans-aortic valve mean pressure gradient by echocardiography and cardiac catheterization were 0.72±0.23 vs. 0.67±0.23 cm²; and 53±18 mmHg, respectively. Concordance of AVA and trans-aortic valve mean pressure gradient by 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.

**Conclusions:** The size of the LA, specially the area obtained in four chambers view is a good independent predictor of the development of AF after TAVI.

**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±6.1 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, specially the area obtained in four chambers view is a good independent predictor of the development of AF after TAVI.

**Table 1. Results**

<table>
<thead>
<tr>
<th>Structure</th>
<th>Mitral valve</th>
<th>Aortic valve</th>
<th>PFO/ASD</th>
<th>LV/Pericardial space</th>
<th>Transaortic imaging</th>
<th>3D imaging</th>
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<td>Average grade</td>
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<td>b) Calcification: 3.7/5</td>
<td>c) Colour Doppler: 4.2/5</td>
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<td>No. of patients</td>
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<td>N=21</td>
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**What’s new in imaging for valvular heart disease? 175**

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Background and aim: Transcatheter aortic valve implantation (TAVI) has been established as 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 AR following the implantation. Our aim was to describe 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 and 12 months, and annually thereafter. Postprocedural AR was graded by means of the following standards: grade I: <10% of LVOT; grade II: 10%–25%; grade III: 25%–40%; grade IV: >40% (disappearing any degree of AR in some patients), probably related to the high adaptability and self-expandability of the nitinol prosthesis.

Results: Any degree of AR was present in the echocardiographic study at discharge in 90 patients (78%); grade I: 53 patients (46%); grade II: 28 patients (24%); grade III: 8 patients (7%); and grade IV: 1 patient (1%). At last echocardiographic follow up there was a significant reduction in the number of patients with postprocedural AR; any degree of AR was observed in 67 patients (58%); grade I: 31 patients (27%); grade II: 24 patients (21%); grade III: 10 patients (9%); and grade IV: 2 patients (2%), p=0.03. Conclusions: At discharge, a high percentage of patients who underwent a successful implantation of aortic valve with the CoreValve prosthesis in our institution had any degree of echocardiographic postprocedural AR. Beyond the first year of follow up, we observed a significant reduction in the paravalvular regurgitation (disappearing any degree of AR in some patients), probably related to the high adaptability and self-expandability of the nitinol prosthesis.

Background and aim: Postprocedural AR following TAVI is a well-known phenomenon, and the most common cause is the oversizing of the aortic annulus which may result in the production of a suboptimal seal between the prosthesis and the native aortic valve. In cases of incomplete sealing, regurgitation may be observed in the acute postprocedural period and may even persist into the long-term follow-up. Thus, the aim of the present study was to describe 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: We analyzed 75 patients consecutively (16 women, 68.5±12 years) who underwent TAVI with the CoreValve prosthesis at one center during the period from April 2008 to March 2014. Aortic valve calcium was assessed using FACS after subsequent RNA extraction, with each sample being placed in a 0.1 N NaOH solution, kept at room temperature for 6 h and then acidified with 0.3 N HCl to pH 7.0. The amount of calcium was determined in duplicate at 540 nm using a colorimetric method to quantify the aortic valve calcium and backscattering indexes was found. We propose that a significant correlation between the gold standard for the determination of aortic valve calcium and backscattering indexes was r=0.8919 (P<0.001, IC 0.8312 to 0.89), the correlation between the area-calcium area backscattering index was r=0.8919 (P<0.001, IC 0.8312 to 0.89) and the correlation between the area-calcium area index was r=0.8919 (P<0.001, IC 0.8312 to 0.89).

Conclusions: The risk of postprocedural AR is clearly related to the severity of aortic valve stenosis, the degree of mismatch between aortic annulus and prosthesis and the severity of native aortic valve calcification. Moreover, we demonstrated that pharmacological or genetic PTP1B inhibition restored NO production and improved endothelial dysfunction in a mouse model of heart failure.

P1110 | BEDSIDE
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 further the deposit of atherosclerotic plaques and calcification calcium is a marker of cardiovascular risk and poor prognosis. Currently there is no validated echocardiographic method to quantify the aortic valve calcium and qualitative methods are highly inaccurate. Our goal is to obtain a new valid and accessible method for the assessment of aortic valve calcification by transthoracic echocardiography.

Methods: We analyzed 75 patients consecutively (16 women, 68.5±12 years) under echocardiography and computer tomography (CT) performed during the same year. We developed two indexes from the backscattering analysis of the ultrasound and we grouped the results into four calcium groups from 0 to severe calcification attending quartiles to compare. CT was used to quantify the amount of calcium attending quartiles to compare. CT was used to quantify the amount of calcium.

Conclusions: A significant correlation between the gold standard for the determination of aortic valve calcium and backscattering indexes was found. We propose a reliable method to assess aortic valve calcification by transthoracic echocardiography.

CLINICAL IMPACT AND MODULATION OF ENDOTHELIAL (DYS)FUNCTION

P1111 | BENCH
Altered molecular signature of cardiac microvascular endothelial cells after chronic pressure overload and transition to heart failure
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Introduction - Cardiac microvascular endothelial cells (MVEC) play an important role in modulating energy supply and contractile performance of the healthy heart, but their molecular signature during pressure overload remains unknown.

Purpose: We investigated the temporal changes in MVEC gene expression during pressure overload and subsequent transition to heart failure.

Methods: We randomised 35 male Tie2-GFP transgenic mice to transverse aortic constriction (TAC) or sham surgery for 2 weeks (n=6, n=5) or 10 weeks (n=14, n=10). We measured cardiac function and dimensions using transthoracic echocardiography (30 MHz, Vevo2100) and determined heart to body weight ratios (HW/BW) as an index of cardiac hypertrophy. The GFP+ cardiac MVEC were selected using FACS for subsequent RNA extraction, PCR sequencing and validation of gene expression using qRT-PCR (Taqlman).

Results: TAC animals displayed time-dependent progressive cardiac dilation, increased cardiac hypertrophy and interstitial fibrosis as compared to sham (Table). Transcriptional profiling at 2 weeks after TAC revealed 23% lower expression levels of CD36 and Meox2 (ns) and upregulation of Col1a1 and Col1a1 (4.7- and 2.8-fold, P<0.05) compared to sham. After 10 weeks, Adami2-1, Clip and Tbias4 were greater than 4-fold increased (P<0.05), as well as ESM-1 (1.6-fold, ns) and NPRA (3-fold, P<0.05).

Conclusion: In the early stage of cardiac hypertrophy after pressure overload, downregulation of fatty acid uptake (CD36, Meox2) and upregulation of collagen production and increased cardiac hypertrophy and subsequent 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 is a crucial actor of Endoplasmic Reticulum Stress (ERS) regulation, a conserved pathway involved in cell homeostasis control. PTP1B expression is induced under ERS conditions, such as misfolded protein accumulation in the ER lumen, and can inactivate the PERK branch and activate the IRE1α branch of ERS. Moreover, recent studies suggested that ERS plays a role in endothelial dysfunction via increased oxidative stress and impaired NO production.

To assess the role of ERS in PTP1B-mediated endothelial dysfunction, we used PTP1B knockout mice (PTP1B−/−) and two different models of ERS induction, involving either in vitro 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 dilation (FMD) in phenylephrine-preconstricted, isolated, perfused mesenteric arteries. Arterial ERS markers were analyzed by Western Blot.

In wild type (WT) mice, both in vivo and in vitro TN induced a severe endothelial dysfunction, (Maximal FMD, %: TN in vivo: Untreated 24.1±2.0; TN 3±0.9 p<0.01; TN in vitro: Untreated 20.5±1.3; TN 8.2±1.7, p<0.01). This endothelial dysfunction was associated with an increase in the ERS markers GRP78 (+136%) and ATF6α (+60%) in mesenteric arteries. In contrast, PTP1B−/− mice showed no alteration of endothelial function when treated with TN (in vivo: 22.4±5.3, p<0.05 vs. untreated WT; TN in vitro: 23.0±5.2, p<0.01 vs. TN WT). This endothelial protection was associated with a lesser increase in GRP78 (+70%) and ATF6α (+25%) expressions. Interestingly, ATF6α was basally upregulated in PTP1B−/− mice, when compared to WT mice, suggesting a negative regulation of ATF6α expression by PTP1B.

This work confirms that ERS induces endothelial dysfunction in resistance arteries. It also demonstrates for the first time that PTP1B is a crucial actor of ERS in the endothelium and that the beneficial effect of PTP1B inhibition on endothelial dysfunction largely involves a reduction of endothelial ERS, potentially revealing powerful new targets for endothelial protection.

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P1111 | 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 functions 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 littersmates 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±5.5% vs. 54.93±6.46%, n=8–12, P<0.05) and concomitant 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 formation. Additionally, obese mice induced by 24-week HFD displayed an impaired endothelium-dependent vasorelaxation to both insulin (46.86±3.68% vs. 64.98±2.85%, n=8, P<0.01) and acetylcholine (46.65±4.93% vs. 100.59±2.35%, n=5, 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 (48.84±3.29% vs. 29.56±2.98%, n=6, P<0.01 for response to insulin; 75.59±4.93% vs. 57.25±3.81%, 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.

P1112 | BENCH
Platelet endothelial aggregation receptor -1: a novel modifier of angiogenesis
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Objective: Platelet Endothelial Aggregation Receptor-1 (PEAR1) is a cell membrane protein, expressed on platelets and endothelial cells (ECs). PEAR1 sustains sRb3-activation in aggregating platelets and attenuates megakaryocyte-via controlling the degree of phosphorylation of Akt. Its role in EC biology is unknown. The aim of this study was to compare the expression of PEAR1 in human endothelium of various tissues and to determine its role for EC function in vitro and for angiogenesis in Pear1−/− mice.

Methods: PEAR1 is present on the membrane of human cultured ECs and it is co-localized with CD31 in various tissues. PEAR1-expression was variable in ECs of different origin. Lentiviral knockdown of PEAR1 in cultured ECs by 70% doubled EC proliferation, in turn enhancing in vitro tube formation on matrigel through the Akt/PKB-dependent p21/CDC2-pathway. Even when physiologically blood vessel formation was unaffected in Pear1−/− mice. angiogenesi-sis in these mice was significantly increased both in a hind limb ischemia ligation model (4.7-fold increase in capillary density in the ligated limb of Pear1−/− mice compared to ligated limbs in WT mice) and in a skin wound healing model (resulting in a 2-fold faster wound closure in Pear1−/− mice compared to WT littermates).

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

P1113 | BENCH
Dual Antithrombotic Effects of Ticagrelor in Arterial Thrombosis: an Antiplaeter 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) or clopidogrel active metabolite (CAM, 1.5±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 mecha-nisms 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 CAM, 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 de-regulated in HAECs. Inhibition of ENT1 by dipyridamole did not mimic the observed effect. In line with this, adenosine receptor antagonists against A1, A2a, A2b or A3 did not reverse ticagrelor-mediated TF reduction. C57BL/6 mice treated with ticagrelor or clopidogrel exhibited equal and next to complete inhibition (>95%) of ADP (10μM)-induced platelet aggregation; however, ticagrelor significantly prolonged time to arterial occlusion as compared with clopidogrel (94.1±8.7 min vs. 72.1±6.5 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.

P1114 | 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 impairment of fibrinolytic status. Concord grape juice (CGJ), a rich source of flavonoids, can modify cardiovascular risk factors. Endothelial function and arterial stiffness are surrogate markers of arterial health.

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

Methods: We studied the effect of 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 (pSm), immediately (Sm0) and 20 minutes after (Sm20) cigarette smoking. Endothelial function was evaluated by flow-mediated dilation (FMD) of the brachial artery. Carotid-femoral pulse wave velocity (PWV) was measured. A score index of aortic stiffness. Serum levels of plasminogen activator in-hibitor 1 (PAI-1) were measured at each study day immediately before smoking and 20 minutes later as a biomarker of fibrinolytic status.

Results: Treatment with CGJ resulted in a significant improvement in FMD (from 8.0±2.9 to 9.6±2.8; p=0.03) and PWV (from 16.3±0.61/16.3±0.61sec/day to 14.8±0.56/14.8±0.56sec/day, 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). Treatment with CGJ decreased pSm values of PAI-1 from 102 (65–134)ng/ml day 0 to 58 (42–75)ng/ml day 7 to 0.39 (20–47)ng/ml day 14, p<0.001 while placebo had no impact on PAI-1 levels (p>0.2). Moreover CGJ significantly ameliorated the acute smoking
induced increase in PAI-1 levels (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 improved von Willebrand factor levels and platelet aggregation.

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 this injury.

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=0.09) but not at 4 and 12 weeks. Arterial sheaths yielded significant numbers of cells (mean 6.3×10^2±4.6×10^3) 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 naive 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 cardioverter defibrillators (ICD). A new 5-year risk score was proposed in the new ESC guidelines, with a class IIa indication for ICD implantation if score >0.6%. Our aim was to evaluate the use of the new score in clinical practice, compare with previous recommendations and study the associations of a high score with parameters not included in the model.

Methods: Consecutive index HCM cases were studied and evaluated according to the guidelines with genetic testing, ECG, echocardiogram, magnetic resonance, Holter and treadmill stress ECG or echo. Conventional SCD risk factors (C-SCDRF): maximal left ventricular wall thickness (MLVWT) >30 mm; non-sustained VT (NSVT); syncope; family history of SCD (FH-SCD); abnormal blood pressure response to exercise (ABPRE). The new risk score was calculated and compared to baseline, radial artery 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: 113 patients (pts), age 57.8±16.3 years, 62 (55%) males, MLVWT 19.3±4.8 mm, left ventricular outflow tract obstruction in 31%. Positive genetic test was 23% (n=27). The new SCD risk score was calculated and compared to baseline, radial artery 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.

Conclusions: Despite similar baseline characteristics, higher use of beta-blockers and less intraoperative hemodynamic shifts, HCM patients who undergo intermediate to 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

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 cardiac genetics department were included. Survival curves were determined using Kaplan-Meier analysis.

Results: There were 274 MYBPC3 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

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

Conclusion: Dutch MYBPC3 founder mutation carriers show great clinical heterogeneity; ranging from phenotype negative at advanced age to SCD at young age. Prognosis in phenotype-negative carriers is excellent.

P1121 | BEDSIDE
Late gadolinium enhancement assessed by CMR in apical hypertrophic cardiomyopathy. A marker of ventricular arrhythmia and adverse events
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Background: Patients with apical hypertrophic cardiomyopathy (ApHCM) have particularities that distinguish it from the most common hypertrophic cardiomyopathy phenotype, regarding both the clinical profiles and genetics. The relationship between myocardial fibrosis and ventricular arrhythmias in these patients is unclear. Our aim was to evaluate, in asymptomatic or mildly symptomatic patients with ApHCM, whether there is a relationship of late gadolinium enhancement (LGE) with ventricular arrhythmias.

Methods: We included prospectively a population of 48 Caucasian patients with ApHCM. Ten patients (20.8%) had episodes of non-sustained ventricular tachycardia (NVST) in the Holter monitoring and 31 (64.6%) had LGE in CMR. During follow-up (29±9 months), eight (16.7%) patients with MACE were identified.

Results: We found an association of NVST with LV end-diastolic volume (OR: 2.849; 95% CI: 1.059–7.558, p=0.04). 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 screening performed to date have been confined to very small groups of patients and to a limited number of genes. We sought to determine the genetic basis of RCM and to establish the yield of modern Next Generation Sequencing (NGS) technologies in this setting.

Methods: A total of 189 unrelated patients with end-stage idiopathic RCM (41±14 years, 44% males) underwent NGS genetic evaluation with a panel of 259 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 (6%), Mutated genes included MYH7 (4), DES (3), MYBPC3 (3), LMNA (2), FLNC (2), TNN1 (2), TNN3 (1), TNN2 (1), TNNC1 (1), TNNT2 (1), TNNI3 (1), TNNT2 (2), LAMP2 (1). A total of 12 patients (38%) exhibited genetic variants of unknown significance and 2 patients (6%) did not show any possible disease-causing mutation. Evaluation of 90 relatives from 25 families identified 18 affected individuals and 6 mutation carriers without clinical phenotype. Familial evaluation confirmed the pathogenicity of disease-causing mutations in 8 families. 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 RASP was significantly correlated with sinus rhythm (β = −0.15, P = 0.021), left ventricular obstruction tract (LQTV) maximal gradient (β = 0.22, P = 0.001) and left atrial volume (β = 0.39, P = 0.0001). Exercise RASP was significantly correlated with resting RASP (β = −0.28, P = 0.001), grade of mitral regurgitation (MR) at rest (β = 0.48, P = 0.0001) and resting LQTV peak gradient when MR was eliminated from the analysis. Regarding prognostic patients, 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), survival after baseline (46±7.1% vs 57.1±6.3%, 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.

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 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 = 0.0001). No further changes were observed during the follow-up period.

Conclusions: This free specific strains of L. plantarum reduces LDL-C and improves the levels of other cholesterol and lipids 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.

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

Results: 78 patients were included in the study, 31 patients in the IG and 39 in the CG. 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, 8 patients in the CG did not achieve the target levels of cLDL. Without MR the strain combination reduced the LDL-C level by 24.1% (−0.05 and −0.33 mmol/L, P = 0.0001). In addition, the three L. plantarum strains reduced triglycerides by 14.3% (−0.05 and −0.33 mmol/L, P = 0.0001). No further changes were observed during the follow-up period.

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

P1126 | BEDSIDE

A combination of three specific Lactobacillus plantarum strains reduces low-density lipoprotein cholesterol and improves other cardiovascular risk factors 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 capacity to hydrolyze plant sterol esters and as 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 (TG)) without receiving cholesterol-lowering treatments, were randomized to receive either a placebo or the three strains combination (1:1:2E+09 CFU) administered in one capsule a day during 12 weeks. Cholesterol, lipid and safety parameters were assessed at baseline and after 12 weeks of intervention. A follow-up of 4 weeks without treatment was also carried out after the intervention.

Results: There were no adverse events or changes in safety parameters during the study. After 12 weeks, and as compared to the placebo, the combination of the three strains reduced LDL-C by 8.4% (−0.25 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 = 0.0001). No further changes were observed during the follow-up period.

Conclusions: This free specific strains of L. plantarum reduces LDL-C and improves the levels of other cholesterol and lipids 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.
Kaplan-Meier analysis demonstrated that patients with the LDL-C/HDL-C ratio was predictive of future CVE, even in the drug-eluting stent era. Furthermore, it is desirable to maintain the LDL-C/HDL-C ratio at less than 2.5 for a more accurate assessment to identify or refute a cancer signal in large RCTs on behalf of IMPROVE IT Trial Investigators.

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

Methods: Kaplan-Meier analysis demonstrated that 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 at less than 1.5 for the secondary prevention after DES implantation.

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 at less than 1.5 for the secondary prevention after DES implantation.
were. 40.0% vs. 65.7% (P < 0.001), 78.7% vs. 91.0% (P = 0.031), and 50.7% vs. 66.2% (P = 0.103), respectively.

Conclusions: Repeat EVT affect poor clinical outcomes in CLI patients with tissue loss.

P1133 | BEDSIDE
Clinical impact of post-procedural fractional flow reserve on future restenosis in superficial femoral artery disease
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Background: Post-stenting fractional flow reserve (FFR) is a predictor of repeat target vessel revascularization after percutaneous coronary intervention. However, little is known about the clinical impact of post-procedural FFR on future restenosis in patients with superficial femoral artery (SFA) disease after endovascular treatment (EVT).

Methods: 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 0.90. The primary rate at 12 months was significantly lower in high FFR group (P < 0.001) compared to low FFR group (P < 0.01), (23.3% vs. 66.7%, P < 0.001).

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 (Tibial Peroneal)-Trunk patency is important for the clinical outcomes of endovascular therapy for femoropopliteal lesions but influence of it is unclear. We sought to evaluate clinical impact of comparison TP-Trunk patency with TP-Trunk stenosis in patients treated after 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 follow. We devide 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: Baseline patients characteristics, lesion characteristics, Primary Patency (PSVR＜2.5), free from TLR and amputation free survival. We compared TP-patient with TP-stenosis by multi factors (Gender, Age, Smoke, CKD (eGFR ＜ 60), HD. Ischemic Heart Disease, AF, HTN, DM, Dyslipidemia, Obesity (BMI ≥ 25), Long lesion (>150mm), Cilostazol, TLR Resion, DFA gail, PTA for POPA, TP-Trunk patency).

Results: Kaplan-Mayer analysis revealed that the, Clinical driven TLR and primary patency (PSVR＜2.5) rate were significantly higher (logrank, p < 0.01) in patient with TP-Trunk paint than in patient with TP-Trunk stenosis. Multi-variant analysis shows that TP-Trunk patency were independently factors associated with clinical driven TLR rate (Hazard ratio (HR): 0.53, 95% confidence interval (CI): 0.42–1.07, P = 0.04)

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

P1135 | BEDSIDE
Predictors of 2-year mortality and risk stratification after surgical and endovascular revascularization for hemodialysis patients with critical limb ischemia due to infragluteal artery disease
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Purpose: As reflected in the latest guidelines, life expectancy of <2 years is the main determinant in selection of revascularization strategy (bypass surgery [BSX] or endovascular therapy [EVT]) in patients with critical limb ischemia (CLI). However, determinants of <2 years life expectancy in hemodialysis (HD) patients with CLI has not been systematically studied. Therefore, we examined predictors of 2-year mortality in this setting.

Methods: From 2007 to 2009, 246 consecutive CLI patients (246 first treated limbs) on HD (age, 69±10 years; 70% male: 45% non-ambulatory status; 69% diabetics and 79% with tissue loss) who underwent revascularization for infragluteal lesions (178 EVT and 68 BSX) were retrospectively enrolled. Overall survival rate after revascularization was evaluated by Kaplan-Meier analysis. Predicators for 2-year mortality after revascularization were determined using a Cox hazards model.

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

Conclusions: Advanced age, low albumin level, and low ejection fraction were independently associated with 2-year mortality after revascularization in HD patients with CLI. Risk stratification by these risk factors would be useful for decision-making in revascularization strategy.
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 LL 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 bare nitinol 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% at 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 283 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% of the OPG was approximately 25 cm.

P1138 | BEDSIDE
Impact of patient’s activity on clinical outcome after femoropopliteal interventional
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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 in wheel chair and bed ridden group (86.8%, 86.2% and 82.4% respectively; p<0.05).
Conclusion: Patient’s activity may be an independent predictor of MACE after FP intervention.

MYOCARDIAL FUNCTION

P1139 | BEDSIDE
ST2-R2 score: degree of reverse remodelling and 4-year survival in patients with heart failure. A multicenter study
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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 relevant 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 scoring and LVEF and LV size changes. Based on the specified subgroups a significant association was observed between 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.

P1140 | BEDSIDE
Right ventricle myocardial perfusion pressure and outcome in pulmonary hypertension due to left heart failure
Background: 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±32 mmHg in the PH group as compared to 107.1±24.8 in the no-PH group (p<0.001). The DPP was similar in both groups, 62.9±17.2 vs 62.9±12.9 mmHg; respectively (p=0.97). No difference in the mortality event rate according to SPP quartiles was observed (p=0.33). In contrary, in DPP quartile analysis, the death rate in the two lower quartiles was significantly increased by 37.4% and 28.8%, as compared with 16.2% and 17.6% in the higher quartiles (p=0.002). In a multivariate analysis, the adjusted hazard ratio (HR) for all-cause mortality was 3.27 (95% Confidence Interval (CI) 1.31–8.18, p=0.01), 2.76 (95% CI 1.10–6.86, p=0.029) and 0.81 (95% CI 0.42–1.56, p=0.03) 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 an alternative to surgery in patients with severe aortic stenosis. The balloon aortic valvuloplasty (BAV) can be used in balloon aortic valvuloplasty (BAV), but is considered to be a bridging procedure, and the low paravalvular leakage (PLV) of BAV is a controversial subject. The objective of this study was to evaluate the impact of direct TAVI on the PLV 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. Prospective collected echocardiographic data before TAVI were retrospectively analyzed in all patients. The VARC-2 criteria were used for designing clinical outcomes. Patients were classified based on LVEF in patients with impaired (LVEF<50%) and patients with preserved LVEF (≥50%). The VARC-2 criteria were used for designing clinical outcomes.

Results: Two hundred and four patients (mean age: 81±7 years) were included in the study. From 130 patients with preserved LVEF, 62 patients (48%) underwent BAV and 68 patients (52%) underwent direct TAVI. Device success rate was equal 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 feasible and has lower paravalvular leakage rates comparing to patients undergoing non-direct TAVI at 1-year.
fraction were detected in PaH, indicating the compensated nature of the observed hypertrophy. Active relaxation was accelerated in the heart’s stroke, while it showed a marked improvement in AB (Tau: −7.7±2.6% PhyH vs. +42.1±11.1% PaH, p<0.01). Load-independent, sensitive indices of LV contractility were increased in both models, in parallel with the degree of hypertrophy. Stroke work increased in both models, whereas mechanical efficiency of LV was improved in PhyH and remained unchanged in PaH (+20.8±4.7% PhyH vs. −4.7±4.9% PaH, p<0.05).

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

P1145 | BENCH
Human iPSC-MSCs is superior to human ESC-CMS for improvement of left ventricular function in a porcine model of post-myocardial infarction heart failure
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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 a single 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/dtmax 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
P1147 | 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 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: −4.05 to 2.17 mmHg, p=0.36) compared to control at 6 months. The proportion of patients who normalized their BP control was achieved in 36% of patients after 2 weeks. The mean change in systolic blood pressure (SBP) was −10±16 mm Hg, and the mean change in diastolic blood pressure (DBP) was −5±9 mm Hg; 85% of patients achieving a decrease in SBP, DBP or both. Most patients (84%) had a good experience and thought the platform was easy to understand and convenient to use as measured by a patient satisfaction survey.

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

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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 artery denervation (RDN) on changes in office and ambulatory blood pressure measures (ABPM) and on changes in nocturnal SBP defined by ABPM 6 months post-RDN compared to baseline 0–1 month post-RDN.

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. Denervation was performed from baseline in office and 24-hr ambulatory blood pressure was determined at 6 months follow-up for patients with OSA. Average nocturnal SBP (1 am to 6 am), average peak nocturnal SBP (average of 3 highest SBPs between 1 am and 6 am) and maximum nocturnal peak SBP were calculated using pooled patient-level ABPM data 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 pattern of nocturnal SBP (defined by ABPM) was observed in 86% of RDN and 87% of control patients (p=0.610). The six-month change in office SBP was significantly greater in the RDN OSA patients compared with control patients (−17.0±22.4 mmHg vs −4.3±26.1 mmHg, p=0.011) while the 24-hr ambulatory SBP change was not significantly different between the groups (−5.0±14.7 mmHg vs −0.8±17.9 mmHg, p=0.142). Average nocturnal SBP was reduced in the RDN but not in the control patients (−5.5±19.6 vs 1.6±21.5 mmHg, p=0.056). This pattern was also observed with average peak and maximum nocturnal peak SBPs (−5.6±20.4 vs 3.2±22.4 mmHg, p=0.021 and −4.8±21.8 vs 4.5±22.4 mmHg, p=0.025, respectively).

Conclusions: Patients with resistant hypertension and OSA appeared to have greater reductions in office SBP and in average peak and maximum peak nocturnal SBP following RDN than 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), thus representing an unique model to examine the hypothesis that sympathetic activity modulates circulating ADMA and its symmetric enantiomer (SDMA).

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

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

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

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

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Background: For blood pressure (BP) management, objective information that is rapidly accessible at any time in an ambulatory setting would enable more efficient medication adjustment, medication use, and/or pharmacologic unresponsiveness should be the focus.

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

Methods: 37 subjects (23 males; age 62±9 years) used the system for 6 weeks. Two digital medicine prototypes consisted of valsartan 80 mg or 160 mg placed in a gelatin hemi-capsule having an exipient tablet as a “stopper”. On the external stopper surface, a poppy-seed size ingestible sensor (IS) made of foodstuff created a biogalvanic current upon ingestion to alert a prototype adhesive wearable system (WS) worn on the torso. The WS 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 were not received 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, means, taking and scheduling adherence was 90% and 83% with some taping 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 use.

Conclusions: Automatically acquiring, integrating, displaying, and communicating (1) physiologic metrics, (2) activities of daily living, and (3) regularity and patterns of correctly confirmed medication ingestion, appears to be feasible in an ambulatory setting. Versions of better tolerated WSs are now available, and development of medicinal 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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Background: 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.

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

Methods: Seven normotensive female Yorkshire pigs underwent unilateral RSD using MRHIFU for safety and efficacy assessment. A fiberoptic temperature probe was invasively placed in the target renal artery to confirm energy delivery and real-time ultrasound imaging during MRHIFU. MRI was utilized 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 assessed 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 between the treated and untreated renal arteries was observed in 85% of animals with treated nerves showing increased cellular infiltration 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.
P1152 | BEDSIDE
Non-invasive coronary flow reserve in patients with resistant hypertension
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Resistant hypertension (RH) (office blood pressure (OBP) 140/90 despite treatment with three antihypertensive agents including one diuretic) is associated with increased risk for cardiovascular events. Coronary flow reserve (CFR) is impaired in patients with hypertension and is an independent predictor of cardiac mortality. However data on CFR in the subset of RH are scarce.

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

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

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

1196 | BENCH
Relative survival and excess mortality following Primary PCI for STEMl: Insights from a 97129 patient national cohort study
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Introduction: Primary PCI (PPCI) studies report 3-year all-cause mortality rates >10% and 6% for those surviving the acute phase. These studies typically lack external validity or are from historical cohorts. Furthermore, long term survival is affected by factors other than baseline variables not relating to the underlying disease. There are no whole-country studies of survival after PPCI which have adjusted for background mortality.

Methods: We performed a nationwide population-based cohort study from 106 UK hospitals comprising 97,129 patients from 2006 to 2013. Data from the British Cardiovascular 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.

1197 | BEDSIDE
Symptom onset to reperfusion trends in patients with ST-elevation myocardial infarction across New York State from 2004 to 2010

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

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

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

Results: There was a statistically significant trend towards shorter OTD, OTB, and DTB times in patients presenting with STEMI in New York State between 2004 and 2010 (median DTB time of 79 minutes (IQR 47, 114) in 2004 to a median time of 59 minutes (IQR 38, 81) in 2010, p<0.01 for trend from 2004 to 2010). In subgroup analysis, gender (male or female), age (<65 or ≥65), and the presence of co-morbid conditions (cerebrovascular disease, chronic obstructive pulmonary disease or diabetes mellitus) did not influence the trend in reperfusion times. A statistically significant trend towards shorter OTD times (p=0.04) was observed in patients with history of myocardial infarction but not in patients with prior CAGB. On the other hand, patients with prior CAGB had a statistically significant trend towards shorter OTD than DTB times (p<0.01) but non-significant OTD times (p=0.38).
Conclusions: Our results show a consistent, statistically significant trend towards shorter OTD, OTB, and DBT 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 AMI decreased from 19% to 13% (p=0.01) and 1-year mortality from 31% to 23.6% (p=0.004, respectively) reflecting a lower rate in non-progammed revascularization and myocardial infarction. This effect is preserved even when corrected for other significant variables (OR 0.54, IC 95% 0.35–0.84, p=0.007). No heterogeneity was detected (I²=0% for all outcomes).

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 (ACE) inhibitors) 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 22% (p=0.002). The detected reduction in mortality rates persisted after adjusting for other significant variables (OR 0.54, IC 95% 0.35–0.84, p=0.007).

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

1199 | BEDSIDE
Complete percutaneous coronary intervention versus culprit only percutaneous coronary intervention for acute ST elevation myocardial infarction with multivessel coronary artery disease: a meta-analysis
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Background: Current guidelines recommend primary PCI in haemodynamically stable acute STEMI patients should be limited to the culprit vessel despite significant stenosis in non-culprit coronary arteries. Recent studies and meta-analyses provide conflicting data.

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

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

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

Conclusion: Complete PCI is significantly associated with decreased risk of cardiovascular mortality, repeat revascularisation, and repeat non-fatal MI in patients with acute STEMI and multivessel CAD.
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 multivariable 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 multivariable 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), with only a single MVD patient (0.18%) experiencing a MI related to a non-culprit lesion.

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

Conclusion: In clinical practice GP IIb/IIIa inhibitors in Germany are used in more than 50% of the patients with primary PCI for STEMI treated with heparin. The use is associated with an improved mortality without an increase in bleeding complications. This data support 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 exploratory coronary intervention study
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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 STEMI pts undergoing pPCI in our center in 2007–2011 (n=807, after exclusion of pts without CM values). CIN was defined as an increase in creatinine >0.5 mg/dl in the first 72 hours; coronary artery disease (CAD) 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 Cigarroa 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 admission and in-hospital left ventricular ejection fraction (LVEF) (p<0.001) had a markedly lower anterior MI, a higher Killip class, a higher baseline eGFR, (p<0.05). CR >1 was a predictor of CIN (OR 3.9 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 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, CK peak, haemoglobin, eGFR and diabetes.

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

1205 | BEDSIDE
New generation drug-eluting stents vs. bare metal stents for primary angioplasty in patients >75 years with ST elevated myocardial infarction: the ESTROFA Mi75 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-
Background: Dyslipidemia during myocardial infarction (MI) has been reported but the mechanism is still unclear. Sterol regulatory element binding protein (SREBP) is a key regulatory transcription factor and it adjusts the lipogenesis through the AMPK-mTOR-SREBP signaling pathway in hepatocytes. The signaling pathway inside hepatocytes could be altered by inflammatory signals secreted by inflammatory cells including dendritic cells (DCs). It has been known that DCs can be activated 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) Sham group, 2) MI control group, 3) MI + DCs group. Mice were treated with the supernatant of MI myocardial cells (from MI group) or normal myocardial cells (from Sham group). The exosomes secreted by the DCs above were injected into another three groups of mice through the tail vein. Lipid profiles in plasma, DC distribution and the protein and the mRNA expression of AMPK-mTOR-SREBP signaling in liver were all 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.

Results: 1. Total cholesterol and LDL cholesterol in plasma were increased at 24 hrs post-AMI and slightly decreased on day 7 post-MI 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 in the liver increased before and after the addition. 2. The protein and the mRNA levels of AMPK-mTOR-SREBP signaling in liver were increased at 24 hrs post-AMI, but these were decreased on day 7 post-MI, which corresponded to the change of plasma cholesterol levels. 3. Injection of exosomes obtained from DCs of mice induced the increase in plasma cholesterol and LDL-c levels in MI group compared with sham group. The protein and the mRNA levels of AMPK-mTOR-SREBP signaling in liver were also increased by the injection of exosomes in MI groups. 3. Addition of exosomes obtained from DCs treated with MI myocardium supernatant induced significant increases in the protein and the mRNA expression of AMPK-mTOR-SREBP signaling in the cultured hepatocytes.

Conclusion: DCs can be activated and secrete exosomes which induce upregulation of AMPK-mTOR-SREBP signaling in hepatocytes, leading to the hypercholesterolemia post-MI.

1216 | BENCH
Serelexin reduces oxidative stress in vitro and atherosclerosis in apoE-deficient mice
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Background: Serelexin (RLX) is recombinant human relaxin-2, a naturally occurring peptide that regulates maternal cardiovascular adaptations to pregnancy with several effects potentially relevant to the treatment of acute heart failure, including increased arterial compliance, cardiac output, and renal blood flow. Results from the RELAX-AHF study showed significant improved dyspnea symptoms and significant mortality benefits within patients with acute heart failure. It is unclear whether serelexin has an effect on atherosclerosis. Therefore, we investigated the effect of serelexin in human coronary artery smooth muscle cells (HCAsmCs) and in a mouse model of atherosclerosis.

Methods and results: In vitro, we investigated the effects of serelexin on oxidative stress (LO-12, DCF) in human coronary artery smooth muscle cells (HCAsmCs). Serelexin incubation of HCAsmCs reduced significantly antioxidant II- induced ROS production (veh: 100%; ang II: 127.3±7.2%, ang II+RLX (10ng/ml, 24h): 108.8±2.1%, p=0.044 vs. ang II). Female 6-week-old apolipoprotein E deficient (C57BL6/ApoE−/−) mice were fed a high-fat (21% fat) diet containing 1.25% cholesterol for 6 weeks and received a continuous treatment with serelexin in two different doses (0.125g/kg/day and 0.05g/kg/day) through subcutaneously implanted osmotic mini-pumps. Additionally, one group of female ApoE−/− mice served as control group treated with vehicle through osmotic minipumps. Total cholesterol, fasting blood glucose, blood pressure and heart rates were no different between the groups. Vascular oxidative stress [LD12-chemiluminescence] was significantly reduced in both serelexin-treated mice (veh: 322.7±13.2; RLX: 0.05g/kg/day: 119.76 RLU/μg (p=0.03 vs. veh.), RLX 0.125g/kg/day: 109 RLU/μg (p=0.002 vs. veh.)). Serelexin treatment in both concentrations significantly improved endothelium-dependent vasodilatation (organ chamber experiments) without influencing endothelium-independent vasorelaxation as compared without serelexin treatment. Small plaque development (Oil red stainings) and aortic root, was significantly reduced in animals treated with the higher doses of serelexin, indicating dose dependency effects of serelexin (veh: 88.8±0.9%, RLX 0.05g/kg/day: 61.8±1.1% (n.s. vs. veh.), RLX 0.125g/kg/day: 57.9±0.9% (p=0.038 vs. veh.).

Conclusion: The presented data demonstrate novel effects of serelexin on vascular oxidative stress and atherosclerotic plaque development. Therefore, Serelexin could serve as a new drug class for treating atherosclerosis-related diseases.
Rising systolic blood pressure leads to a continuous progression towards hypertensive heart disease: a prospective population study

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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±12.4 years) underwent 3D-CMR combined with computational modelling. The relationship between SBP and wall thickness (WT), relative wall thickness (RWT), end-systolic wall stress (WS) and fractional wall thickening (FWT) were assessed 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 asympotmic concentric hypertrophic adaptation of the septum and anterior wall with associated normalization of WS. In the lateral wall an increase in WS with rising SBP was not balanced by a commensurate hypertrophic response. In normotensives, SBP was positively associated with WT (β=0.08) and RWT (β=0.06) in the septal and anterior walls, and this regional hypertrophic response was progressively stronger amongst pre-hypertensives (β=0.08) and hypertensives (β=0.21). Males had a greater hypertrophic response than females with the most robust interaction between SBP and gender in the septum (β=0.67). FWT was positively associated with SBP in the inferior and lateral walls (β=0.10) but not where SBP-associated hypertrophy was predominant.

Conclusions: SBP is associated with a continuous progression towards the hypertensive cardiac phenotype, which we show to be defined by concentric hypertrophy of the septum and eccentric remodeling of the lateral wall. We observed that rising SBP is associated with a 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.

Association of orthostatic hypertension with cardiovascular and all cause mortality in the elderly program

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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 (oHyp) 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 oHyp, 4073 had a normal response, and 438 had orthostatic hypotension (SBP decrease by 20 mm Hg or more, oHypo).

Results: Compared with normal response, oHypo was associated with higher 17-year cardiovascular death in an analysis adjusted for age, gender and SBP (HR 1.16, 95% CI 1.06–1.27, p=0.001). Similar findings were observed for all-cause mortality. The higher risk was no longer significant after additional adjustment for creatinine, diabetes, body mass index, smoking, left ventricular failure, and HDL cholesterol. The higher mortality associated with oHypo 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.
Purpose: To compare OHCA management and outcomes according to whether they occur during off or working hours.

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

Results: Of the 11430 reported OHCA, 7240 (63%) occurred during off hours. Witnesses were more often present but less frequently initiated BLS and used AED as compared to patients who presented during working hours. In hospital discharge, despite similar rates of hypothermia, coronary angiography and angioplasty.

Conclusion: Survival rates of OHCA were lower during off hours mainly due to a lower rate of witness-initiated BLS and AED use rather than a difference in hospital management or the rate of public awareness and training programs in improving OHCA prognosis during off hours.

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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 during an out-of-hospital cardiac arrest (OHCA). Based on 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 efforts and survival after OHCA.

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 3771 (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, 10 min [interquartile range (IQR) 6–16] vs. 17 min [IQR 11–24], P < 0.0001). Moreover, the CPR-to-ROSC time was significantly shorter in 1-month survivors with CPC 1–2 than those in CPC 3–5 (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 (adjusted 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 CPR-to-ROSC time ≤18 min achieved ROSC within 25 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 >5.5 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.

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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 PEA/ASY vs. VF. This study analyzed the autopsy findings of 100 autopsied SCD cases with PEA/ASY vs. VF as a presenting rhythm at the time of cardiac arrest.

Methods: Prevalence of PEA/ASY vs. VF occurring within one hour after onset of witnessed collapse was analyzed by the emergency personnel of patients with SCD. Underlying structural heart disease was diagnosed by medical-legal autopsy in the Finnish study of genotype and phenotype profile of SCD (FinGesture) 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 medico-legal autopsy. PEA/ASY 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 vs. 62.7), body mass index (mean 30.9 vs. 27.4), gender or in the time of delay between the onset of cardiac arrest and the ECG recording (mean 19±15 minutes in PEA/ASY vs. 16±14 minutes in VF). PEA/ASY was more prevalent than VF in cases with non-ischemic cardiac disease (35.3% vs. 31%, p < 0.001) at autopsy. Usage of psychotropic medication was also more common in PEA/ASY 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: PEA/ASY 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 PEA/ASY.

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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 risk for 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: WCD patients (mean 57 years old, range 11–90, 78% male) were grouped into 8 cardiovascular indications: non-ischemic cardiomyopathy (CM), 12%, acute ischemic CM, 27%, ICD implant, 12%; myocarditis, 10%; genetic, 1%; heart transplant candidate, <1%; heart failure, <1%; dilated CM, 37%. Patients wore the WCD for a median of 58 days with median daily use exceeding 22.4 hours. 64% of patients had daily use >90% and 91% of patients wore the WCD for >10 days. Longer duration of wear correlated with longer median daily use.

Results: A total of 120 patients experienced WCD treatment. 94 (1.6%) patients had VT/VF and 2 (0.03%) patients experienced episodes of asystole. Inappropriate treatments occurred in 0.4% of all patients and were mostly due to noise artefacts (54%) or fast supraventricular tachycardia (38%). Higher therapy rates occurred among ICD implant and acute ischemic CM patients. 79% of all treatments were presented within 50 days of WCD use, and 90% of all therapies occurred within 80 days. In total 112 (93%) patients survived beyond the first 24 hours after WCD therapy.

Conclusions: The majority of patients had >90% daily use over 8 weeks of median total wear. SCA presented in 1.6% of patients, and all VT/VF episodes were appropriately detected and treated. Post-treatment survival was 93%. This confirms the overall value of the WCD in German treatment pathways, with the opportunity for earlier ICD implant and among patients with clinical diagnosis different than had been reported in previously published WCD studies.

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

Methods: In a multidisciplinary program for the evaluation of unexplained falls and/or syncope in elderly patients we investigated all patients for OH and PPH. This diagnostic program of 2 days included a comprehensive geriatric assessment and after a meal.

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 for the diagnosis of OH more active standing BPM should be performed in the work-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.

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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 encephalopathies. 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 LQTS type 2 (LQT2) have an increased prevalence of cerebral affection compared to other LQTS subclasses.

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

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

**Results:** Of the 15 patients, 11 (73%) had experienced 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 LQTS 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:** Syncopes in LQT2 patients were frequently associated with tonic-clonic activity, spells and urine incontinence, which could also be consistent with epilepsy. In addition, 2/15 had co-existing diagnoses of epilepsy and LQT2. The majority of the EEGs showed minor to moderate changes with intermittent theta activity or spells. Two patients (13%) had been diagnosed with epilepsy and received anti-epileptic medication prior to their LQTS diagnosis.

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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 syncopal episodes. Serotonin uptake 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 VVS and a diagnostic, positive head-up tilt test (HUT). Their psychological, stress-related profile was assessed by the Anxiety Sensitivity Index (ASI) questionnaire, a simple, 16-item questionnaire, assessing fear of anxiety-related sensations, previously studied in VVS. An anxiety screening test (Beck Anxiety Inventory) was also systematically evaluated. Patients scoring positive for ASI (n=60, 57% of the assessed population) were randomized in a 2:1 fashion to receive either 10–40 mg fluoxetine daily (n=40) or placebo (n=20), and were followed-up for 1 year.

**Results:** No difference was observed between the two treatment groups regarding baseline clinical characteristics as well as anxiety levels, as assessed by the Beck Anxiety Inventory score. Following a 12-month period, a significant difference was observed between patients receiving fluoxetine and those with placebo, regarding the distribution of syncope-free time during the study period (p=0.05). A significant difference was also observed between the 2 groups regarding presynopal events as well as the total number of patients who experienced syncope and 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.
transsected 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, α1AR activity in PoTS was more homogeneous and higher than both VVS and controls (p<0.05) while VVS also was higher than the control group (p<0.01). Moreover, sera from PoTS shifted α1AR-phenylephrine dosage curves to the right.

**Table 1**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Alpha-1AR AAb (% above BB)</th>
<th>Beta-1AR AAb (RLU)</th>
<th>Beta-2AR AAb (RLU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n=13)</td>
<td>63±1.7</td>
<td>390±187</td>
<td>512±253</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>

Antiadrenergic serum activity among patients with PoTS, VVS, and normal age-matched controls. *p<0.01 vs controls; †p<0.05 vs VVS. One-way ANOVA-test for difference between groups: a1AR-AAb, p=0.0004; b1AR-AAb, p=0.0001; b2AR-AAb, p<0.0001.

**Conclusions:** These data support a pathophysiological relationship between α1/2 adrenergic AAbs and PoTS; and suggest they are not restricted to classical PoTS alone but may also be present in other forms of dysautonomia such as recurrent VVS as a part of an autoimmune spectrum.

Acknowledgements: The Lundström Endresshedsfonden, the Anna Lisa and Sven-Erik Lundgrens Foundation; the Ernhold Lundströms Research Foundation; the Stockholm County Council, University Hospital, and the Karolinska Elderly Care Research Foundation.

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

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**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, categories 1 to 2; CPC 1–2) in children transported to hospital without a prehospital ROSC after OHCA.

**Methods:** Of 9093 OHCA children, 7332 children aged <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 pre-hospital 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) 1–1.6] vs. 12 year [IQR 0–11], P<0.001), and actual shock delivery (25/73 [34.2%] vs. 314/7259 [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-asystole rhythm (ventricular fibrillation [VF]/pulseless ventricular tachycardia [VT]; adjusted odds ratio [aOR] 15.9; 95% confidence interval [CI] 8.05–32.0, pulseless electrical activity [PEA]; aOR 5.18; 95% CI 2.76–9.82) and (2) bystander-witnessed arrest (aOR 3.21; 95% CI 8.44–57.9). In witnessed-arrest children with a non-VF/PEA 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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Following a statewide quality improvement initiative, increased by-

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bystander CPR and first responder defibrillation for both: results form a

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and no new echocardiographic abnormal findings were revealed in any patient.

atrial fibrillation. No patient developed AV conduction disturbances over the time

did not induce any sustained ventricular arrhythmia. During the long-term follow-

were detected. Mean EF was 59±3%. Family history of sudden death was present

of 85.2±47.3 months, ECG was found abnormal in 3 cases (1 long QT, 1 Brugada

in the absence of structural and ischemic heart disease (normal echocardiogra-

All survivors of OHCA presenting with VF , and normal baseline ECG

Methods:

the last 14 years. The long-term follow-up and the evolution over the time of ECG

The aim of this study was to investigate the clinical and ECG features

structural heart disease is rare, with a broad differential diagnosis that includes

Out-of hospital cardiac arrest (OHCA) in the absence of evident

Background:

LONG-TERM RISK AND MORTALITY IN PATIENTS WITHOUT OBSTRUCTIVE CORONARY ARTERY DISEASE BY CORONARY ANGIOGRAPHY

K.K.W. Olesen1, M. Madsen2, G. Egholm1, T. Thim1, L.O. Jensen2,

H.E. Boetker1, H.T. Soerenensen2, M. Maeng1, 3 Aarhus University Hospital,

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Department of Clinical Epidemiology, Aarhus, Denmark; 3 Odense University Hospital,

Department of Cardiology, Odense, Denmark

Introduction: Patients with medically treated diabetes mellitus have a risk of my-
ocardial infarction (MI) equivalent to non-diabetic patients with a previous MI, and

Therefore, it has been suggested that prophylactic treatment of these patients with

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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.

BEST POSTERS IN POST MYOCARDIAL INFARCTION OUTCOMES

LONG-TERM RISK AND MORTALITY IN PATIENTS WITHOUT OBSTRUCTIVE CORONARY ARTERY DISEASE BY CORONARY ANGIOGRAPHY

K.K.W. Olesen1, M. Madsen2, G. Egholm1, T. Thim1, L.O. Jensen2,

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Introduction: Patients with medically treated diabetes mellitus have a risk of my-
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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 (normal cardiocapogra-

phy/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 sec-

ondary 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

type 2 pattern and 1 early repolarization pattern in inferior leads). In the remaining

were diabetes at the time of examination. CAD was present in 41,010 (n=5,475 diabetic

patients, while 30,414 had no CAD (n=3,066 diabetic). Mean follow up was 4.3

years. Diabetic patients with CAD at CAT exhibited the highest risk of MI dur-

ing follow-up followed by non-diabetic patients with CAD. However patients with-

out CAD, despite presence or absence of diabetes, exhibited similar low rates of

MI. In terms of all-cause death, diabetic patients with CAD were at highest

risk, followed by diabetic-patient with CAD and diabetic patients without CAD

showing equally high mortality risk, with non-diabetic patients without CAD at

the lowest risk of death.

Conclusions: Patients with diabetes but no CAD exhibited the same low risk of

MI as non-diabetic patients without CAD. This challenges the general assumption

of diabetic patients as a uniform group of high-risk patients with regard to risk of

future MI.

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

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Department of Cardiology, Odense, Denmark

Introduction: Chest pain despite the absence of obstructive coronary artery dis-

ease (CAD) has previously been associated with favorable long-term risk of death

and future myocardial infarction (MI). However, recent large-scale studies are sug-

gesting otherwise, leaving risk assessment of these patients unclear.

Purpose: Examine long-term risk of myocardial infarction (MI) and all-cause mor-

tality in patients without obstructive CAD verified by coronary angiography (CAG)

compared to a sampled background population from the Western Danish popula-

tion.

Methods: Population-based retrospective cohort study. Patient cohort was estab-

lished using every CAG procedure from January 1st 2003–December 31st 2012 in

the Western Denmark Heart Registry. Analyzes were restricted to patients without

obstructive CAD at time of premier CAG examination, further stratified according
to procedural priority: acute/subacute or elective procedures. Further sensitivity

analyses was performed in elective patients with stable angina pectoris. Patients

with prior history of MI, PCI or CABG were excluded. Subcohorts were compared
to a background population from the Western Denmark population. Maximum follow up of 7 years with endpoints of MI and death.

Total number of endpoints were counted. Cumulated event curves were constructed. Short-term risk difference and relative risk were estimated for the
initial 6 months after CAG. Crude and adjusted long-term HR were generated using Cox's proportional hazard regression analyses.

Results: 31,805 patients undergoing first time CAG patients were eligible for analyses of whom 9,241 were acute/subacute procedures and 22,493 were elective procedures. In sensitivity analyzes 13,110 elective patients had stable angina pectoris. 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. 0.755–0.965) in all patients. Elective patients with stable angina 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 patients 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


Background and aim: Number of PCI performed by center is a determinant of mortality in STEMI patients. The decision to propose reperfusion therapy is a cornerstone of STEMI patient management in the pre-hospital setting, and guidelines suggest that the rate of reperfusion-decisions is a quality indicator. We sought whether the number of STEMI managed by mobile intensive care units squad (MICU) and emergency medical system departments (SAMU; Service d' Aide Médicale Urgente) was a determinant of the rehospital referral-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 by the SAMU. 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 [25–167] min. The annual number of STEMI 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 fibrinolyis: 24%). There was no correlation between total case-load for each SAMU or MICU.

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.

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 stress echo (SE) and exercise-electrocardiography test (EET) over time in the last 39 years.

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

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

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

Conclusion: Over the last 39 years, we observed a steady decline of positivity for all tests, except imaging and non-imaging, exercise and pharmacoalological, 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...
markers such as ECG changes during EET or wall motion abnormalities during SE.

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 (58.8±9.9 years) patients who were referred for DSCE. Ischemic response was defined as wall-motion deterioration and/or perfusion abnormality in two or more consecutive myocardial segments. Patients were classified as diabetics and non-diabetics. Furthermore, they were stratified as appropriate (A), uncertain (U) and inappropriate (I). Mean follow-up lasted 57±10.1 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 uncertain and 22.7% as inappropriate. Mean follow-up lasted 57±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 uncertain and 22.7% as inappropriate. Mean follow-up lasted 57±10.1 months. End points included all-cause mortality, cardiac death, the need for late revascularization (>3 months) and hospitalizations.

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.

P1343 | BEDSIDE
Should we perform exercise echocardiography on patients with left bundle branch block and suspected coronary disease?
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Introduction: Exercise stress echocardiography (ESE) is recommended for the evaluation of suspected obstructive coronary artery disease (OCAD) in ambulatory patients with left bundle branch block (LBBB), with a class I indication in the AHA/ACC guidelines. Supportive data is derived almost exclusively from Dobutamine stress echocardiography (DSCE), which is an appropriate test for exercise-induced ischemia.

Methods: We evaluated 114 consecutive patients with LBBB referred for ESE to investigate for OCAD at our institution. The left ventricular contractile response (LVCR) post stress was categorised as normal or abnormal. Patients with an abnormal response were sub categorised as (a) regional ischaemic response or (b) globally abnormal due to either global hypokinesis or global failure of myocardial contraction to augment. Subsequent anatomic imaging (angiography or CTCA) results were evaluated with significant OCAD defined as stenosis > 70%.

Results: There were 114 consecutive patients (54% females, mean age 63 (SD 6±10) years) who exercised to achieve > 85% of the age predicted maximum heart rate. Only 51 patients (46%) demonstrated a normal LVCR to exercise. 63 (55%) had an abnormal LVCR. Of these there were 45 with a globally abnormal response and 18 who had a regional ischaemic response. Of the patients with abnormal LVCR, 42 (67%) had anatomic imaging, only 19 of whom had obstructive CAD. This included 13/13 with an ischaemic response and 6/29 with globally abnormal response.

Conclusion: Compared to the AHA/ACC guidelines, SE appears a suboptimal test to evaluate for OCAD in patients with a LBBB, as greater than 50% patients will have an abnormal LVCR, the majority due to global abnormality where OCAD cannot be excluded. We suggest alternative testing e.g. pharmacologic stress imaging study or CT coronary angiography.

P1344 | BEDSIDE
Objective criteria of LAD lesion during exercise stress echocardiography: coronary flow velocity reserve during exercise
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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 been approved as coronary flow assessment during exercise. The objective of this 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.

Materials and methods: We enrolled 302 patients: 1) 232 non-selective subjects who were referred to stress echocardiography before coronary angiography; 2) 70 controls without CAD who were not significantly different from the main group according to age and gender distribution (mean age 59±8 vs. 57±10 years, 71% vs. 59% men, p=NS). All the patients performed a supine bicycle 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 significant differences between velocity flow data regarding the subgroup without proximal stenosis of this artery: velocity in LAD at the peak of exercise (49±29 vs. 66±22 cm/s, p<0.0003), ΔV (16±20 vs. 28±22 cm/s, p<0.0001), and CFVR (1.5±0.6 vs. 1.9±0.7, p<0.0001). The patients with the middle lesions of LAD had a significant higher velocity at rest versus group without such LAD lesions (42±23 vs. 33±15 cm/s, p<0.003). The patients with LAD lesions had a lower flow velocity at the peak of exercise (55±30 vs. 74±18 cm/s, p<0.00005), a lower ΔV (19±21 vs. 42±16 cm/s, p<0.000001), and a lower CFVR (1.5±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.

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 recordings (AP) 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 (VSFP1) was used 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
assess AP characteristics and single-cell arrhythmias. This method provides a basis for high-throughput QT assays for safety pharmacology. Patient-derived cells with a reduced repolarization reserve may be particularly suited to detect even subtle drug effects.

PI347 | 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 each an anti-CD25 antibody in CD1 mice or the dybythia toxin 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). Bioplex 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. 4±4%), increased number of major events (aneurysms, cardiac ruptures and deaths); histological analysis revealed that Treg depletion resulted in increased infiltration by CD45+ inflammatory cells (8±4% vs. 25±7%), paralleled by decreased collagen deposition. In accordance, injection of EGFP+ Tregs, which persisted in the heart for at least 1 week after injection, also reduced infarct size and preserved cardiac contractility (EF at 1 month: 35±6% in control vs. 55±11% in Treg-injected mice). Of note, close to the site of Treg injection, we observed 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 chemoattractant).

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 we all as following myocardial infarction, when they sustain cardiac function and improve lesion healing.

PI348 | BENCH
Improved vascularization and increased expression of contractile protein mediate beneficial effects of transplantation of adipose tissue mesenchymal cells expressing telomerase and myocardin in murine R. Madanna1, L. Petrov2, M.A. Teberino1, Y.J. Geng3, P. Ferdinandy4, S. Zacchigna1, V. Martinelli2, G. Colussi1, M. Arzini1, A. Nordio2, S. Moimas1, G. Sinagra2, M. Gacca1, 1International Centre for Genetic Engineering and Biotechnology (ICGEB), Molecular Medicine, Trieste, Italy; 2University Hospital Riniuti, Trieste, Italy

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

Objectives: We examined the therapeutic efficacy of transplanted AT-MSCs expressing MYOCD and TERT in a murine model of myocardial infarction (MI), and underlying mechanisms.

Methods: AT-MSCs from the adipose tissue of aged (12-month-old) male C57BL/6 mice were transduced with lentiviral vectors encoding TERT and MYOCD. Twelve-month-old C57 mice underwent coronary artery ligation (Lig), followed by randomization into 4 groups (n=5/group): Sham operation, MI control (saline 20 μL), MI followed by intramyocardial injection with mock-transduced AT-MSCs (2.5±10⁵ cells/20 μL), or aged AT-MSCs expressing TERT and MYOCD (2.5±10⁵ cells/20 μL).

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

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

PI349 | BENCH
Prolyl hydroxylase inhibition induces SDF-1 and CXCR4 expression to increase CXCR4+ cell homing and myocardial repair

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

Methods: To evaluate the effects on HIF-1α mediated SDF-1 and CXCR4 expression, genetically tagged SDF-1-EGFP and CXCR4-EGFP mice were subjected to optimal doses (80mg/kg i.p.) of the prolyl hydroxylate Inhibitor dimethyloxalyl-glycine (DMOG). To examine the time frame of SDF-1 and CXCR4 expression in vivo (HEK cells) and in vivo (BM & heart), DMOG was treated at different dosing regimens (50μM to 100μM & 80mg/kg i.p.) and time intervals (1 to 6 hrs), FACS and immunohistochemical analyses of CXCR4+ bone marrow (BM), peripheral blood, and heart cells as well as infarct size measurements were performed under normoxic and ischemic conditions and with and without DMOG treatment.

Results: SDF-1-EGFP mice treated with DMOG showed robust induction of SDF-1 in heart vessels. In vivo, 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 (6hrs). In vivo, CXCR4 expression was significantly upregulated in BM (6hrs) 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+, of transgenic CXCR4-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 (6hrs). In vivo, CXCR4 expression was significantly upregulated in BM (6hrs) 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+, CD45+ and CD45- cells, as well as stem cell populations like ACC133 and Lin-ckit1-3a-c1+8e-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+/CD68 ratio in favor of M2 macrophages associated CD206+ population in infarcted hearts associated by attenuated infarct remodeling.

Summary and conclusion: Our data suggest that inhibition of prolyl hydroxylase may be a promising target for HIF-1α mediated SDF-1 activation to increase CXCR4+ cell homing and myocardial repair.
Lack of progression or regression of left ventricular hypertrophy in children with sarcomeric gene disease

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Background: The muscular dystrophies are inherited diseases characterized by severe muscle wasting and weakness. Cardiac involvement is disease specific and varies from asymptomatic ECG changes to conduction disorders requiring pacing or end-stage dilated cardiomyopathy.

Purpose: The purpose of the study was to evaluate cardiac involvement in patients with several forms of hereditary muscular dystrophies.

Materials and methods: We evaluated 180 patients with genetically verified hereditary muscular dystrophies (MD) at mean age of 33±12.1 years, 112 males - 53 patients with dystrophinopathies (45 with Duchenne MD, 8 with Becker MD), 42 patients with myotonic dystrophy type 1, 21 patients with distal myopathies, 13 patients with limb-girdle (LG), 34 patients with facioscapulohumeral (FSH), 17 patients with mitochondrial myopathy. We performed clinical examination, 12 lead ECG, conventional 2D echocardiography, Doppler and tissue Doppler echocardiography. LV systolic dysfunction was found in 21 patients (11.7%) - in 24.4% of Duchenne MD patients, 50% of Becker MD patients, in 4.8% of myotonic dystrophy patients, in 14.3% of patients with distal myopathies, in 2.9% of patients with LG, in 53.3% of patients with distal myopathies, in 26.2% of myotonic dystrophy patients, in 52.4% of distal myopathies patients, in 7.7% of LG, in 26.5% of FSH patients and in 29.4% of patients with mitochondrial myopathy. RV involvement was found in patients with Duchenne MD. Pathological ECG findings were recorded in 80% of patients with Duchenne MD, in 55% of patients with Myotonic dystrophy, in 23.8% of patients with distal MD, in 23.1% with LG, in 29.4% with FSH and in 23.5% with mitochondrial myopathies. In one patient with myotonic dystrophy a permanent pacemaker was inserted because of AV block. Conclusion: Myocardial involvement seems to be a frequent and heterogeneous finding in hereditary muscular dystrophies, and genotype appears to be an important cause of this variability. Cardiomyopathy is most common and severe in patients with dystrophinopathies. ECG changes and conduction disturbances are more common in patients with myotonic dystrophy. Our findings imply that patients with muscular dystrophies require close cardiovascular as well as neurological follow-up.
coagulant prescription were higher in overweight, whereas those of the elderly, heart failure, and history of stroke/SE were higher in underweight. A total of 156 stroke/SE and 532 death occurred during follow-up. The Kaplan-Meier curves for the incidence of death/stroke/SE and those of stroke/SE are shown in the figure. Even after adjustment by sex, components of CHADS2 score, and oral anticoagulant prescription, overweight was associated with lower risk of death/SE/kg as compared with normal (hazard ratio: 0.60, p < 0.01), whereas underweight was associated with higher risk of death/stroke/SE (hazard ratio: 1.89, p < 0.01).

Conclusion: In real-world Japanese AF patients, overweight was significantly associated with lower risk of death/stroke/SE, whereas underweight was significantly associated with higher risk of death/stroke/SE.

P1358 | BEDSIDE

Diabetes, intakes, erythrocyte membrane phospholipid fatty acids and cardiovascular risk


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Atrial fibrillation (AF) increases the risk of stroke/systemic embolism and death. There is no standard definition and estimates of its prevalence in obese adults range from approximately 20–30%. Possible predictors of MHO are shorter lifetime 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 predicted MHO 20 years later. We hypothesized 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, >1.30mmol/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) of 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 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 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 specific cut points.
further data collected in a subset of participants through periodic resurveys to estimate usual intake levels for the whole cohort. Cox regression models were used to yield adjusted hazard ratios (HRs) among 474,191 participants free of major prior diseases at baseline.

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

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

**BEST POSTERS IN MORPHOLOGY VERSUS FUNCTIONAL ASSESSMENT... THE GREAT DEBATE CONTINUES ON PAPERS**

P1361 | BESIDE

**Comparison of physiological coronary artery stenosis severity assessed by fractional flow reserve and optical coherence tomography findings in stable angina pectoris**

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**Background and aim:** Acute coronary syndromes were widely believed to result from rupture of thin-capped fibrotheroma (TCFA) and thrombosis at the site of a mild to moderate stenosis. In contrast to this belief, a new mechanism of possible etiopathogenetic relevance was proposed, in which stent expansion is a risk factor for neointimal hyperplasia (NH). Debate continues whether this new mechanism was supported by the data. In this study, we aimed to compare the stenosis severity assessed by fractional flow reserve (FFR) and lesion instability by Optical Coherence Tomography (OCT) in patients with stable angina pectoris (SAP).

**Methods and results:** We investigated 198 lesions of 181 SAP patients who underwent OCT imaging and FFR measurement before PCI. Physiological stenosis severity was assessed by FFR, and lesions were divided into two groups on the basis of FFR values; severe stenosis group (group S): FFR < 0.75 (n=78, 39%), moderate stenosis group (group M): FFR < 0.75 (n=120, 61%), according to the previous study. OCT findings were compared among these two groups. TCFA was defined as lipid-rich plaque (lacr. ≥90%) with fibrous cap thickness <70μm. The median FFR values in all lesions, group S, and group M were 0.77 (interquartile range [IQR]: 0.69–0.83), 0.65 (0.55–0.71), and 0.81 (0.78–0.87), respectively. There were no significant differences in patient characteristics except for the frequency of previous myocardial infarction (group S: 15%, group M: 36%, P = 0.002). In OCT 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±0.33 mm, group M: 1.35±0.33 mm, P < 0.01), % diameter stenosis (group S: median 55.2%, IQR [48.7–62.9], group M: 53.0% [48.0–57.8], P = 0.002), and lesion length (group S: 13.3mm, [10.5–16.5], group M: 13.6mm, [10.6–18.1], P = 0.01). In a stepwise logistic regression, age, % diameter stenosis (group S: 0.69 (0.60–0.79), 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 current concept that lesions responsible for acute coronary syndromes in SAP may be mild in most cases provided that plaque rupture of TCFA evenly results in coronary events in the wide range of stenosis severity.

P1362 | BESIDE

**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:** The Index of microcirculatory resistance (IMR) is a readily available, wire-based method for invasively assessing coronary microvascular function in the catheterization laboratory. Although previous studies reported that high IMR value after primary percutaneous coronary intervention (PCI) was frequently observed and was associated with adverse clinical outcome in ST-segment elevation myocardial infarction patients, the relationship between target lesion characteristics and microvascular function remains elusive.

**Purpose:** We investigated the relationship between target lesion characteristics assessed by OCTs findings of the culprit lesion and microvascular function by OCT after PCI in patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS).

**Methods and results:** Fourty-five hemodynamically stable NSTE-ACS patients (male: N=36, age: 64.0±10.4 years, unstable angina: N=19, NSTE-ACS: N=26) with single de novo culprit lesion were enrolled. We assessed the presence and extent of post-PCI microvascular dysfunction (MVD) before PCI, at 2 hours post PCI, and at follow-up. OCT analysis was performed before PCI and IMR was measured immediately after PCI with the use of a pressure-temperature sensor wire. The median IMR value was 24.0 (interquartile range [IQR]: 11.2–15.1). IMR < 0.75 value after PCI was significantly associated with age (P = 0.03). There was no significant relationship between post-PCI IMR values and cardiac troponin I (cTnI) levels at all measurements (on admission, before PCI and after PCI). There was a significant relationship between high post-PCI IMR values and the presence of plaque rupture (P < 0.05), whereas the presence of OCT-derived thin-cap fibrotheroma, and red thrombus showed weak correlation with high IMR values (P > 0.07).

**Conclusion:** High IMR values after PCI in the target vessel were significantly associated with OCT-detected high-risk lesion characteristics, although there was no significant relationship between post-PCI IMR value and the marker of myocardial necrosis in NSTE-ACS patients.

P1363 | BESIDE

**The impact of in-stent neointimal hyperplasia on long-term clinical outcomes: an observational study from the optical coherence tomography registry**

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**Background:** Although pathological studies have indicated the development of neointimal hyperplasia (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).

**Methods:** 175 consecutive patients (314 lesions) who underwent OCT examination > 1 year after bare metal or drug-eluting stent implantation were enrolled (149 sirolimus- [SES], 67 paclitaxel- [PES], 61 everolimus-eluting stents [EES], and 37 bare metal stents [BMS]). We assessed the presence of NA by the follow-up OCT and compared MACE between NA+ and NA- patients.

**Results:** Forty-six patients (54 lesions) had NA at the follow-up OCT. Both SES and PES exhibited earlier onset of NA and occurred at a constant rate at each period as compared with BMS. In EES group, NA was observed in 13.1% between 12 and 36 months (Figure). Patients with NA had higher low-density lipoprotein (LDL)-cholesterol and C-reactive protein (CRP) levels at follow-up. In multivariate logistic analysis, LDL-cholesterol and CRP levels at follow-up were independently associated with the presence of NA (odds ratio [OR]: 1.022, P = 0.008, OR: 1.01, P < 0.001, respectively) and MACE (P < 0.001). A higher incidence of MACE at follow-up. Multivariate Cox hazard analysis showed that the presence of NA was an independent risk factor for MACE (hazard ratio: 2.909, P = 0.012).

**Conclusions:** Drug-eluting stents exhibited greater trends for atherosclerotic changes occurring in earlier time point than BMS. High LDL-cholesterol and CRP levels may be risk factors for NA development in patients treated with coronary stents. Moreover, the presence of NA was independently associated with MACE.
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 vs distal).

Results: Of 17380 pts undergoing FFR measurement: a) 2781 (16%) pts presented lesions with FFR in the gray zone; b) 1459 fulfilled the inclusion/exclusion criteria and were included in the present analysis: 449 treated with revascularization (revasc) and 1010 with medical therapy (MT). Clinical characteristics were similar among pts treated with revascularization or MT, except for male gender. Diastolic dysfunction, NYHA classes, overall mean heart rate and smoking history were higher in the revasc group (p<0.0001). In pts with an FFR between 0.70 and 0.75, MACE’s were more frequent after MT than after revasc (11 [21%] vs 5 [12%], respectively, p=0.026). In an pts with an FFR between 0.81 and 0.85, MACE’s tended to be less frequent after MT than after revasc (11 [21%] vs 5 [12%], 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 paralleled by an increase in overall mortality (p=0.032).

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 apanes 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). Beyond a ‘passive’ component due to the increased left ventricular pressure, an “active” component due to pulmonary vasculature reactivity may be present. The mechanism behind pulmonary vasoconstriction being not fully understood, we hypothesized that central apneas (Cheyne-Stokes respiration – CSR) through chemoreflex stimulation may contribute to PAH in HF.

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

Results: Eleven patients (20%) showed significant CSR, as defined by a 24-hour apnea/hypopnea index >15. HF patients with CSR, compared with patients with normal breathing, presented with higher systolic arterial pulmonary pressure (SBPAP, 15.9 mmHg, p=0.01), with no difference in systolic and diastolic function. Furthermore, patients with central apneas also presented with enhanced HRV (median 0.79, interquartile range -0.62–1.27 vs 0.43, OR 0.19–0.69 L/min, p<0.05) and HCVR (1.18, 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 ng/L, p<0.001), sPAP was indeed correlated with HR (R=0.29, p<0.001) and norepinephrine (R=0.29, p<0.001). Other heart failure medication and endoventricle ejection fraction (≥75 bpm) 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 Ends HR ≥75 bpm (p<0.05 for differences).

Conclusions: IR remains statistically significant predictor for in-hospital mortality, increased apoptotic-derived EMPs labelled as CD144+/CD31+/annexin V+ and CD31+/annexin V+ microparticles. Therefore, HOMA-IR (OR=1.10, 95% CI: 1.05–1.17, p=0.032) and CD144+/CD31+/annexin V+ EMPs. Using C-statistics for Models with HOMA-IR, ENOS-derived apoptotic and activated microparticles were phenotyped by flow cytometry.

Results: These were not significant differences between both cohort patients in EMPs labelled as CD144+/CD31+, CD144+/annexin V+, and CD62E+ microparticles. No significant correlation of increased HRV and EMPs concentrations were observed in subjects with CHF and 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 (EMPs) in patients with CHF.

Methods: The study retrospectively involved 300 CHF patients aged 48 to 62 years who were underwent multipal 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. Endoventricle ejection fraction <50% and any revascularization) up to 5 years. Data were also analyzed according to their lesion location (proximal vs distal).

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 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 heA트 failurE). Data were collected from February to June 2012 by 793 cardiologists across Germany. Data are 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±10 years, 63% male, 87% in NYHA class II or III, atrial fibrillation (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 (≥75 bpm). 42% of the study population had a HR of ≥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 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 non-diabetic patients with chronic heart failure
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Background: Increasing attention has been paid to insulin resistance (IR) as a key mechanism for the development of chronic heart failure (CHF) 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 (EMPs) in patients with CHF.

Methods: The study retrospectively involved 300 CHF patients aged 48 to 62 years who were undergone multipal 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.

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

Methods and results: A new mouse model that over-expresses human LOX was generated by conventional methods. Transgene expression was determined by real-time PCR in 8 different tissues including aorta, heart, kidney, white adipose tissue, liver, and brain. The maximal expression of human LOX was found in aorta followed by heart and WAT. Neither the expression of endogenous LOX nor that of other LOX-like (LOXL) isoforms was modified by transgene expression in aorta, heart, kidney, or WAT. We tested the impact of LOX over-expression on cardiovascular remodeling in TgLOX mice and their wild-type (WT) littermates after chronic infusion with Ang II (1.4 μg/kg/min) or saline by using osmotic minipumps (n=10 per group). Ang II-induced aortic diameter dilation studied by echography was similar in TgLOX and WT mice after Ang II infusion. However, the mortality rate due to aortic rupture was higher in WT mice (20%) compared to TgLOX mice (0%). Cardiac function was evaluated by echocardiography. We observed that Ang II infusion decreased ejection fraction (EF) and fractional shortening (FS) in TgLOX mice, while they were augmented in WT mice. A stronger hypertrophic response induced by Ang II was observed in TgLOX mice as evidenced the increased LV mass and left ventricle posterior wall (LVPW) thickness in diastole and systole and the higher HW/BW ratio compared with WT mice. Accordingly, the left ventricular inner diameter (LVID) in diastole and systole 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-HEMC in both transgenic and WT mice. The values of cardiac output and stroke volume remained similar in both groups. Although overexpression of LOX (the Ang II-induced expression of pro-inflammatory (Emr-1, IL-6, Mmp-9) and fibrosis-related (Serpin-1, Col-1α1) 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 in patients with resistant hypertension.

Methods: A total of 1052 participants from Ibaraki hypertension assessment trial multi-center registry treated for RH with (n=195) or without RH (n=800) were followed up for 4±1 years. RH was defined as uncontrolled hypertension (≥ 140 mmHg for systolic BP or 90 mmHg for diastolic BP) despite treatment with three or more anti-hypertensive medication classes, or controlled hypertension treated with four or more anti-hypertensive medication classes. Major adverse cardiovascular events (MACE, a composite of acute coronary syndrome, stroke, and all-cause mortality) and annual BP control were compared between the RH and non-RH groups.

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. 77.7% at 1 year, p=0.001; 38.9% vs. 31.0% at 2nd year, p=0.081; 36.1% vs. 25.5% at 3rd year, p=0.037; 35.1% vs. 25.5% at 4th year, p=0.040; 32.1% vs. 22.3% at 5th 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=0.032). Multivariate analyses adjusted for age, however, revealed that independent risk factors for MACE were uncontrolled hypertension at the 1st year (adjusted HR 2.5, 95% CI 1.3–4.7; p=0.004) and higher level of serum creatinine (adjusted HR 2.2, 95% CI 1.1–4.5; p=0.030), but not RH. Subgroup analysis showed that a risk for MACE in RH group was increased by female gender (adjusted HR 6.8, 95% CI 1.2–38.2; p=0.030) 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 uncontrolled hypertension during follow-up.

P1372 | BEDSIDE

Arterial hypertension, endothelial microparticles, and endothelial dysfunction

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Background: Membrane microparticles (MPs) are submicron membrane vesicles 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 effect of conventional treatments on these processes is unknown.

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 mechanical characteristics of the arterial system in healthy subjects (n=10), patients with isolated arterial hypertension (n=8), patients (n=10) with CAD and arterial hypertension (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 patients with stable CAD.

Results: As compared to matched healthy controls, patients with arterial hypertension 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±0.9%). 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), respectively. 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 be a marker of endothelial injury but may also induce endothelial dysfunction.

P1373 | BEDSIDE

Guideline adherence and clinical outcomes in hypertensive crises

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Background: A guideline for the management of hypertensive crisis was published in The Netherlands in 2010, providing diagnostic and therapeutic state-
P1374 | BEDSIDE
Blood Pressure control, presence of depressive symptoms and clinical outcomes at 4 years in patients with cardiometabolic disease
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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 phenomenon”. Comorbid depression is common in these patients and associated with poor prognosis; with substantial evidence that depression may be associated with lower BP control. 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 for survival analysis.

Results: Out of 35537 patients, 2068 (5.8%) had at least one vascular event during 4 years follow up. Depression (defined as ≥ HADS-D=7) had a significant interaction with SBP (p=0.04) and DBP (p=0.01) in predicting a new vascular event. In the sub-group analysis based on SBP control categories, patients with uncontrolled SBP and depression had a higher risk of a new vascular event ( Hazard Ratio HR 1.38; 95% Confidence Interval (CI) 1.14–1.67, p<0.001) compared to those with uncontrolled SBP but without depression. Similarly, patients with tightly controlled SBP and depression had a higher risk of a subsequent vascular event (HR 1.42; 95% CI 1.17–1.71) compared to those with tightly controlled SBP and without depression. 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 values, 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.

P1375 | BEDSIDE
Mechanisms and predictors of sudden cardiac death
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Introduction: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is associated with sudden death risk, however its diagnosis remains challenging. We aimed to assess whether vectorcardiographic (VCG) parameters specific to the right heart would help to differentiate ARVC with otherwise normal ECG’s from control subjects.

Methods: 12-lead resting ECGs from 115 patients meeting Task Force 2010 definition criteria were assessed. 52 (age 41±13.9 years, 64% males) did not fulfill degradation or repolarization criteria and were compared with age- and gender-matched control subjects (n=52, age 42±16 years, 63% males). A 3-dimensional spatial QRS-T (QRS-T) angle, a right-sided adjusted spatial QRS-T (RT SGRS-T) angle and a root mean square of both left and right sided depolarization (ωQRS) were assessed along with conventional QRS duration (QSRd), corrected QT interval (QTc) and PR duration.Right side adjusted parameters were calculated from the pseudo orthogonal lead system based on the leads V1, V5 and II and which utilized specific maximum QRS voltages into their calculations (ie. R-wave of V1, S-wave of VI).

Results: All parameters tested significantly differentiated those with ARVC and normal variant ECG’s from control patients (p<0.05). The right-sided QRS-T angle and right-sided QRS-T root mean square best differentiated the two sets of patients. RMS values of the RT SGRS-T and P wave analysis ischemic EF >75% and 14±8.5±26.2mV vs 9±4±3±2mV (p<0.01). Sensitivity and specificity for the right spatial QRS-T angle at a cut-off of 70.8 degrees and 86.5±26.8mV gave sensitivity and specificity for ARVD with normal variant ECG of 69.2% and 94.1%, respectively and 57.7% and 94.1% for the right sided QRS-T angle and right-sided root mean square.

Conclusion: ARVC disease process may lead to development of subtle ECG abnormalities that can be distinguishable using right-sided VCG markers better than the spatial QRS-T angle or other traditional ECG parameters. Right-sided VCG parameters allowed correct identification of ARVC patients in a subgroup of patients with normal variant ECGs. Larger validation studies are warranted including whether these parameters have value for early detection of disease progression.

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±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 [C.I]: 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 (QFRS) 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. QFRS during RV pacing was defined as the presence of >2 notches on the R/S 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: 345 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 QFRS was observed in 159 subjects in any myocardial segment. On multivariate analysis RV pacing-induced QFRS was associated with higher mortality and appropriate ICD therapies. On multivariate analysis RV pacing-induced QFRS was associated with a higher total mortality (p<0.01, HR 4.0, 95% CI 2.1–7.6)
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: +28 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). 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 expression 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 ERP and high-grade NSVT and additionally increased risk 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.
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.

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 were obtained from a prospectively recorded nationwide, population-based registry of out-of-hospital cardiac arrest (OHCA) and patients were divided into a monophasic (n=943) or biphasic (n=6,866) waveform defibrillator cohort. The primary endpoint was 1-month favourable neurological outcome (cerebral performance category scale, category 1 or 2; CPC 1–2) and the secondary endpoint was 1-month survival after cardiac arrest.

Results: The rates of 1-month survival and 1-month CPC 1–2 were significantly higher in the biphasic waveform defibrillator cohort than in the monophasic waveform defibrillator cohort (29.9% vs. 24.9% and 20.2% vs. 15.7%, all P<0.01, respectively). Multivariate logistic regression analysis using 10 prehospital confounding variables showed that biphasic waveform defibrillation was significantly associated with improved 1-month survival (adjusted odds ratio [aOR] 1.36; 95% confidence interval [CI], 1.15–1.61) and 1-month CPC 1–2 (aOR 1.43; 95% CI 1.17–1.75). In the multivariate logistic regression model for subgroup analyses, significant benefits of biphasic waveform defibrillator use for 1-month survival and 1-month CPC 1–2 were found with collapse-to-first-shock delivery time <10 minutes (aOR 1.34; 95% CI 1.12–1.60, aOR 1.48; 95% CI 1.20–1.84, respectively).

P1383 | BEDSIDE
The Efficacy of electrical therapy using biphasic AEDs in the 2010 CPR guidelines for Patients with Out-of-Hospital Cardiac Arrest Due to Ventricular Fibrillation
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Background: The 2005 guidelines for CPR with electrical therapy recommended a single shock instead of 3-shock sequences recommended in the 2000 guidelines. The 2010 guidelines stressed that it is necessary to improve CPR quality. Moreover, there was insufficient evidence to recommend any specific biphasic waveform. We compared the effects of electrical therapy based on the three guidelines.

Methods: From the data of the All-Japan Utstein Registry, a prospective, nationwide, population-based registry of out-of-hospital cardiac arrest (OHCA), we included adult patients who had bystander-witnessed OHCA due to cardiac etiology and in whom shockable arrest was recorded as an initial rhythm. Study patients were divided into three groups based on the different CPR guidelines: 3-shock protocol in the 2000 guidelines (2000G), 1-shock protocol in the 2005 guidelines (2005G), and 1-shock protocol in the 2010 guidelines (2010G). The primary endpoint, favorable neurological outcome at 30 days after OHCA, was compared between using biphasic AEDs and monophasic in the three groups.

Results: The 17,005 patients met the inclusion criteria (figure). The figure shows the comparison of favorable neurological outcome between using biphasic AEDs and monophasic in the three groups. Adjusted odds ratios for favorable neurological outcome were 1.5 (95% CI, 1.3 to 1.7) after biphasic AEDs, and 2.2 (95% CI, 1.9 to 2.5) after the 2005G group and the 2010G group as compared with the 2000G group, and 1.6 (95% CI, 1.3 to 1.8) after biphasic AEDs and 1.2 (95% CI, 1.1 to 1.3) after the 2010G group as compared with the 2005G group.

Conclusion: The majority of MVP and SCD subjects in this cohort had biphasic biphasic AEDs and frequent VFVs, 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 resuscitation in the Greater Paris Area.

Results: Among the 11,420 OHCA, 4,333 (38%) were women. Compared to men, their survival rate till hospital admission was lower (18% vs. 26%). and they had a lower rate of angiography procedures by OHCA (2% vs. 6%) and by survivor till hospital admission (40 vs. 60%). When angiography was performed, it was less often followed by angioplasty (26 vs. 36%).

Prognosis and management by gender

<table>
<thead>
<tr>
<th>Overall</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of OHCA (n)</td>
<td>11,420</td>
<td>7,068</td>
</tr>
<tr>
<td>Alive at hospital admission (%)</td>
<td>23.07</td>
<td>26.26</td>
</tr>
<tr>
<td>Angioplasty per OHCA (%)</td>
<td>54.06</td>
<td>59.66</td>
</tr>
<tr>
<td>Angioplasty per survivor (%)</td>
<td>4.26</td>
<td>5.71</td>
</tr>
<tr>
<td>Angioplasty per survivor (%)</td>
<td>18.49</td>
<td>21.75</td>
</tr>
<tr>
<td>Angioplasty per angiography (%)</td>
<td>34.19</td>
<td>36.45</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.
Conclusions: In witnessed OHCA patients with an initial shockable rhythm, biphasic waveform defibrillation was significantly associated with improved 1-month survival and 1-month neurological outcomes compared to the outcomes with monophasic waveform defibrillation.

P1385 | BEDSIDE
ADR2 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 ADR2 gene coding for the β2 adrenergic receptor is associated with sudden cardiac death (SCD) in heart failure.

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

Methods: We recruited 349 patients between 2008 and 2013 during the prospective MAP-IDM study. 213 patients who experienced primary VF (cases) were compared to 181 patients with STEMI but without VF (controls). None of the patients had other cardiac history. Patients were genotyped for the ADR2 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 ADR2 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/Gln cases was twice faster than in the Gln/Glu and Gli/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 (spring/summer: 87±110 min; P<0.05).

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

P1386 | BEDSIDE
AKAP9 mutations identified in young patients with idiopathic ventricular fibrillation or polymorphic ventricular tachycardia

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Background: A-kinase anchoring protein 9 (AKAP9) is a member of a large AKAP family, which recruits signaling molecules and presents them to down-stream targets to achieve efficient spatial and temporal control of their phosphorylation state. In heart, AKAP9 is known to recruit protein kinase A and protein phosphatase 1 in regulating IKs. AKAP9 mutations are causative for long QT syndrome. Right ventricular (RV) conduction delay has been associated with long QT syndrome. The last mutation (c.11135G>C, p.I2287V) was a 19-year-old boy who suffered VF after running and was successfully resuscitated by AED. He had a syncopal episode at the age of 12 years. On 12-lead ECGs of the 5 patients, AKAP9 mutations were identified in young patients with idiopathic VF and PVT, especially in the young, suggesting new insights on the mechanisms underlying juvenile fatal arrhythmia.

Purpose: To identify 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.

Methods: We enrolled 27 cases in the present study. AKAP9 mutations were detected by Sanger sequencing or amplicon-based targeted next generation sequencing.

Results: AKAP9-M1311K had several episodes of syncope, and PVT was recorded after urination during Holter recording. A 25-year-old woman with AKAP9-I2287V lost consciousness after lunch. After admission, PVT was recorded on ECG monitoring. The forth mutation (c.9253T>G, p.D3986G) 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, PR, QT and QTC intervals and QRS durations were within normal range. Among the VF and PVT patients, AKAP9 mutation carriers were significantly younger than non-carriers (mean age, 17±6 years vs. 38±19 years, P<0.001).

Conclusion: We identified 5 AKAP9 mutations which might be associated with idiopathic VF and PVT, especially in the young, suggesting new insights on the mechanisms underlying juvenile fatal arrhythmia.
Clinical Electrophysiology, Frankfurt am Main, Germany; 2 McMaster University, X. Vinolas5, J. Neuzner 6, M. Glikson 7, J. Wang8, J.S. Healey2 on behalf of RV conduction in males.

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, homoyzgous T allele carriers of C1236T (HR 1.90; 95% CI 1.09;3.30; allele frequency 0.43) and C3435T (HR 1.72; 95% CI 1.03;2.87; allele frequency 0.43) had a significantly increased risk of SCD in a recessive model. Interaction between the ABCB1 polymorphisms and digoxin use was significant for C1236T (p=0.04) and G2677T (p=0.03) in the age and sex adjusted model.

Methods: In this study, we showed that in digoxin users, homoyzgous T allele carriers of the ABCB1 gene had an increased risk of SCD compared to digoxin users with none or one T allele. This implies that the ABCB1 genotype modifies the risk of cardiac digoxin toxicity. If these findings can be replicated in an independent cohort, testing ABCB1 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.

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

P1390 | BENCH
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 pathogenic mechanisms are not well understood.

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

Results: In ARVC/D, compared to dilated cardiomyopathy (DCM) and controls, we found significantly increased mRNA levels of the desmosomal molecule desmoglein-2 (ARVC/D vs. DCM/control: p=0.006;0.001) and plakophilin-2 (ARVC/D vs. DCM/control: p=0.01/0.004), of the proapoptotic molecule PERP (ARVC/D vs. DCM/control: p=0.008/0.008), of the proadipogenic molecule carnitine-palmitoyltransferase-1b (CPT1B) (ARVC/D vs. DCM/control: p=0.05/0.008) and calcium channel associated molecule phospholamban (ARVC/D vs. DCM/control: p=0.006/0.002). 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: We demonstrated that a previous history of malignant events was associated with longer RVED's. Our findings supported the RV conduction delay mechanism behind BS and demonstrated for the first time that the predominant malignant male Brugada phenotype might also be the result of a more delayed mechanism behind BS and demonstrated for the first time that the predominant RV conduction delay mechanism.
Hospital of Getafe, Getafe, Spain; 2 University Hospital of Fuenlabrada, Madrid, Spain.

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 variants were 32% and 97%, respectively.

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 ≥55ms) and were compared with 32 first degree relatives (age 36.7±13.4 years, 58.3% males). The angles encompassing the down-slope and up-slope of the S-wave were measured in V1 and V2 using a protractor.

Results: The S-wave angle inV2 significantly differentiated ARVC with normal variant ECG patients from family members who do not meet 2010 taskforce criteria (p-values 0.015). Utilizing a V2 S-wave angle of 11 degrees as the upper limit of normal cut-off value, the sensitivity and specificity for ARVC with normal variant was 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.

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 each Spanish province and second stage units were 20 randomly selected persons drawn from each 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 (0.02%), both were women, 55 and 54 years old. – Type 2: ten cases (0.11%), nine of them were males, mean age 52.2 years old. For QTc analysis we excluded individuals with left bundle branch block and individuals without sinus rhythm. We analyzed data from 7,889 patients. 52.5% were women, mean age 58.3 years. These are our 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.

Differences in risk factors and outcome of cardiac arrest in southern Spain 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=30447, baseline examination 1991–1996, age 58±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 (1.34–2.8) (P<0.001)). Civil status and level of education were significantly associated with CA in any of the groups. No midlife risk factors differed significantly with regards to survival after CA but presence of shockable rhythm at the time of CA and in-hospital CA were associated with better survival-to-discharge rates.

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.

Sudden cardiac death and channelopathies and cardiomyopathies

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Background: Hypertrophic cardiomyopathy (HCM) remains the most common cause of sudden death (SCD) in the young. Two main mechanisms are postulated: LV hypertrophy and late gadolinium enhancement (LGE) is independently associated with an increased risk of SCD events. Our aim is to establish the relation between LGE extension and the novel SCD risk-prediction model.

Potential role of quantitative contrast-enhanced cardiovascular magnetic resonance for the evaluation of sudden death risk in intermediate-risk patients with hypertrophic cardiomyopathy

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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 every 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: 59 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). 5 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 inherited 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±18 bpm vs. 56±14 bpm, p=0.29), while maximum HR was lower on nadolol (120±20 bpm vs. 139±24 bpm, p<0.001). At exercise, incidence of arrhythmias was lower on nadolol (60%) than on metoprolol SR (96%) and no medication (92%) (both p<0.01). Also severity of arrhythmias was lower on nadolol than metoprolol SR (score 1.2±1.3 vs. 2.4±0.9, p<0.01) and no medication (1.2±1.3 vs. 2.5±1.2, p<0.01) (Figure). Arrhythmic score from Holter was lower on nadolol than no medication (0.8±1.0 vs. 1.2±1.0, p=0.03).

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

P1398 | BEDSIDE

Deletion of SCN5A and SCN10A detected using NGS as a probable cause of Brugada syndrome. Results of a copy number variants cohort screening

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Background: Brugada syndrome (BS) is a genetic channelopathy associated with risk of sudden death, affecting predominantly young males and displaying autosomal dominant inheritance. SCN5A and SCN10A are the genes most commonly associated with BS in the literature. A responsible mutation is identified in only about 30% of BS patients with the rest remaining genetically undetermined.

Copy number variants (CNVs) are the major type of structural variation in human genome and are important sources of human genetic and phenotypic variation. CNVs have been associated to predisposition to human diseases. Up to date there are no described associations between CNVs and BS. Next generation sequencing (NGS), unlike traditional Sanger sequencing, allows the detection of structural variants. Our aim was to explore the presence of CNVs in a cohort of BS patients who were sequenced using NGS.

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

Results: Fifty-nine patients were screened. An associated mutation was found in 25% of probands and 15% of the identified variants were located in SCN5A. One CNV was found in a proband (1% of the probands, 3% of those with definite diagnosis, 6.6% of the mutations found). The CNV found is a heterozygote deletion of the whole SCN5A and SCN10A genes.

The patient is a 13 years old male who was referred due to typical atrial flutter after exercise. He showed a Brugada type 1 pattern on the ECG. There is no family history of sudden death. Electrophysiological study (EPS) was performed without inducible ventricular arrhythmias which were not inducible with EPS. The patient is currently under exercice beta blocker treatment and is asymptomatic. We screened 59 patients with the rest remaining genetically undetermined.

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. NGS analysis should be performed routinely during genetic tests for BS.

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VENTRICULAR ARRHYTHMIAS

P1399 | BEDSIDE

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

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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 ischemic heart disease who underwent RFCA were retrospectively analyzed. We screened 10 patients, 10 VTs originated from left Purkinje system and the other was scar-related VT. These Purkinje-related VTs were fast (mean cycle length, 287±54 msec) and could be eliminated by RFCA targeting diastolic Purkinje potentials during VT. During the mean follow-up of 42±42 months, 5 patients (26%) experienced VT or VF recurrence; however, there was no VF storm. In 3 patients with VF recurrence, VF only occurred within five days after RFCA session and spontaneously disappeared. Two other patients experienced an ICD shock therapy for VF and incessant nonsustained polymorphic VT and received additional medical therapies. While there was no arrhythmic death during the follow-up periods, there were 2 deaths for heart failure and 4 deaths for non-cardiogenic causes.

Conclusions: VF ablation in patients with ischemic heart disease resulted in good long-term outcomes in the majority of the patients. However, 32% of the patients had the concomitant Purkinje-related monomorphic VT; moreover 31% of the patients experienced the newly occurrence of monomorphic VT which did not exist before VF ablation. These Purkinje-related monomorphic VTs were also successfully suppressed by RFCA to the Purkinje system, and possibility of conversion from VF to monomorphic VT should always be kept in mind.
P1400 | BEDSIDE
Early repolarization pattern: a marker of increased risk in patients with catecholaminergic polymorphic ventricular tachycardia
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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 prevelance 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 defined as “notching” or “slurring” at the terminal portion of QRS with ≥0.1 mV elevation at least in 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 interolateral leads in 5 (10%) patients. All patients with ERP were symptomatic at presentation (23 of 23 pts with ERP vs 19 of 28 pts without ERP, p=0.003). Syncope was also more frequent in patients with ERP (18 of 23 pts with ERP vs. 11 of 28 pts. without ERP, p=0.005).

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

P1402 | BEDSIDE
Ventricular tachyarrhythmia during pregnancy in patients with structural heart disease: results from the ROPAC registry
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Background: The occurrence of ventricular tachyarrhythmia (VTA) during pregnancy may have devastating effects on both mother and baby, but literature is scarce. We investigated the incidence, onset, predictors and outcome of VTA in pregnant women with heart disease.

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

Conclusions: VTA occurred in 1.4% of pregnant women with structural heart disease and presented mainly in the third trimester. Cardiomyopathy and NYHA class ≥1 were independent pre-pregnancy predictors. VTA during pregnancy has impact on preterm birth and low birth weight rates.

P1400 | 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 length (CL), 1–3 extras, 2 pacing sites) and LV endocardial electroanatomical 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>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/patient (IQR 2–5) were induced. Mean SA was 71±39cm² (32±13% of total LV area), DS 32±29cm² (39±22% of SA), and BZ 38±21cm² (61±22% of SA). LP were present in 79% of the pts (12±15/pat, mean duration after offset QRS 57±27ms) and vLP in 33%. The presenting VT CL was >320ms in 56 pts (67%, mean CL 420±64ms) and <320ms in 27 pts (33%, mean CL 290±72ms). Pts with fast VTs had smaller SA (42±10% vs 38±12% of total LVA: 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%; 4.5% vs 17±2% respectively: all P<0.001). Of importance, in 27% of pts with fast VTs no LP were found compared to 4% in pts with VTCL>320ms (P=0.025; no vLP in 82% vs 58%; P=0.013).

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

P1403 | BEDSIDE
Ventricular arrhythmias induced by sodium channel blocker is a risk stratification tool in patients with Brugada syndrome
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Background: There is no evidence to detect high-risk patients with Brugada-type ECG in whom ST elevation was augmented by pilsicainide. The objective was to clarify whether pilsicainide induced ventricular arrhythmias (VAS) and T-wave alternans (TWA) can identify high-risk patients.

Methods: We administered intravenous pilsicainide (1mg/kg) to 273 patients (265 men; 47±13 years of mean age) with Brugada-type ECG (spontaneous type 1 ECG – 179 patients) and evaluated changes of ECG morphology and the occurrence of VAS. Baseline characteristics of them included 13 patients with history of ventricular fibrillation (VF), 88 with history of syncope.

Results: During 94.7±50.6 months of mean follow up, 4 patients died suddenly, 25 patients experienced VF events and 2 patients died from cancer. Intravenous pilsicainide unmasked typical type 1 ST-segment elevation in 77 patients with non-spontaneous type 1 ECG. TWA induced by pilsicainide was observed in 30 patients (11%) but it was not significant predictor for fatal arrhythmic events (sud-
den death (SD), VF, and ventricular tachycardia (VT)). Pilsicainide also induced VAs in 41 patients (15%; 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 PI-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 diluted cardiomyopathy
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Background: Current guidelines assign a IB indication for implanting a cardioverter defibrillator (ICD) in patients with non-ischaemic diluted cardiomyopathy (DCM) who have an left ventricular (LV) ejection fraction (LVEF) <35% and who are NYHA functional class II or III. However, studies have shown that LV function often improves in patients recently diagnosed with idiothetic DCM, and that the incidence of appropriate shocks in this population is low. Thus, the optimal timing of assessment for ICD implantation is uncertain.

Purpose: We aimed to assess whether the indication for ICD implantation changed over time in patients with recent-onset DCM, and the prevalence of serious arrhythmic events in this population.

Methods: 102 consecutive patients referred to our tertiary care hospital with idiopathic DCM, an LVEF < 35% and who were in NYHA class II or III. Device implantations and arrhythmic events were subsequently evaluated at pre-test ECG: type 2 or 3 ST morphology according to the 2° Consensus Conference criteria; r' wave duration ≥0.10 s in V1-V2; QRS duration in V1 ≥0.10 s; QRS duration in V6 ≥0.14 s; QRS r' wave duration in V1-V2; QRS S 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 ≥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).

Results: Seventy-seven patients (91% men, 66.7±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). Endocardial approach in patients with transmural scar was associated with an increased risk of recurrence (hazard ratio 2.78; IC 95% 1.01–7.6; p=0.004).

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.
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.

P1407 | BENCH
Implantable cardioverter-defibrillator in hypertrophic cardiomyopathy patients: what can we expect with new guidelines?
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Sudden cardiac death (SCD) continues to be the most devastating complication of hypertrophic cardiomyopathy (HCM). The new guidelines of the European Society of Cardiology (ESC) define the current standard for estimation of SCD risk as an integral part of clinical management. The aim of this study was to compare the 2014 and 2011 implantable cardioverter-defibrillator (ICD) recommendations in HCM patients (pts), and correlate them with the presence of fibrosis.

Methods: We studied 80 HCM ambulatory pts, in our hospital. All of them had performed cardiac magnetic resonance for late gadolinium enhancement (LGE) evaluation. The recommendation for ICD was assessed using previous (ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy - 2011) and current guidelines (ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy - 2014). SCD risk was calculated by current guidelines. All statistics analyses were performed using SPSS 20.0 version.

Results: The mean age of our population was 50±18 years and 65% were male. The majority of pts were in NYHA class I (71%) or II (27%) and had septal HCM (69%). LGE was present in 65 (82%) pts, mainly in the septum (51%) with a focal distribution. A diffuse pattern was found in a minority of cases (26%). By 2011 guidelines, 51% of pts had a class IIa recommendation for ICD and 49% had no ICD indication (class III). In comparison, by 2014 guidelines, we found much more pts without ICD indication (82%; p<0.001), fewer pts with a class IIa recommendation for ICD (8%; p<0.001) and 10% of pts had a class IIIb indication. HCM SCD risk by current guidelines did not correlate with the presence of fibrosis.

Conclusion: In our population, we found several differences in regarding recommendation for prophylactic ICD between previous and current guidelines. Overall there were fewer pts with ICD indication than before and fibrosis did not correlate with calculated SCD risk.

P1408 | BEDSIDE
N-terminal pro-B-type natriuretic peptide is elevated and strongly associated with higher mortality in comatose out-of-hospital cardiac arrest patients - a TTM substudy
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Background: We hypothesized that elevated N-terminal pro-B-type natriuretic peptide (NT-proBNP), a biomarker of increased left ventricular strain, following out-of-hospital cardiac arrest (OHCA) is associated with higher cardiovascular and overall mortality.

Purpose: In this sub-study of the Target Temperature Management (TTM)-trial we assessed the association between NT-proBNP concentrations, all-cause mortality, and cause of death in patients comatose after OHCA. The TTM-trial reported similar mortality and neurological outcome with targeting either 33°C or 36°C.

Methods: Two TTM-centres participated in the biomarker substudy. Of the 700 patients included, 647 patients (92.4%) had NT-proBNP measured on day 1, 2, and 3 and was stratified into quartiles. Outcome was 180 days-cause mortality and cause of death.

Results: Median NT-proBNP in the 4 strata was 466, 1140, 2298, and 6524 pg/ml.

A significant association with 180-day survival rates (P<0.0001) was found (Figure). In a multivariate model adjusting for age, sex, time to ROSC, lactate on admission, bystander CPR, initial rhythm, creatinine, body mass index, ST-elevation myocardial infarction, and TTM allocation group, the lowest NT-proBNP levels (Q1) was associated with lower mortality (HR=0.53 (0.35–0.82) p<0.01) compared to Q4. Increasing quartiles of NT-proBNP on day 1 was associated with cardiovascular (Q1: 3.1%, Q2: 8.0%, Q3: 12.4%, Q4: 36.4%, p<0.0001) and, to lesser degree, neurological death (Q1: 17.4%, Q2: 27.2%, Q3: 38.3% Q4: 30.3%, p<0.01). Mortality ratio in NT-proBNP Q4/Q1: Neurological 1.7 vs. Cardiovascular 1.1. Similar findings were seen on day 2 and 3.

Conclusion: NT-proBNP is elevated and strongly associated with all-cause mortality and especially risk of cardiovascular death in comatose OHCA patients.

P1409 | BEDSIDE
Genetic screening identifies a high proportion of mutations in patients with idiopathic ventricular fibrillation and sudden cardiac death
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Introduction: Several gene defects are associated with idiopathic ventricular fibrillation (IVF) and sudden cardiac death (SCD). The development of NGS-based mutation screening provides a unique opportunity to estimate extensively the spectrum and prevalence of rare variants in genes associated with cardiac diseases.

Methods: Cohort 1 was composed of 75 patients resuscitated from cardiac arrest related to IVF. All patients have undergone a complete clinical cardiac examination including 12 lead-ECG, cardiac echography, coronaryography and exercise test. Cohort 2 was composed of 99 victims of SCD related to ventricular fibrillation younger than 45 years old and without explanation for the SCD at the time of the examination.

Genetic screening was based on the use of the HaloPlex™System (Agilent Technologies) prior to HiSeq sequencing (Illumina). The custom kit covers 163 genes related to IVF. All patients have undergone a complete clinical cardiac examination including 12 lead-ECG, cardiac echography, coronaryography and exercise test.

Results: In cohort 1, the mean age was 36±10 years with a male predominance (52 males, 69%). In cohort 2, the mean age was 37±7 years with a male predominance (76 males, 79%). In cohort 1, we identified 50 probable mutations in 35 patients (47%). In cohort 2, we identified 30 probable mutations in 24 patients (24%).

Conclusion: Our study identified mutations in almost 50% of IVF patients after a complete clinical cardiac evaluation. These results suggest that molecular analysis must be part of the work up in this kind of patients. In young patients affected by unexplained SCD, the molecular analyses are less contributive probably because of a more important percentage of patients affected by ischemic cardiomyopathies.

P1410 | BEDSIDE
Novel camodulin 2 mutation causes unexplained cardiac arrest in two unrelated infants

Background: Calfomulin 1 (CALM1) mutations have been found to cause cardiac arrest in infants at very early age. Underlying etiology described is Long QT Syndrome (LQTS), Calfomalinergic Polymeric Ventricular Tachycardia (CPVT) and Idiopathic Ventricular Fibrillation (IVF). Data about CALM2 mutations are lacking. We present two unrelated children with sudden cardiac arrest and a novel camodulin 2 mutation (Asn98Ser) with a subtle phenotype of LQTS and CPVT.

Methods and results: Two unrelated children aged 4 and 7, who were born to healthy parents, were studied in aplastic cardiomyopathies. In young patients affected by unexplained SCD, the molecular analyses are less contributive probably because of a more important percentage of patients affected by ischemic cardiomyopathies.

Conclusion: Our study identified mutations in almost 50% of IVF patients after a complete clinical cardiac evaluation. These results suggest that molecular analysis must be part of the work up in this kind of patients. In young patients affected by unexplained SCD, the molecular analyses are less contributive probably because of a more important percentage of patients affected by ischemic cardiomyopathies.
a highly conserved across the species residue, and the location in the protein was adjacent to critical calcium binding loops in the calmodulin carboxyl-terminal domain, predicting a high pathogenic effect. In the second case (non survivor, 7 years) it was a de novo mutation, but in the first one parents refused to be studied. Conclusions: Human calmodulin 2 mutations are associated with a life-threatening condition in early infancy. Phenotype can be variable, with a low clinical penetrance. This is the first time for this gene to be associated with CPVT.

BASIC MECHANISMS OF ARRHYTHMIAS

P1410 | 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 PS was constructed to test the hypothesis.

Results: The percentage of RV activated within 5ms decreased from baseline 53±6% to 43±8% during early ischaemia (<20 min), and paradoxically then increased to 59±8% (p<0.001), with more surface breakthroughs and complex activation during late ischaemia (Figure). This phenomenon was abolished if treated with the gap junction enhancer rotigaptide. In the computer model, a 6% reduction in conductivity was sufficient to render quiescent PMJs active. Increasing the fraction of functioning PMJs accelerated endocardial activation, increasing surface breakthroughs and the complexity of activation, matching the experiments.

Conclusion: At baseline, most PMJs are quiescent. Ischaemia-induced closure of gap junction channels causes more PMJs to become functional due to reduced source-sink mismatch. The resultant altered and more complex activation patterns may be pro-arrhythmic as they increase the pathways for meandering wavefronts and the likelihood of wave collision.

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P1411 | BENCH
Circadian variations of myocardial expressions of BMAL1 in regulating the occurrence of ventricular arrhythmia (VA) in CHF.
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Purpose: We sought to investigate the role and mechanism of the CLOCK-BMAL1 in regulating the occurrence of ventricular arrhythmia (VA) in CHF.

Methods: Circadian variations of myocardial expressions of β1-AR and β2-AR in Purkinje cells and BMAL1 were examined. Then, luciferase and ChIP assay were applied to determine whether CLOCK-BMAL1 transcriptionally regulate β1-AR expression. Adenovirus infections were applied to overexpress CLOCK and/or BMAL1 in the guinea pig ventricular cardiomyocytes and the action potential durations were measured. Electrocadiograms of Langendorff-perfused hearts with isoprenaline (ISO). ISO + CGP-20712A (β1-AR selective antagonist, CGP) and ISO + ICI111855 (β2-AR selective antagonist, ICI) at CT3 and CT15 were recorded and VA were induced by PES.

Results: Sham operated animals showed circular oscillations in the expression of β1-AR and CLOCK-BMAL1 (P<0.05), but not in β2-AR (P>0.05). Importantly, the expression of β1-AR and CLOCK-BMAL1 were attenuated in CHF at CT15 (P<0.05). Luciferase and ChIP-PCR analysis revealed that BMAL1 could bind to the enhancer of β1-AR to regulate arrhythmia severity after CHF (P<0.05). Ad-CLOCK and Ad-BMAL1 co-infection resulted in overexpression of β1-AR and a greater incidence of arrhythmic activity in myocytes. During ISO and ISO + ICI infusion, the diurnal variation in response of β-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 affects repolarization of ventricular myocytes and regulated ISO-induced arrhythmogenesis through β1-AR.

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P1413 | BENCH
Fibrillatory 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 cardiomycyte mitochondrial remodelling 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 (Ψm) 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 antibiobin-2 expression, however levels of anti-fibrillatory stress were reduced levels of USA30 suggest possible ubiquitination of Mfn-2. Silencing RNA-induced knock down of Mfn-2 prevented mitochondrial remodelling in response to fibrillatory stress.

Conclusions: Fibrillatory stress induced mitochondrial hyperfusion, increased the frequency of mitochondria:SR contacts, synchronised Ψm to calcium release events and facilitated subsequent stress free rapid activation in atrial cardiomyocytes. This "mitochondrial remodelling" appears to be mediated by Mfn-2. The mechanism(s) and respiratory implications of mitochondrial remodelling remain to be elucidated. Further work is required to determine whether interruption of mitochondrial remodelling is potentially anti-arrhythmic.

Background: Circadian variations of myocardial expressions of β1-AR and β2-AR (P<0.05) were recorded. The expression of β1-AR and β2-AR were attenuated in CHF at CT15 (P<0.05). Luciferase and ChIP-PCR analysis revealed that BMAL1 could bind to the enhancer of β1-AR to regulate arrhythmia severity after CHF (P<0.05). Ad-CLOCK and Ad-BMAL1 co-infection resulted in overexpression of β1-AR and a greater incidence of arrhythmic activity in myocytes. During ISO and ISO + ICI infusion, the diurnal variation in response of β-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 affects repolarization of ventricular myocytes and regulated ISO-induced arrhythmogenesis through β1-AR.

Acknowledgement/Funding: This work was supported by grants from the National Natural Science Foundation of China (No. 8117062 and No. 81470457)

P1414 | BEDSIDE
Attenuation of CLOCK-BMAL1 decreases the occurrence of ventricular arrhythmia in chronic heart failure
Nanjing Medical University, Nanjing, China; People's Republic of China

Background: Circadian rhythms influence the incidence of SCD in chronic heart failure (CHF), however, the underlying mechanisms are not well defined.

Purpose: To investigate the role and mechanism of the CLOCK-BMAL1 in regulating the occurrence of ventricular arrhythmia (VA) in CHF.

Methods: Circadian variations of myocardial expressions of β1-AR, β2-AR and cardiac gene CLOCK and BMAL1 were examined. Then, luciferase and ChIP assay were applied to determine whether CLOCK-BMAL1 transcriptionally regulate β1-AR expression.

Results: Adenovirus infections were applied to overexpress CLOCK and/or BMAL1 in
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 mM Eq K+) followed by K+-deficient (1 mM Eq) 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 Biolab software.

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 not changed by melatonin, however, treatment prevented dephosphorylation and abnormal topology (lateralization) of Cx43.

Conclusions: Our results suggest that acute treatment with melatonin protects against low potassium induced VF in part due to prevention of abnormal expression and distribution of myocardin Cx43.

P1414 | BENCH
Heterozygous plakoglobin deficiency results in increased bifurcental beta-catenin expression
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Background: The cell-cell 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 dilation, gap junction protein connexin-40 (Cx40) 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 and preclinical (beta-catenin) plakoglobin−/− mice.

Methods: Echocardiography on 19–wkd old PG+/− and WT (n=13–15) 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+/− 1.65±0.03mm vs WT 1.65±0.03mm). Decreased PG in PG+/− LV (PG+/− 0.65±0.01 vs WT 0.86±0.01; p<0.05) and RV (PG+/− 0.68±0.01 vs WT 0.83±0.01; p<0.05) and Cx43 in LV (PG+/− 0.55±0.07; RV PG+/− 0.09±0.02 vs WT 0.14±0.02; p<0.05). Electrophysiological investigations showed that inducibility of AF episodes was not significantly different among all groups. Significant more episodes of VTs were inducible in PG+/− mice compared to all other groups (Cx40hetA96S/TAC group inducible 77%, PG+/− mice 88%, WT/TAC 60% and WT/TAC-sham 60%).

Conclusions: 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
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 reentry substrate, propagates atrial and ventricular capture and inhibits 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 neurones of the dorsal vagal motor nucleus (DVMN) project to the heart and protect cardiomyocytes against acute ischemia/reperfusion injury, we now investigated the role of the Cx40A96S mutation in AF associated to hypertensive heart disease and cardiac hypertrophy after transaortic constriction (TAC) operation in the murine heart.

Methods: Investigated groups consisted of mice with Cx40hetA96S/TAC (n=15); WT/TAsham (n=11) and with WT/TAC+ (C40hetA96S/TAC + sham; 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 episodes was not significantly different among the investigated groups (C40hetA96S/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 lasted longer in the TAC operated mutant mice compared to WT (C40hetA96S/TAC group (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 (C40hetA96S/TAC group (69%) versus Cx40hetA96S/TACsham (33%), WT/TAC (29%) and WT/TACsham (9%), 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 diameter electrodes), and paced horizontally (H) & vertically (V) (1–28Hz). For each pacing interval, 2s of unfiltered unipolar Eg (total number analysed ~1.5 million) were characterized in time (duration, amplitude, line length, fractionation score) & frequency (dominant frequency (DF), DF/dv/dt) domain and correlated to fibrosis using a 700μm x 700μm overlaid grid in Fiji (fig A). 20 month old atria underwent optical mapping using di-4-ANEPPS.

Results: Induced AF was rare in isolated atrial preparations. Eg features displayed anisotropy with only one pacing direction showing correlation with fibrosis (fig B). Overall Eg data from each grid confirmed Eg correlation with fibrosis (fig C). APD90 was inversely correlated to Eg duration and fractionation score (r=-0.63, r=-0.66, p<0.01 for both).

Conclusions: Unipolar Egs correlate with fibrosis in one direction demonstrating the importance of fibrosis in tissue anisotropy. Optical mapping reveals fractionated Eg are not summated individual action 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 Kcne3−/− mice

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Abstract P1420 – Table 1. Biophysical properties of hERG channels

<table>
<thead>
<tr>
<th>Temperature (°C)</th>
<th>Tail current density at 20 mV (pA/pF)</th>
<th>The potential of half-maximum inactivation (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>25°C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WT</td>
<td>34.8±4.7 (15)*</td>
<td>−74.2±9.6 (45)*</td>
</tr>
<tr>
<td>G584S</td>
<td>10.1±6.4 (13)*</td>
<td>−47.2±2.4 (17)*</td>
</tr>
<tr>
<td>D609G/WT</td>
<td>10.8±2.5 (10)*</td>
<td>−22.4±2.3 (18)*</td>
</tr>
<tr>
<td>35°C</td>
<td>58.2±8.6 (16)</td>
<td>−94.6±20.2 (18)*</td>
</tr>
<tr>
<td>40°C</td>
<td>72.1±9.6 (16)*</td>
<td>−65.5±3.6 (10)*</td>
</tr>
<tr>
<td>25°C</td>
<td></td>
<td>−31.2±0.6 (2)</td>
</tr>
<tr>
<td>35°C</td>
<td></td>
<td>−43.0±2.6 (10)</td>
</tr>
<tr>
<td>40°C</td>
<td></td>
<td>−54.9±1.8 (8)</td>
</tr>
</tbody>
</table>

*P<0.01 vs TCD at 35°C; †P<0.05 vs TCD at 35°C; ‡P<0.05 vs WT at 25°C; §P<0.05 vs WT at 35°C; ¶P<0.05 vs WT at 40°C.

Rationale: The molecular pathology of atrial fibrillation (AF) remains elusive. KCNEs are a group of Kv channel ancillary subunits that modulate Kv channel function. Mutations in human KCNE3 have been associated with AF.

Objective: We used mice with global Kcne3 deletion to study the molecular pathology of KCNE3-associated AF.

Methods and results: Holter ECG recordings revealed spontaneous episodes of paroxysmal AF in Kcne3−/− mice. Invasive electrophysiology studies demonstrated reduced atrial effective refractory period (AERP). Episodes of paroxysmal AF were also inducible by in vivo programmed electrical stimulation in Kcne3−/− mice. The cellular correlate for AF predisposition was a significant increase in Kv current densities in atrial cardiomyocytes with increased IKs. Kcne3 deletion also resulted in hyoperaldestromonism with adrenal gland zona glomerulosa hyperplasia. Electrophysiological alterations in Kcne3−/− mice were aldosteronedependent and were caused by increased Rab4, Rab5, 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 Kcne3+/+ mice, and reduced spontaneous AF episodes and arrhythmia induction in Kcne3−/− animals.

Conclusions: Kcne3 gene disruption causes AF in mice. The underlying arrhythmogenic substrate for this phenotype is an increase in aldosterone-dependent recycling of Kv1.5 channels via activation of specific Rab GTPases downstream of the Akt/AS160 pathway. The findings uncover detailed molecular mechanisms underpinning a channelopathy-linked form of AF. Furthermore, they highlight the necessity of considering extracardiac mechanisms even in monogenic arrhythmia syndromes.

Acknowledgement/Funding: DFG, Friede Springer Herzstiftung, Fritz-Thyssen-Stiftung.
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 (popdc1-S191F) by TALEN-based gene editing. Homozygotes revealed skeletal muscle biopsies, suggesting that membrane trafficking of POPDC1 may affect the gating properties of the potassium channel TREK1. Membrane localization was reduced, consistent with the ultra-conserved DSPE motif directly involved in cyclic nucleotide binding.

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
Aliiskiren suppresses extracellular matrix genes in atrial fibrillation - a global mRNA profiling in the canine experimental atrial fibrillation model


Introduction: We have previously reported atrial structural remodeling involving the extracellular matrix (ECM) synthesis in a canine model of atrial fibrillation (AF). Aliiskiren, a direct renin inhibitor suppressed AF inducibility and atrial tissue fibrosis; however, the underlying molecular mechanisms remain unclear. In the present study, we analyzed the global responses in mRNA expressions in atria by using 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 and they were divided into 3 groups as follows; 1) pacing control group (n=6): continuous atrial rapid stimulation of 400 bpm was delivered for 3 or 6 weeks without any drug administration, 2) pacing + aliskiren group (n=6): aliskiren (30 mg/kg/day) was orally administered in similarly paced dogs as the control, and 3) sham group (n=3): no pacing and no drug administration. The total RNA was purified and the global mRNA expressions were profiled by Affymetrix 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 periostin 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. RhoA and RhoA exhibited up-regulation in both 3 and 6 week pacing control, and this up-regulation was suppressed in the pacing + aliskiren group, while transforming growth factor-b (TGF-b) did not exhibit a significant difference.

Conclusions: Aliiskiren 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 TSP-1 and periostin via activation of RhoA, which was 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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Background: EHRA recommends the use of implantable loop recorders in patients with infrequent unexplained palpitations (UP). However, there is little published evidence about this topic.

Purpose: We investigated the clinical benefits of using an insertable cardiac monitor (ICM) in patients with UP.

Methods: The observational, multicenter, international INSIGHT XT study prospectively enrolled 1003 patients implanted with an ICM for arrhythmia diagnosis, irrespective of the clinical indication. Remote monitoring was not routinely used. This report focuses on 68 patients whose primary indication for an ICM was UP.

Results: The mean age was 59.6±15.5 years and 57.4% were female. The median follow-up time was 15 months (IQR: 12–24). At baseline, 65% had hypertension, 44% had hypercholesterolemia and 7.4% had diabetes. The stroke risk CHA2DS2VASc score was low to moderate (0–1) in 31%, and high (≥2) in 69% of patients (means SD: 2.4±1.6). Palpitations at baseline were associated with symptoms of presyncope/syncope (50%), chest pain (22.1%), dyspnea (32.4%) and fatigue (14.7%), The median time to first follow-up diagnosis was 4.4 months (Q1-Q3: 1.8–6.5). Fifty-five patients (81%) had at least one arrhythmia detected, among which 91% had recurrent palpitations. Cardiac arrhythmias were ruled out in 13% (n=9) and palpitations remained unexplained in 6%. ICM guided clinical actions included pacemaker implant (13.2%), ablation (2.9%), and initiation/continuation of AAD (63.2%), antplatelets (38.2%) and OAC (14.7%) therapies.

Arrhythmias detected by ICM

<table>
<thead>
<tr>
<th>Arrhythmia</th>
<th>% (number of diagnoses)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation/atrial flutter/brady-tachy syndrome</td>
<td>36.8% (25)</td>
</tr>
<tr>
<td>Sinus arrest/bradycardia</td>
<td>26.5% (18)</td>
</tr>
<tr>
<td>Atrial tachycardia</td>
<td>23.5% (16)</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>22.1% (15)</td>
</tr>
<tr>
<td>Sinus tachycardia</td>
<td>14.7% (10)</td>
</tr>
<tr>
<td>High degree atrioventricular block (2nd–3rd)</td>
<td>8.8% (6)</td>
</tr>
<tr>
<td>Other arrhythmias</td>
<td>28% (19)</td>
</tr>
</tbody>
</table>

Conclusion: The use of an ICM enabled physicians to rule out or identify arrhythmias in 9 out of 10 patients with unexplained palpitations. This resulted in therapeutic and clinical actions in many cases.

Acknowledgement/Funding: Medtronic, Inc
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 wavefront 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 heterogenous with rotors appearing to be dominant subtype. No rotors or sustained focal activity were observed.

P1425 | BENCH
The risk variant rs131433087 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: We carried out an in vitro 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 atrial appendage of 45 patients without atrial fibrillation were genotyped for two risk variants on chromosome 4q25 and ionic currents were measured using perforated patch clamp technique. Comparison of the normal (CC) and the risk variant (CT) of the single nucleotide polymorphism at rs2200733 as well as the GG and CT variant at rs131433087 revealed that the cell size, measured as the cell capacitance, was significantly larger in myocytes from 17 patients with the GT risk variant than in those from 28 patients with the normal GG variant (77±8 vs. 56±5 pF, p=0.02). By contrast, there was no difference between myocytes from patients with GT (n=7) and CT (n=38) variants (62±9 vs. 64±5 pF, p=0.88). Similarly, the frequency of transient inward currents activated by spontaneous calcium release from the sarcoplasmic reticulum was almost 4-fold higher in the GT risk variant than in the normal GG variant (1:41±03 vs. 0.37±0.10 events/min, p<0.001) 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 sarcoplasmic 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=29) 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: −2.63±0.25; CT: −2.74±0.59; GG: −2.88±0.32; GT: −2.68±0.35 pA/pF), its inactivation or its current-voltage relationship.

Conclusions: A risk variant rs131433087 on chromosome 4q25 predisposes human right atrial myocytes to present hypertrophy and increased calcium current density (CC: −2.63±0.25; CT: −2.74±0.59; GG: −2.88±0.32; GT: −2.68±0.35 pA/pF), its inactivation or its current-voltage relationship.

P1427 | BEDSIDE
ST-segment elevation in Brugada syndrome patients is associated with conduction 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 (coved-type ST-segment elevation and a negative T-wave in right precordial leads).

Purpose: We aimed to determine the pathophysiological basis of the ST-segment elevation in BrS-ECG with the use of data from various epicardial and endocardial right ventricular activation mapping procedures in 6 BrS patients and 6 non-BrS controls.

Methods: In 8 patients (2 BrS, 6 controls) with atrial fibrillation an epicardial 8x6 electrode grid electrode (interelectrode distance 1 mm) was placed epicardially on the RV outflow tract (RVOT) prior to Video Assisted Thoracic Surgical Pulmonary Vein Isolation (VATS-PVI). In two other BrS patients endocardial, epicardial RV (CARTO) and body surface mapping (BSM) was performed. In two additional BrS patients we performed decremental pre-excitation of the RVOT during endocardial RV mapping. During VATS-PVI and CARTO mapping.

Results: BrS patients (n=4) showed greater activation delay and more fractionated electrograms in the RVOT region than controls (n=6). The area with ST-segment elevation on the BSM-ECG was anatomically correlated with the area on the RVOT-PVI with the use of data from various epicardial and endocardial right ventricular activation mapping procedures in 6 BrS patients and 6 non-BrS controls.

P1428 | BENCH
Current and expression of HERG mutation L599Sfs*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 HERG protein expression levels and the ubiquitination levels. Immunostaining of the gene-transfected cells was also performed to evaluate the cellular localization of the HERG proteins. We conducted patch-clamp of the cells transfected with WT and A78T genes for the measurement of Ikr. HEK293 cells were co-transfected with A78T mutant gene and either Hsp70, 90, 40, and 27 to investigate whether these HSP family can improve the stability of A78T-HERG protein.

Results: In transfected HEK293 cells, the level of the mature form of A78T-HERG at 155kDa was remarkably lower than that of WT-HERG associated with significant increases in its ubiquitination. There were no changes in the levels in its immature form at 135kDa. A78T-HERG was predominantly localized in the cytosol, whereas WT-HERG was predominantly localized on the plasma membrane. This localization was also supported by the small amplitude of Ikr through A78T-HERG associated with small tail currents. Heat shock for 1 hour significantly increase of mature form of A78T-HERG associated with increase of amplitude of Ikr. It has been also tested whether HSP family could stabilize A78T-HERG. Hsp90, 70 and 27 but not Hsp40 increased the mature form of the A78T-HERG proteins, indicating their stabilization.

Conclusions: A78T-HERG showed the impairment of trafficking to plasma membrane, and was degraded by the ubiquitin-proteasome pathway. Hsp70, 90, and 27 significantly increased the mature form of A78T HERG, and Hsp family might be a potential target in the treatment of LQT2 resulting from A78T HERG mutation.
Pathology and function of conduction tissue in Fabry disease cardiomyopathy

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Background: Cardiac arrhythmias are common in Fabry disease (FD) and may occur in the pre-hypertrophic cardiomyopathy (CM) suggesting an early compromise of conduction tissue (CT). Being FD X-linked, CT may be variously involved in male and female FDCM, affecting CT function and arrhythmogenesis.

Purpose: To evaluate the CT infiltration in patients with FDCM.

Methods: Among 72 pts with endomyocardial biopsy diagnosis of FDCM, 11 (4M, 7F) mean age 54.6±8.2 years, maximal wall thickness (MWT) 20.5±1.7 mm) had CT included in histological specimens and 4 also at electron-microscopy. CT glycosylation was evaluated by lectin histochemistry, immunofluorescent assay, western blotting; currents were observed by whole-cell patch clamp.

Results: Expression of HERG mutant gene L539fs/47−558W was transfected into HEK293 cells. After incubated with dilated K+ channel (K-channel) expression were observed by real-time PCR, confocal laser scanning, immunofluorescent assay, western blotting; currents were observed by whole-cell patch clamp.

Conclusion: HERG mutant L539fs/47−558W channel is dormant presenting no functions. The activation and deactivation gating did not significantly change in WT and heterozygous channels. The prolonged inactivation time and reduced number of inactivating channels improved the availability of the channel. I-V curve showed the HERG in WT group and in WT+L539fs/47 group increased with the K+ concentration. The chronic extracellular low K+ concentration up-regulated the HERG currents in both wild-type and heterozygous mutant, especially in the latter.

Methods: Pediatric patients with genotyped LQTS and healthy age- and sex-matched controls underwent phase contrast MRI to analyze radial (VR) and longitudinal (VZ) myocardial velocities during systole and diastole in LV base, mid, apex. 12-lead and 24-h holter ECG were recorded to assess heart rate corrected QTc duration and arrhythmogenic risk.

Results: We included 9 LQTS patients (4 boys, 5 girls, average age 12.1±1.1 years) and 9 healthy controls (4 boys, 5 girls, average age 10.6±0.5 y, p=n.s.). 7 patients had LQT1 (KCNQ1 mutation), one patient had LQT2 (KCNH2 mutation) and one patient LQT4 (KCN1E mutation). None of the patients has experienced ventricular tachycardia yet and all patients received anti-arrhythmic beta blocker therapy. QTc duration was significantly prolonged in LQTS patients compared to healthy controls. 472±15.9 ms vs. controls, 417±8.1 ms; p<0.01), Heart rate was slightly but not significantly slower in LQTS patients (LQTs, 69±5.1 min-1 vs. controls 82±3.9 min-1).

Using phase contrast MRI, we revealed prolonged time-to-diastolic peak velocities – as marker for duration of contraction and early relaxation – in longitu- 
dinal (VZ) and radial (VR) directions (base, VZ: LQTS, 424.2±13.7 μm/s vs. controls, 476±19.6 μm/s, p<0.01; Vr: 424.2±12.7 vs. 383.9±8.2, p<0.05; Vr: 426.6±13.2 vs. 385.3±19.1, p<0.05, apex, Vr: 431.4±12.2 vs. 395.5±6.9, p<0.05). In addition, peak diastolic velocities were reduced in LQTS patients in LV mid and apex, indicating impaired diastolic relax- 
ation (mid, Vz: LQTS, −8.87±0.75 vs. controls, −10.72±0.50, p<0.05, apex, Vz: −3.74±0.36 vs. −5.39±0.58, p<0.05). This ab- 
normal EPS; extensive in 3 females with atrial and/or ventricular arrhythmias and short HV interval; massive in 4 males with atrial fibrillation and/or ventricular ar- 
rythmias and short HV. Short P-R AH with increased refractoriness was addition- 
ally found in 3 pts with extensive/massive CT infiltration. A male with the shortest 
HV presented infrahassistion block during decremental atrial stimulation. There was no correlation with age, MWT and type of gene mutation.

Conclusion: The antiarrhythmic agent ranolazine also has an antiarrhythmic potential. An antiarrhythmic effect has recently been demonstrated in an animal model of long-QT-syndrome. The present study was conducted to characterize the electrophysiologic effects of ranolazine in an experimental whole-heart model of short QT syndrome as a model for J wave syndromes.

Methods and results: 12 rabbit hearts were isolated and Langendorff-perfused. After obtaining baseline data, pinacidil, an IKATP channel opener, was infused in a single dose (1 μM). Eight ventricular and epicardial monophasic action potentials and a 12-lead ECG showed a significant abbreviation of QT interval (~34ms, p<0.05) and ac- 

tion potential duration at 90% of repolarization (APD90; −31ms, p<0.05). This ab- 

breviation of ventricular repolarization was accompanied by a significant increase of number of APDs. Patients will be randomized to receive 

pinacidil 8 of 12 hearts. In 8 hearts, the heart was perfused with pinacidil (10μM) leading to an increase of QT-interval (~29ms, p<0.05). APD90 (~18ms, p<0.05) and ERP (~28ms, p<0.05) as compared with sole pinacidil treatment. Furthermore, ad- 
mistration of pinacidil led to a significant decrease of spatial dispersion of repolarization (~13ms, p<0.05).

Under baseline conditions, ventricular fibrillation (VF) was inducible by a stan- 
dardized pacing protocol including programmed stimulation and aggressive burst stimulation in 4 of 12 hearts (16 episodes). After application of 1M pinacidil 8 of 

12 hearts were inducible (34 episodes). Additional infusion of 10M pinolinol 

led to a significant suppression of VF. Only one episode could be induced in 1 of the other animals.

Conclusion: In the present pharmacologic model of early repolarization, admin- 
istration of pinacidil led to an increased inducibility of VF due to a reduction of ERP. Additional treatment with ranolazine reversed this effect and demonstrated potential antiarrhythmic properties based on an increase of ERP and the reduction of QT interval. We propose that FDCM is a frequent in male and variable in fe- 
tile due to skewed X-chromosome inactivation; its extensive/massive involve- 
mence causes accelerated conduction with prolonged refractoriness and electrical instability.

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A novel metric quantifies wavetail and wavefront interaction and identifies sites of potential reentrant activation

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Background: Initiation of re-entry depends upon the time interval between the arrival of the premature wavefront distal to the initial region of block and regaining of excitability in tissue proximal to the initial region of block (Re-entry Vulnerability Index (RVI), ms). Locating critical regions susceptible to such unidirectional block has clinical relevance.

Purpose: To 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 when complete re-entry did not occur (bidirectional block). Simulations also showed that phase singularities associated with spiral wave re-entry (and to cluster inside regions of low RVI).

Figure 1

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

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P1434 | BENCH
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 electrophysiology 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 VT/VF in 51 patients [53.1%], recurrent syncpe 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 asynchronous 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 | BENCH
Preserved myocardial viability predicts response to cardiac resynchronization therapy better than targeted left ventricular placement
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Background: Recent studies have demonstrated that left ventricular (LV) lead placement directed toward the site of latest mechanical activation by echocardiography improved outcome in patients with cardiac resynchronization therapy (CRT), therefore attention has shifted back to mechanical dyssynchrony. However 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).

**Conclusion:** Our findings demonstrate that preserved myocardial viability plays a more important role in predicting response to cardiac resynchronization therapy compared to targeted LV lead placement.

**Results:** Among 93 patients, 52 (55.9%) patients. It was noted that 87 of 93 patients (93.5%) had criteria of 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 E wave - a peak early LV filling velocity (p=0.02). Multiple linear regression analysis was used to identify factors associated with the severity of electrical dyssynchrony. Sixty two parameters were analyzed altogether. The severity of electrical dyssynchrony was related to male gender (p=0.004), CAD (p=0.011), ESV, and E wave - early peak LV filling velocity (p=0.02).

**Conclusion:** The incidence of LBBB among patients <70 years of age, and to identify factors associated with the severity of electrical dyssynchrony.

**Methods:** This study included 124 Petite™ 58ERB leads which were 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™ 58ERB leads and to clarify the failure characteristics of pacing leads with a hexafilar coil.

**Methods and results:** This study included 124 Petite™ 58ERB 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™ 58ERB leads, ten lead failures occurred. In seven cases, the lead impedances leaped almost simultaneously 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™ 58ERB leads have a certain reason for electrical dysfunction.
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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Introduction: Identification of atrial fibrillation (AF), even in the absence of symptoms and without 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 implantation and type of lead fixation used.

Methods: We analyzed prospectively the incidence of AHREs >5 min compatible AF and the presence of IBL on CT-scan in patients with dual-chamber CIED and no history of AF attending to time from implantation (<3 months vs. ≥3 months from implantation) and the type of atrial lead used (active vs. passive vs. VDD).

Results: We evaluated 124 consecutive patients (62% men, aged 74±10 years-old) during a mean follow-up of 27±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/ICD/CRT devices (12%). Time from implantation was <3 months in 89 patients (72%) and ≥3 months in 35 (28%), with 30 patients (33%) from <3 months implantation group and 9 patients (11%) at 3 months of follow-up and 28 (31%) over the 3 first months and 14 patients (40%) from >3 months group (41% and 12 patients (34%) respectively) showed AHREs; p=ns. The type of fixation used was active in 64 patients (52%), passive in 41 (33%) and VDD leads in 19 (15%). AHREs were detected in 1 VDD patient (5%) and in 13 atrial lead patients (12%) at 3 months of follow-up and in 6 (31%) and 34 patients (32%) respectively over the 3 first months; p=ns. AHREs were present in 5 passive fixation patients (12%) and 8 active fixation patients (12.5%) at 3 months and in 17 (41%) and 17 patients (28%) respectively after; p=ns. In this population, the prevalence 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 AHRE 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.

Device therapy

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 and without 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 implantation and atrial lead characteristics, time from implantation and atrial high rate episodes compatible with silent atrial fibrillation in study group (35/61 vs 23/57, p=0.08).

Methods: We evaluated 124 consecutive patients (62% men, aged 74±10 years-old) during a mean follow-up of 27±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/ICD/CRT devices (12%). Time from implantation was <3 months in 89 patients (72%) and ≥3 months in 35 (28%), with 30 patients (33%) from <3 months implantation group and 9 patients (11%) at 3 months of follow-up and 28 (31%) over the 3 first months and 14 patients (40%) from >3 months group (41% and 12 patients (34%) respectively) showed AHREs; p=ns. The type of fixation used was active in 64 patients (52%), passive in 41 (33%) and VDD leads in 19 (15%). AHREs were detected in 1 VDD patient (5%) and in 13 atrial lead patients (12%) at 3 months of follow-up and in 6 (31%) and 34 patients (32%) respectively over the 3 first months; p=ns. AHREs were present in 5 passive fixation patients (12%) and 8 active fixation patients (12.5%) at 3 months and in 17 (41%) and 17 patients (28%) respectively after; p=ns. In this population, the prevalence 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 AHRE 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.

Device therapy

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.

There were no differences in basic echocardiographic parameters such as LVEDD, LVSVD, EF, LA. There was a trend towards greater percentage of paroxysmal atrial fibrillation in study group (35/61 vs 23/57, p=0.08).

Conclusions: Long lasting ventricular pacing in patients with SSS increases left ventricle diastolic dysfunction and myocardial fibrosis parameters. This could negatively influence the atrial arrhythmogenesis.

Device therapy

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 interatrial 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 influence 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.
Conclusion: We reviewed all venography cine sequences acquired during implant procedures in the cath lab of our institution between November 2013 and November 2014. We only included studies performed before the first venous access attempt was made. 89 patients were included in the study (PM: 52 pts., ICD/CRT-D: 37 pts.). Implants were performed on pts. left side in 73 and the right side in 16 cases.

Using imaging software, the course of the vein was described by measuring the angulation of the axillary vein and the clavicle relative to the body’s longitudinal axis and the vein’s intersection with the rib cage margin. A virtual needle trajectory was drawn and its overlap with the axillary vein’s course assessed for both methods.

Results: Of the 89 patients analyzed, a fluoroscopy-only guided lateral puncture as described by Burri et al. would have been successful in 55 (62%) of patients, whereas the more medial first rib approach described by Antonelli et al. would have been successful in 64 (72%) of patients. Failure was neither predicted by patient demographics, nor the BMI nor by any signs apparent from the fluoroscopy without venous contrast.

Conclusion: If performed strictly as described, both the lateral and the first rib approach have a relatively high failure rate. Subsequent iterative changes of the needle position increase patient discomfort, the risk of patient injury and of long-term mechanical damage to the lead. On the other hand, venogram-guided puncture of the axillary vein was performed without any complications in all 89 pts. included in this study. Venography is a simple, quick, inexpensive and low-risk procedure. As the course of the axillary vein is highly variable and clinically unpredictable, contrast venography should always be performed before axillary vein puncture is attempted.

P1444 | BEDSIDE Effectiveness of closed loop stimulation pacing in preventing disabling cardiacinhibitory vasovagal syncope. A single-center experience

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Background: Vasovagal syncope (VVS) is a benign disease. However, in rare occasions, cardiacinhibitory 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 (CLS) pacing is effective in the prevention of recurrences of cardiacinhibitory vasovagal syncope.

Methods: Patients with severe and recurrent vasovagal syncope and positive Head Up Tilt Test (HUUT) with significant cardiacinhibition received a DDD-CLS pacemaker (REVISION; YOLOS DR, Biotronik GmbH Co.) and were reviewed. Severere cardiacinhibition during HUUT was defined as bradycardia <40 bpm during >10 seconds or prolonged asystole (>3 seconds). Pacemakers (PM) were implanted if a minimum of 5 syncopal events had occurred.

Results: A total of 18 patients had a DDD-CLS PM implanted (10 males, mean age 49 years, range 27–76). Tilt test was positive in 17 patients and 4 patients had a subcutaneous holter recording implanted. Structural heart disease was present in 2 patients (aortic mechanical 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 HUUT contributes to a major reduction in the risk of subsequent syncope.

THROMBOSIS AND COAGULATION

P1445 | BENCH Oxidative profile of intracoronary thrombi in STEMI patients increases with elapsed pain-to-PCI time

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Background: Distal embolization of intracoronary thrombi can be a complication in patients with primary PCI and myocardial infarction (STEMI), which is associated with impairment of myocardial perfusion and poor clinical outcome. Increasing evidence suggest thrombus composition as a key component for incidence of embolization during primary percutaneous coronary intervention (PCI).

To this respect, we have recently reported that elapsed pain-to-PCI time and hence ischemic time has impact in the composition of STEMI thrombus.

Purpose: The present study was aimed to identify thrombus proteins related to oxidative stress, with a dynamic evolution in relation to pain-to-PCI elapsed time, and with potential relevance to the evolution of the ischemic process.

Methods: STEMI patients presenting for PCI were included in the study (n=28). Intracoronary thrombi obtained during PCI were analyzed by 2D-electrophoresis and MALDI-ToF mass spectrometry. Differential proteomic profiles were identified by comparing early thrombus (<3hours pain-to-PCI) (T3) and aged thrombus with longer evolution (>6hours) (T6) by using the PD-Quest analysis software. In silico analysis of protein function and networks was performed with the Ingenuity Pathway Analysis (IPA) software.

Results: Oxidative thrombus of longer evolution time (>6 hours) presented changes in proteins that are involved in the mitochondrial electron transport chain of the cell and therefore regulate the steady state concentrations of active species. Thus, T6 thrombi showed 4-fold increase in the complex II protein succinate dehydrogenase (p=0.002) and a 3-fold decrease in the mitochondrial membrane ATP synthase, which might turn in the impairment of ATP production and the increase of protons generated by electron transport complexes of the respiratory chain. Besides, thrombi with more than 6 hours evolution showed a significant decrease in proteins, as superoxide dismutase (20fold, p=0.01) and peroxiredoxin-2 (20fold, p=0.01), which are directly involved in eliminating anion and radical oxygen species.

Conclusions: Oxidative thrombus of longer evolution creates an oxidative niche at culprit site that exacerbates vascular and ischemic damage worsening patient outcome.

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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 than those having the ability to produce larger and more active platelets we performed RNA sequencing in megakaryocytes cultured with or without dimethylsulfoxide (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 CDC45, chromatin assembly factor 1α, and MCMs. In contrast, genes that were upregulated in higher ploidy megakaryocytes were significantly enriched for transcripts involved in haemostatic and coagulation pathways including VWF, coagulation factor XIII, thrombin receptor-like 2, PDGFα, thrombospondin 1 and plasminogen activator inhibitor type 1. Furthermore, glycoprotein IIb (part of the fibrinogen/VWF receptor) and tubulin β1 (involved in microtubule changes in platelet release) were both significantly upregulated in higher ploidy megakaryocytes. Both of these genes are specific to megakaryocytes and platelets.

Conclusions: 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.
Conclusion: Primary PCI success rate assessed by cTFC and TMPG is significantly correlated with body mass index (BMI) and CLT and negatively with anaemia presence (decreased red blood cells count - RBC and haemoglobin concentration - HGB) and high density lipoprotein (HDL). Final TIMI perfusion grade was positively correlated with RBC, HGB and tissue plasminogen activator (t-PA).

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Background: Slow reflow after primary percutaneous coronary intervention (pPCI) significantly affects short- and long-term prognosis. It occurs in almost 30% of ST-segment elevation myocardial infarction (STEMI). Many patient- and procedure-related factors influence this phenomenon. However, the impact of coronary thrombus components was not extensively studied.

Methods: Patients were pretreated with acetylsalicylic acid, clopidogrel and placebo-controlled trials systematic review and meta-analysis of randomized placebo-controlled trials. The aim of the meta-analysis was to evaluate the effect of statin therapy on VWF:Ag levels.

Results: The study comprised 50 patients and follow-up of 6 months. ST was the primary endpoint, and adverse cardiac events (death, myocardial infarction and target lesion revascularization) were the secondary endpoints. Results: Seven studies with 2568 patients were included in the present analysis. Diabetes mellitus was present in 22% of the patients. The target vessel was the proximal left anterior descending coronary artery in 46%, with 15% of lesions involving a bifurcation. 25% of lesions were classified as type C, with moderate or severe calcification in 13% and thrombus in 15% of them.

After a mean follow-up of 6.5 months (range 6–12), the rates of any and definite/probable ST were 1.5% (0.7–2.3) and 1.4% (0.6–2.2) respectively, while subacute and late ST occurred in 0.9% (0.2–1.6) and 0.5% (0.2–0.9) of the patients, respectively. MACE occurred in 6.5% (4.7–8.2) of patients, driven by 3.3% (1.7–4.8) rate of target vessel revascularization, 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<0.001) and in those with long lesions (B 0.19: 0.06–0.23; p<0.001), and was reduced by intravascular imaging (B 0.22: −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.

Conclusion: Stent thrombosis reduces von Willebrand factor antigen levels: A systematic review and meta-analysis of randomized placebo-controlled trials

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Purpose: The aim of the meta-analysis was to evaluate the effect of stent therapy on plasma vWF:Ag levels.

Methods: The search comprised PUBMED, Cochrane Library, Scopus, and EMBASE databases up to 31 January, 2015, to identify randomized controlled trials (RCTs) that investigate the effect of stent therapy on plasma WVF:Ag levels.

Results: Random-effect meta-analysis of 21 treatment arms with 1434 individuals revealed a significant decrease in plasma WVF-Ag levels following stent therapy (standardized mean difference [SMD]: −0.54 IU/dl, 95% confidence interval [CI]: −0.87, −0.21; p<0.001). This effect size was robust and removing each of the included treatment arms from analysis did not change statistical significance of the pooled estimate. In subgroup analysis, the greatest effect was observed with simvastatin (SMD: −1.54 IU/dl, 95% CI: −2.92, −0.17; p=0.028), followed by pravastatin (SMD: −0.81 IU/dl, 95% CI: −1.18, −0.40; p=0.035), fluvastatin (SMD: −0.34 IU/dl, 95% CI: −0.69, 0.02; p=0.065), atorvastatin (SMD: −0.23 IU/dl, 95% CI: −0.57, 0.11; p=0.179), with the lowest effect for rosuvastatin (SMD: −0.20 IU/dl, 95% CI: −0.71, 0.30; p=0.431). Overall, the effect size calculated for lipophilic statins (atorvastatin, simvastatin and fluvastatin) (SMD: −0.56 IU/dl, 95% CI: −0.94, −0.19; p=0.003) was greater than that of hydrophilic statins (mavacamtrastin and pravastatin) (SMD: −0.38 IU/dl, 95% CI: −0.76, −0.01; p=0.046). The lowering effect of statins on plasma WVF-Ag levels was greater in the subset of studies lasting ≥12 weeks (SMD: −0.70 IU/dl, 95% CI: −1.19, −0.22; p=0.005) compared with the ones <12 weeks (SMD: −0.34 IU/dl, 95% CI: 0.01, 0.552). Finally, low-intensity statin therapy was associated with a significant reduction in WVF-Ag levels (SMD: −0.66 IU/dl, 95% CI: −1.07, −0.24; p=0.002) while the impact of high-intensity treatment was modest (SMD: −0.28 IU/dl, 95% CI: −0.82, 0.27; p=0.320).

Conclusion: This meta-analysis showed a significant association between plasma WVF-Ag levels and stent therapy, with the largest effect for low-intensity, lipophilic statins administered for at least 12 weeks.
P1451 | BENCH
The safety profile of new cationic dextran heparin antidotes
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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 (Kalaska et al. et al. Eur J Pharmacol, 2012) and Dex40-GTMAC2 and GTMAC3 (Kalaska et al. PLOSOne, 2015, accepted). Our technology is worldwide patented (US20130043516A1; WO2013157967) and could replace an old, immunogenic and hypotensive protamine-based procedure applied during intravascular or cardiac interventions.
Purpose: Aim of the present study was to compare cationically modified dextran and protamine with respect to their efficacy and acute/chronic toxicity.
Materials and methods: Experiments involving 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 direct potential blood clotting (osmotic resistance) of Dex40-GTMAC3 and protamine was measured in whole blood. Blood pressure, heart rate (HR), blood count and histopathology were estimated 1 hour after treatment (administered antidotes contains and blood chemistry were measured in 7, 14 and 28 day 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 (0.2±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±5.7 sec.; p<0.001) prolonged by UFH (300.0±0 vs. 28.9±1.3 sec. in the vehicle treated group; p<0.001), while platelet factor 4 did not. Dex40-GTMAC3 showed no significant acute and chronic toxicity, while Dex40-GTMAC2 decreased blood pressure, HR and changed blood morphology. Dex40-GTMAC3 did not induce hemolysis and did not cause any long-term changes in organs as examined in routine histology.
Conclusion: Dex40-GTMAC3 as a novel, easy to synthesize, potent and safe heparin antidote may become a potential marketable therapeutic.
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P1452 | BEDSIDE
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 is 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 administered patients with RB or WR.
Methods and results: We enrolled 28 consecutive NVAF patients administrated with RB (n=13) and WR (n=15) in this study. Blood samples were collected 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 APTTs (13.4±2.0 vs. 23.4±6.9 sec at 6 AM, 23.4±6.9 sec at 11 AM, 23.4±6.9 sec at 3 PM and 23.4±6.9 sec at 6 AM the next day, respectively, p<0.001) 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±0.4 at 6 AM the next day, respectively, p<0.001) were measured in 28 patients receiving RB or WR. PT-INR was significantly lower than in those for WB. PT-INRs were formed 4 times a day at 6 AM, 11 AM, 3 PM and 6 AM the next day for RB (193.3±75.5 vs. 121.6±50.6 and 174.6±39 vs. 126.1±55.9, 183.2±36.2 vs. 114.7±51.4, respectively, p<0.001) and its value was measured at each time for RB were significantly higher than those for WR. In contrast, the protein C (103.2±19.9 vs. 52.3±11.7% at 6 AM, 121.2±30.3 vs. 55.7±13.7% at 11 AM, 100.2±18.1 vs. 53.1±14.0% at 3 PM, and 104.1±18.2 vs. 51.0±14.8% at 6 AM the next day, respectively, p<0.001) and its value was measured at each time for WR were significantly higher than those for RB. There were significant circadian variation in PT and PT-INR in RB group, but not in the other coagulation assays in both groups.
Conclusion: The protein C and its activity as physiological anticoagulant factor for RB were constantly and significantly kept higher than those for WR throughout the day as opposed to the other coagulation assays. These findings may explain the specific lasting anticoagulant effect of RB, and not WR.

P1453 | SPOTLIGHT
Potential clinical benefits and cost savings associated with inclusion of apixaban in the formulary for treatment of patients with venous thromboembolism
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Background: Budget impact analysis estimates of the likely impact of a new drug on the healthcare decision maker’s annual budget and is generally required before national or local formulary approval or reimbursement.
Purpose: The goal of this study was to assess the impact of apixaban in patients with venous thromboembolism (VTE) on the NHS health care budget in the United Kingdom.
Methods: A model was developed to analyze the impact on 5-year total health care costs of introducing apixaban for acute treatment and secondary prevention in a representative VTE population. Market share projections were based on current market research data, with assumptions regarding future market shares. Clinical effects of apixaban and LMWH/VKA were derived from AMPLIFY, and effects of other NOACs were obtained from indirect treatment comparisons. Cost inputs measured in 2012 values were obtained from published data sources. Outcome measure was the percentage change in healthcare budget comprising pharmacy and medical costs in patients treated over several treatment durations.
Results: Use of apixaban instead of other treatments was predicted to lead to a reduction in recurrent VTEs, major and CRNM bleeds. Model projections if apixaban market share is drawn solely from rivaroxaban were that the total healthcare budget would be reduced by 0.3% to 0.9% in patients treated for 3 months to five years. Drawing market share from LMWH/VKA only, resulted in a change in budget savings of 0.7% and an increase of 4.0% in patients treated for 3 months to five years.
Conclusion: Apixaban is predicted to provide better clinical outcomes, with treatment acquisition costs largely offset by savings in the medical costs in most of the treatment pattern scenarios. 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 (NOACAs) 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 NOACAs 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 aggregation in dabigatran was measured if the administration of dabigatran compared to the measurement before the intake of dabigatran (before: 77±25 vs. on dabigatran: 90±28 AU/min, p=0.0327). Patients receiving rivaroxaban showed no differences compared to the control group (89±32 vs. 84±30 AU/min, p=0.4559).

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Conclusion: This data demonstrates that TRAP induced platelet aggregation is enhanced in cardiac patients taking dabigatran while this is not the case for rivaroxaban.

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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 were due to trauma. Platelet function was measured in a subset of 36 splenectomized patients in whom splenectomy occurred after trauma, and in 7 matched non-splenectomized controls. The response to adenosine diphosphate (ADP), arachidonic acid (ASPI), protease-activated receptor (PAR-4) and thrombin receptor activating peptide 6 (TRAP-6) was tested by multiple parallel-plate impedance aggregometry (Multiplate). Flow cytometry was used to detect circulating monocyte-platelet aggregates (MPA) in whole blood of both groups. We also compared against (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). Multiplate analyses revealed increased platelet activatability in splenectomized patients (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<0.15). 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.

P1458 | BENCH Microvascular obstruction in STEMI patients during pPCI is related to the size of the aspired coronary artery thrombi and pre-PCI Neutrophil Extracellular Trap levels
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Background: Patients with an acute ST-elevation myocardial infarction (STEMI) routinely undergo primary Percutaneous Coronary Intervention (PCI) with thrombus aspiration (T) but microvascular flow can remain impaired (MVO), an important factor in the prognosis of STEMI patients. Coronary thrombi often contain Neutrophil Extracellular Traps (NETs), toxic thrombogenic DNA complexes that are upregulated in pro-thrombotic states and may induce endothelial injury, contributing to MVO.

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

Methods: 30 STEMI patients undergoing pPCI-T without a history of revascularization, kidney or liver failure and known malignancy were enrolled. Arterial blood was drawn pre-and post-PCI and from the culprit artery during T. Thrombi were collected and size and composition was determined. NETs were measured in blood by capture ELISA and in thromb by immunohistochemistry. Angiography was used to calculate corrected thrombolysis in myocardial infarction (TIMI) frame count (cTFC).

Results: Non-parametric testing revealed that length and area (Figure 1) positively correlated with cTFC (p<0.05; p<0.03 resp.). While NETs in thrombi are not related to cTFC, circulating NETs in pre-PCI and post-PCI blood were negatively correlated to cTFC (p<0.01 and p<0.05 resp.). cTFC was not related to age, gender, occlusion site, ischemia duration or toponnin T. Linear regression (R2=0.57 ANOVA p=0.03) revealed that pre-PCI NETs levels and thrombus size were both independent predictors for cTFC (p<0.03; p<0.04 resp.). Leukocytes, ischemia duration or toponnin T levels were not.

Conclusion: Microvascular obstruction in STEMI patients during pPCI is related to the size of the aspired coronary thrombi and pre-PCI NETs levels.

P1456 | BEDSIDE Platelets are permanently activated after splenectomy
M. De Maat1, H. Van Beusekom2 on behalf of CorTAsk Investigators. P1456 | BEDSIDE

Figure 1

Platelets are permanently activated after splenectomy
Deutsche Forschungsgemeinschaft (OL 371/1–1 to Christoph B. Olivier).

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Enhanced in cardiovascular patients taking dabigatran while this is not the case for rivaroxaban.

Conclusion:

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To study NETs in thrombus and circulating blood in STEMI patients in

Purpose:

with advanced atherosclerosis: effects on endothelial function, inflammatory and coagulation markers

Background: It is well established that C-reactive protein (CRP) is a mediator of atherosclerosis and strongly related to coronary artery disease (CAD). In addition, studies have shown that specific polymorphisms of CRP gene are related with mechanisms leading to atherosclerosis.

Purpose: Therefore, we examined the effect of the least studied 3872 A>G (rs1205) polymorphism on inflammatory and coagulation markers as well as on the risk for CAD.

Methods: The study population consisted of 380 patients with angiographically documented stable CAD and 293 controls. The 3872 A>G polymorphism was
determined by PCR and HPY CHIV restriction enzyme. The endothelial function was determined with flow mediated dilation (FMD). High sensitivity CRP (hsCRP) (mg/l) and D-dimers (μg/l) were determined with immunonephrometry, while fibrinogen (mg/dl) with the Clauss method. Interleukin-6 (IL-6) (pg/ml), TNF-α (pg/ml) and sCD40L (pg/ml) were measured by ELISA.

**Results:** We found that the G allele carriers presented with significantly higher levels of all inflammatory markers compared to AA homozygotes both in CARD (IL-6: 3.10±1.36 vs. 2.27±1.77, p=0.0018; TNF-α: 6.19±1.15 vs. 4.88±0.99, hsCRP: 2.31±0.69 vs. 1.92±0.92, p=0.002 for all) and in controls (IL-6: 5.2±2.06 vs. 1.6±0.54, HS-CRP: 1.10±0.49 vs. 0.88±0.65, p<0.001 for all). On the contrary, G carriers, compared to AA homozygotes, had not significant effect on any of the coagulation markers, both in CARD (fibrinogen: 444±132.9 vs. 463±142.6, sCD40L: 2.14±1.79 vs. 1.38±2.51, D-dimers: 3.46±1.67 vs. 1.0±0.1 p<0.001 and in controls (fibrinogen: 380±103.9 vs. 365±72.9, sCD40L: 0.73±1.93 vs. 1.13±1.67, D-dimers: 264±222.9 vs. 312±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 (CARD: 4.15±2.09 vs. 3.76±2.34, p=0.0118, controls: 6.89±2.9 vs. 6.17±2.92, 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 influencing inflammatory mechanisms and endothelial dysfunction.

**P1459 | BEDSIDE**

Plateletcrit and platelet distribution width as predictors of ST elevation myocardial infarction in young patients

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**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%) male), Group 3 as the control group; 112 age-matched controls 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 (8.3±1.0, 8.5±1.1, p=0.022). 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±6.3, p<0.001) and MPV (8.5±1.12 vs. 8.5±0.71, p=0.003) were significantly higher than group 3. At multivariate logistic regression analysis of young and non-young STEMI patients 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 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 MPV, 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 on admission.

**P1460 | BEDSIDE**

Usefullness of platelet indices as predictors of stent thrombosis in ST elevation myocardial infarction


**Introduction:** Platelets especially larger and hyperreactive ones aggravate the formation of intra coronary 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:** Our study consisted of 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 patients were categorized into 3 groups according to MPV, PDW, PCT tertiles, respectively.

**Discussion:** In addition to MPV, other platelet indices PDW and PCT seem to be independent predictors of ST in STEMI. These indicators may utilize risk stratification upon admission of acute STEMI patients.
Therefore we investigated the influence of morphine on platelet inhibition with clopidogrel and prasugrel in patients with primary PCI.

**Methods:** In the ETAMI trial patients with STEMI <12 hours scheduled for primary PCI were randomized to loading doses of either 600 mg clopidogrel or 60 mg prasugrel in the pre-hospital phase. The platelet reactivity index (PRI) was measured with the VASP assay at 2 and 4 hours after intake of the loading doses.

**Results:** A total of 62 patients were enrolled in the ETAMI trial, from these 32 (51%) received morphine in the acute phase. The PRI after 2 hours (50.4 ± 32.7% versus 66.3 ± 22.2%, p < 0.035) and after 4 hours (39.1 ± 27.5% versus 54.5 ± 49.3%, p < 0.05) were significantly lower with prasugrel compared to clopidogrel. The PRI values at baseline and after 2 and 4 hours according to co-medication with morphine are given in the table.

<table>
<thead>
<tr>
<th>Clopidogrel</th>
<th>Prasugrel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine (n=5)</td>
<td>No morphine (n=18)</td>
</tr>
<tr>
<td>Baseline</td>
<td>80.2±11.3</td>
</tr>
<tr>
<td>2 hours</td>
<td>72.8±15.3</td>
</tr>
<tr>
<td>4 hours</td>
<td>59.1±23.1</td>
</tr>
</tbody>
</table>

Mean PRI values.

**Conclusion:** Both with clopidogrel and prasugrel inhibition of platelets is delayed by concomitant administration of morphine at 2 hours after the loading dose. However after 4 hours the influence of morphine is observed only after clopidogrel.

**P1463 | BEDSIDE**

Patients receiving dual antiplatelet therapy and concomitant oral anticoagulation with dabigatran show increased platelet reactivity


**Background:** Patients suffering from atrial fibrillation have an increased incidence of concomitant coronary artery disease (CAD). Following PCI a dual antiplatelet therapy (DAPT) is conducted to prevent in-stent restenosis and CAD progression. As a result of the RELY-trial the oral anticoagulation (OAC) with dabigatran during DAPT is safer than AOC with phenprocoumon. The current guidelines recommend dabigatran as the treatment for patients receiving DAPT with the need of OAC. However, a trend of elevated rates of myocardial infarction (MI) in the dabigatran treatment arm recently raised some concerns.

**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 h and 24 h 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 baseline 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).

Regarding the platelet reactivity following stimulation with ASPI and collagen no changes between the vitamin K-antagonist and Dabigatran group could be observed.

**Conclusion:** The observed trend towards increased rates of myocardial infarction in patients receiving dabigatran deduced from the RELY-trial could be due to elevated platelet reactivity. However, the effect of clopidogrel does not seem to be reduced by dabigatran co-medication.

**P1464 | 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 population based Danish medical registries. In the nested-case control analysis, the Periprocedural DAPT was evaluated by explicit record review for patients with adverse cardiac events (cases) and for control patients matched by age, gender, oral anticoagulant medications, and type of surgery.

**Results:** In the cohort of 22,654 patients treated with DES, we identified 1944 patients (8.5%) who underwent surgery within 12 months. The most frequent types of surgery were cardiac and vascular (40%), abdominal (23%), and orthopedic (13%) procedures. Among surgical patients, 62 (3.2%) had an adverse cardiac event within the first 30 days after surgery. The nested case-control analysis included 62 cases with adverse cardiac events and 207 matched control patients. DAPT was prescribed periprocedurally for 69% of cases vs 76% of controls while 13% vs 15% received a single antiplatelet agent, and 18% vs 9% disrupted both antiplatelet agents periprocedurally. The risk of adverse cardiac events was not associated with the periprocedural DAPT strategy.

**Conclusions:** Cardiac and non-cardiac surgery were common within the first year of DES implantation. Surgery was associated with a relatively high risk of adverse cardiac events within 30 days. Periprocedural compliance to DAPT was much higher than previously reported, which may explain why the risk of adverse cardiac events was not associated with the periprocedural DAPT strategy.

**Acknowledgement/Funding:** TRYG, Knud and Edith Eriksen’s foundation. Aarhus University Hospital, Department Of Cardiology

**PLATELETS AND ANTIPLATELETS THERAPY I**

P1465 | BEDSIDE

The relation between thrombelastography and long-term poststenting ischemic events: 2 years follow-up in East Asian patients after 600mg-dose clopidogrel loading

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**Background:** Recurrent ischemic event occurrence during dual antiplatelet therapy following stent thrombosis, remains a major concern. We sought to determine whether thrombelastography was a good ex vivo platelet function measurement to facilitate risk stratification and personalized antiplatelet therapy.

**Methods:** We investigated the prognostic utility of the strength of adenosine diphosphate (ADP)-induced (MAADP) platelet-fibrin clots measured by thrombelastography in 759 East Asian patients undergoing elective PCI. A 600mg-dose clopidogrel loading was administered on the day before procedure (,<12h). High on-clotplatelet reactivity (HPR) was defined by published consensus criteria. Ischemic and bleeding events were assessed over 2 years.

**Results:** The prevalence of HPR was 36% measured by TEG (n=273). Over all, 58 (7.6%) first ischemic events occurred. Patients with ischemic events had higher MA-ADP (P=0.0001 for all comparisons). By receiver operating characteristic curve analysis, MA-ADP >34mm had the best predictive value of long-term ischemic events, with an area under the curve = 0.79 (95% CI 0.72–0.87, ρ < 0.0001). The univariate Cox proportional hazards model identified MA-ADP >34mm and female as significant independent predictors of first ischemic events at the 2-year time point (P<0.0001). Eleven bleeding events occurred. Receiver

**TEG MA ADP quartiles**
operating characteristic curve and quartile analysis suggests MA-ADP ≤21 mm as a predictive value for bleeding.

Conclusions: The quantitative assessment of ADP-stimulated platelet-fibrin clot strength measured by thrombelastography can serve as a future tool in investigations of personalized antiplatelet treatment designed to reduce ischemic events and bleeding.

P1468 | BEDSIDE

The vasculo-angiogenic and vaso-protective effects of cilostazol in patients with high risk for cardiovascular disease
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Background: We have found that cilostazol may have beneficial effects on endothelial progenitor cells (EPCs) in vitro and can provide vasculo-angiogenic effec-tive in vivo.

Purpose: This study, for the first time, investigated the vasculo-angiogenic effects of cilostazol on EPCs and flow-mediated dilatation (FMD) in patients with high risk for cardiovascular disease (CVD).

Methods: Seventy-one eligible patients (37 received 200 mg cilostazol and 34 took placebo per day for 12 weeks) who had high-risk profile for CVD but without pre-existing CVD were consecutively enrolled in this double-blind and placebo-controlled study. Circulating number and EPCs and in vitro functions were assessed, and plasma biomarkers were measured by enzyme-linked immunosor-bent assay. 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 [percentages: 9.9±6.1 vs. 17.7±6.1%, P=0.002; 8.7±3.0 vs. 15.2±4.8%, P<0.001, respectively, plasma-levels of vascular endothelial growth factor (VEGF)-A165 and FMD significantly increased [72.5 (32.9–120.4) vs. 57.6 (20.0–143.7)%, P=0.002]. There were no significant differences in other parameters and biomarkers between the two groups.

Conclusion: Cilostazol has significantly beneficial effects on mobilization of EPCs with better endothelium-dependent function partly mediated by modifying some metabolic and angiogenic markers in patients with high-risk profile for CVD.

Acknowledgement/Funding: CKUH-10203022; DOH-102-TD-B-111-002; MOHW103-TDU-B-211-113002

P1476 | 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 aspirin and 75mg/d clopidogrel were enrolled in the study. The effect of antiplatelet was assessed by thrombelastography platelet mapping assay (agonist: 20μmol/L ADP), results were recorded as the percentage inhibition of platelet aggregation (IPA). According to the percentage of IPA inhibition, patients with IPA ≥70% were included in the experimental group and patients with IPA <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 rs3737224, A-allele at rs1126458) 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 rs3737224; P=0.0495 for rs1126458).

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 (eNOS) is also expressed in platelets and, through NO production, is able to inhibit platelet aggregation and gregation. 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.

Methods: We enrolled 632 consecutive patients undergoing elective PCI loaded with DAPT consisting of 500 mg aspirin (ASA) plus 600 mg clopidogrel. Blood samples were collected at the time of PCI to: a) genotyping with SNaPshot 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 troponin 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 not 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 with 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).

Conclusion: 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 LIGUID 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. 7.0 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 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 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 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.
Underlying inter-individual variability on cyclooxygenase platelet inhibition. Conclusions: Compared with intravenous LA, oral aspirin showed significantly higher inter-individual variability on cyclooxygenase platelet inhibition. Acknowledgement/Funding: This study was supported by a grant from the Fundación Mutua Madrileña (FMM012).

P1470 | BENCH
Associations of plasma microRNAs with platelet proteins and platelet function
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Objectives: Platelets shed microRNAs (miRNAs). Plasma miRNAs change upon platelet activation. It is currently unclear which plasma miRNAs are of platelet origin and best correlate with residual platelet reactivity in patients on dual anti-platelet therapy.
Methods and results: Next-generation sequencing of small RNAs was performed in platelet-poor and platelet-rich plasma. Selected platelet-related miRNAs were then measured in plasma samples from the population-based Bruneck cohort (year 2000 follow-up). Levels of miR-126, miR-223, miR-24 and miR-21 strongly correlated with plasma concentrations of platelet proteins such as P-selectin, platelet factor 4 and platelet basic protein (rp=0.50–0.63, n=670, p<0.001). Next, platelet-related miRNAs were analysed in plasma of 125 patients with a history of ACS (STEMI, NSTEMI or unstable angina) who have undergone detailed assessment of platelet function 30 days after the acute event, including optical aggregometry using agonists arachidonic acid and collagen, flow cytometry, stimulated phosphoprotein (VASP) phosphorylation assay and VerifyNow P2Y12 assay. Significant positive associations were obtained for miR-126 with the VerifyNow (rp=0.347, n=39, P=0.033) and VASP assay (rp=0.224, n=125, P=0.013). MiR-223 (rp=0.231, P=0.003) and other abundant platelet miRNAs also showed significant correlations with the VASP assay.
Conclusions: Platelets are a major determinant of plasma miRNAs as evidenced by the abundance of platelet miRNAs in plasma and their strong correlation to platelet proteins. Notably, levels of platelet-related plasma miRNAs correlate with platelet function tests in ACS patients on dual anti-platelet therapy.
Acknowledgement/Funding: British Heart Foundation; Foundation Leducq

P1472 | BENCH
Plaque instability and platelet reactivity: 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 tagging 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 aggregation (MA-ADP). The primary endpoint was a composite of cardiovascular death, non-fatal myocardial infarction (MI), stent thrombosis, and ischemic stroke at two-year follow-up after DES placement. The secondary endpoint was the incidence of bleeding events.
Results: The prevalence of post-procedure HPR was 36% measured by TEG (n=53). Overall, 11 (7.5%) first ischemic events occurred. Patients with ischemic events had higher MA-ADP (P<0.0001 for all comparisons). Using multivari- ate 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 ABCB1 C3435T LOF alleles and the post-procedure HPR were independent predic tors 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=0.64).

P1473 | BESIDE
The role of CYP2C19 and ABCB1 polymorphisms on platelet reactivity
under dual antiplatelet therapy
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P1474 | 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-PCI Registry
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Results: Between 2009 and 2012 a total of 6227 patients with PCI for STEMI were included. 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 ABCB1 C3435T 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).
who did not undergo coronary angiography as compared with those who did. Almost one-third of ACS patients are managed without revascularization during the index hospitalization. In this population, a lower use of revascularization therapies employed during hospitalization significantly differ between patients who received coronary angiography compared to those who did not, with unfractioned heparin and novel P2Y12 inhibitors more frequently used in the first group, and low-molecular weight heparins and clopidogrel in the latter group. Duration of P2Y12 inhibitor therapy, determinants of post-discharge bleeding events in ACS 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. HPRPG was considered for ASPi test > 862 AU/min (for ASA) and ADP test values > 417 AU/min (for ADP-antagonists). Fasting samples were obtained for main chemistry parameters and vitamin D levels assessment.

Results: 5,623 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<0.01), 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 HPRPG 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 (r=-0.11, p=0.028). Significant impact of lower vitamin D on HPRPG was observed among the 221 patients receiving ticagrelor, while a less relevant impact was observed with clopidogrel.

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 antplatelet agents.

P1476 | BEDSIDE
Vitamin D levels and high-residual platelet reactivity in patients receiving dual antiplatelet therapy with clopidogrel or ticagrelor
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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. HPRPG was considered for ASPi test > 862 AU/min (for ASA) and ADP test values > 417 AU/min (for ADP-antagonists). Fasting samples were obtained for main chemistry parameters and vitamin D levels assessment.

Results: 5,623 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<0.01), 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 HPRPG 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 (r=-0.11, p=0.028). Significant impact of lower vitamin D on HPRPG was observed among the 221 patients receiving ticagrelor, while a less relevant impact was observed with clopidogrel.

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 antplatelet agents.

P1477 | BEDSIDE
Real world evaluation of 1st and 2nd generation antplatelet and anticoagulant therapy in patients following percutaneous coronary intervention (PCI)

Background: PCI with drug eluting stent (DES) necessitates dual antiplatelet therapy (DAPT). However, DAPT with requirement for anticoagulation remains problematic as duration of triple therapy is undetermined. Moreover, newer anti-platelet agents in conjunction with anticoagulants have not been tested in randomized clinical trials.

Purpose: We present real world data on patients undergoing PCI and compare bleeding and MACCE (death, MI, stroke, target lesion or vessel revascularisation) on different antplatelets and anticoagulants.

Methods: 424 consecutive patients underwent PCI through 2013. The indication for PCI was ACS (51%) or symptomatic angina. Results: Male 71%, 8% <50yrs and 30% >75yrs. DAPT regimen with aspirin: clopidogrel 54%, prasugrel 23%, ticagrelor 10%. Other antplatelet due to intoler-
### P1478 | BEDSIDE

**Diabetes mellitus and platelet reactivity in patients under prasugrel or ticagrelor treatment**

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**Background:** The influence of diabetes mellitus (DM) on platelet reactivity (PR) in prasugrel or ticagrelor treated patients is not well studied.

**Purpose:** We aimed to assess the impact of DM on PR in patients receiving either prasugrel or ticagrelor.

**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 (in PRU) at one month post intervention.

**Results:** Ticagrelor (vs prasugrel) and insulin-treated DM significantly affected PR in the overall population with a 58.4% decrease in PR compared to prasugrel or ticagrelor treated patients, while PR under ticagrelor is not affected by DM status or insulin/non-insulin treatment.

**Conclusions:** In patients on novel antiplatelet agents, apart from a lower PR provided by ticagrelor 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.

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### P1479 | 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 STElevation myocardial infarction (STEMI) and is likely due to delayed 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 2 hours post loading. Per hour increase in pain-to-antiplatelet loading time and novel P2Y12 receptor antagonist use were independently associated with lower probability for HPR with a relative risk (95% confidence intervals, CI) of 0.87 (0.80 to 0.95) and 0.41 (0.31 to 0.55), p=0.002 and p<0.001, respectively.

**Conclusions:** In STEMI patients undergoing primary PCI, a patient-level data meta-analysis revealed the pain-to-antiplatelet loading interval as a newly described factor affecting platelet reactivity shortly after P2Y12 receptor antagonist loading.
reactivity assessment at 30–90 days post-discharge. Diabetic status was defined for an history of diabetes treated with or without drug therapies, fasting glucose ≥126 g/dl or HbA1c >6.5% at the moment of admission. Aggregation was assessed by multiple-electrode aggregometry. HRPR during ticagrelor treatment was defined as ADP test results >417 ALU/min.

Results: 86 out of 224 patients (38.4%) were diabetics. Diabetic status related to older age (P<0.05), higher BMI (P<0.009), renal failure (P=0.016), hypertension (p=0.02), treatment with diuretics (p=0.02), higher levels of WBC, glycemia, HbA1c, and lower levels of HDL-cholesterol (p<0.01, respectively).

Platelet aggregation in diabetics was significantly greater compared to non diabetics (p=0.046 for ASPI test, p=0.031 for COL test, p=0.04 for TRAP test and p=0.002 for ADP test). 29 patients (12.9%) displayed HRPR with ticagrelor with an almost double rate in diabetics as compared to non-diabetics (18.8% vs 9.4%, p=0.06; adjusted OR 2.11, 95% CI 0.94–4.76, p=0.07).

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).

Conclusion: Present study shows among post-ACS patients, that diabetic status is associated with a higher platelet reactivity despite dual antiplatelet therapy with ASA and ticagrelor, and especially in those patients with poor chronic glycemic control. In fact, diabetes emerged as independent predictor of HRPR with ticagrelor.

P1484 | BENCH

**cMRP4 expression in platelet of patients under chronic aspirin treatment is influenced by microRNA 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 pathological pathways, including modulation of drug activity. microRNA are abundant also in platelets, where they might participate to the multi-dependent mechanisms of platelet resistance. Recently over-expression of the multidrug resistance protein-4 (MRP4), an ATP Binding Cassette membrane transporter, actively involved in the efflux of pharmacological and physiological compounds, has been suggested as a mechanism of platelet resistance.

**Purpose:** To establish whether microRNAs may induce MRP4 modulation in patients under aspirin treatment.

**Methods:** MRP4 mRNA expression was analyzed by RealTime PCR on 2 cohort of 25 platelet samples of patients under ASA treatment versus a control group. To test which microRNAs were present in platelets we run a microarray panel of 176 microRNA. We compared the pool of the cohorts under aspirin treatment, with a pool of the healthy volunteer. Different microRNAs were dys-regulated in presence of aspirin. We selected highly dys-regulated microRNAs, with a difference of the fold induction >2. A panel of 176 microRNA was run on the pool of each cohort. MicroRNA-26b was transfected in platelet with microRNA mimic technology and flow cytometry was performed to analyse MRP4 platelet expression.

**Results:** We found a higher MRP4 mRNA expression in platelets of patients under aspirin treatment with a 2- fold increase compared to control. MicroRNA analysis revealed the absence of the two MRP4 targeting microRNA, mir-124a-3p and micrR-19b-3p, which targets MRP4, was found significantly down-regulated in the two cohort of patients under ASA treatment, compared to control group (p<0.005). Platelet transfusion with mirRNA 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 microRNA-26b as putative therapeutic target in aspirin resistance.

**Acknowledgement/Funding:** grant from Catholic University 70112072
Mild therapeutic hypothermia (TH) is standard of care after cardiac arrest of any cause. However, its impact on on-treatment platelet reactivity and outcome remained 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.

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P1485 | BEDSIDE
The impact of therapeutic hypothermia on on-treatment platelet reactivity and clinical outcome in cardiacogenic 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 in patients with acute myocardial infarction (AMI) complicated by cardiacogenic shock and undergoing PCI with P2Y12 receptor inhibitor treatment is unclear.

Methods and results: 145 patients with AMI complicated by cardiogenic shock and undergoing primary PCI in two centers between January 2009-May 2012 were analysed. Of these, 64 (44%) patients received TH treatment. The median (IQR) ADP-induced platelet aggregation following thienopyridine loading dose administration (clopidogrel in 95 and prasugrel in 50 patients) did not differ between the two groups (419 [283 - 684] for TH vs. 355 [207–710] AU x min for non-TH patients, P=0.22). After 30 days follow-up, no significant differences were observed between both groups for mortality (42 vs. 44%, HR: 0.93, 95% CI [0.56–1.53], p=0.77), MI (9 vs. 7%, HR: 0.99 95% CI [0.27–3.7], p=0.99) and TIMI minor bleedings (22 vs. 21%, HR 0.99 95% CI [0.45–2.18], p=0.98). TIMI major bleedings were numerically higher in the TH vs. non-TH cohort (31% vs. 15%, HR: 2.1 95% CI [0.95–4.63], p=0.07). Three definite stent thrombosis (ST) were observed in this registry and all STs occurred in the TH group of patients (p=0.09).

Conclusion: Results of this registry suggest that TH does not negatively impact on platelet reactivity in shock patients receiving either clopidogrel or prasugrel. The numerically higher rate of major bleedings and the clustering of STs in the TH cohort warrant further investigation.

P1486 | BEDSIDE
Short versus prolonged dual antiplatelet therapy (DAPT) duration after coronary stent implantation: a comparison between the DAPT trial and 9 other trials evaluating DAPT duration

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Aims: The Dual Antiplatelet Therapy (DAPT) trial demonstrated that DAPT beyond 1-year after drug-eluting stent (DES) implantation, as compared with aspirin therapy alone, significantly reduced the risk of major cardiovascular and cerebrovascular events, which were driven by the interaction between aspirin and coronary artery stenosis. Other trials evaluating monotherapy (MI) vs. dual antiplatelet therapy (DAPT) in the treatment of acute coronary occlusion (MI).

Methods and results: By a systematic literature search, we identified 9 trials comparing prolonged- versus short-DAPT in addition to the DAPT trial. The result from the DAPT trial (N=9961) with public–private collaboration was discordant with the pooled result from the 9 other investigator-driven trials (N=22174) in terms of the effect of prolonged-DAPT on MI (odds ratio [OR] 0.48 [95% CI 0.38–0.62] versus pooled OR 0.88 [95% CI 0.67–1.15]; P=0.001 for difference), non-fatal MI (8 vs. 7%, HR: 0.99 95% CI [0.27–3.7], p=0.99) and TIMI minor bleeding (21 vs. 15%, HR: 1.45 95% CI [0.97–2.17], p=0.08) compared to the short-DAPT trials. The annual risk of MI among aspirin mono-therapy in the DAPT trial was much higher than that in the other trials (2.7% versus 0.6–1.6%), although the baseline clinical, angiographic, and procedural characteristics were comparable across trials.

Conclusions: Given the discrepancy between the DAPT and other trials, further studies are mandatory to define the optimal DAPT duration after coronary stent implantation.

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

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Background: Platelet adhesion to subendothelial collagen after plaque rupture results 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.

Purpose: The present study explored whether Janus Kinase 3 participates in the regulation of platelet activation and arterial thrombosis 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. Furin-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 wild-type platelets. Consequential, 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 and especially with myocardial infarction 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.

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Background: Antiplatelet drugs (AP) are often co-prescribed with oral anticoagulants (OAC) in patients with atrial fibrillation (AF) and associated vascular disease, or if the patient is at high vascular risk, even though there is little evidence of added efficacy and there is potential for excess harmful bleeding, especially intracranial haemorrhage. For patients with vascular disease, there has also been the perception that AP should be added to non-vitamin K antagonist OACs (NOACs).

Methods: We examined concomitant use AP in GLORIA-AF (a prospective, global, observational study program of patients with newly diagnosed non-valvular AF), in relation to vitamin K antagonist (VKA) and NOAC use.

Results: Of 10675 patients in Phase II (median age 71 years, 54.5% male; median CHA2DS2-VASc score 3), 20.6% had coronary artery disease (CAD), 10.5% had a prior myocardial infarction and 3.3% had peripheral artery disease (PAD). The majority were OAC naive (n=8539, 80.0%), with only 12.3% on AP alone and 7.6% on an antithrombotic therapy. AP was co-prescribed with VKA in 5.4%, and with NOACs in 6.6% of patients. Amongst males with a CHA2DS2-VASc=1 (moderate risk), AP was co-prescribed with VKA in 4.4% and with NOACs in 5.1%. In male AF patients with CHA2DS2-VASc≥2, AP was co-prescribed with VKA in 6.8% and with NOACs in 8.5%. In females with CHA2DS2-VASc<1 (low risk), AP was co-prescribed with VKA in 2% and with NOAC in 1.2%. In females with CHA2DS2-VASc≥2, AP was co-prescribed with VKA in 4.5%, and with NOAC in 5.4%. Regional variation was evident, with VKA+AP most common in North America (6.6%) and Asia (6.7%), vs Europe, 4.2% and Latin America, 2.3%. NOAC+AP was more common in North America (11.4%) and Latin America (11.1%), compared with Europe (4.0%) and Asia (3.1%). AF patients with PAD had higher use of VKA+AP (10.1% vs no PAD, 5.1%) and NOAC+AP (14.6% vs no PAD, 6.2%), as did AF patients with coronary artery disease (CAD), with VKA+AP (11.4% vs no CAD, 3.8%) and NOAC+AP (15.2% vs 4.3%).

Conclusion: These observational data show that a minority of AF patients are prescribed AP in combination with OAC, with co-prescription being similar between NOACs and VKAs. Combination therapy with AP in patients taking OAC is 2–3 fold more common where PAD or CAD was present.

Acknowledgement/Funding: This study was funded by Boehringer Ingelheim.
P1490 | 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 8th June 2014; for randomised control trials with clinical outcomes for P2Y1 inhibitors in adult diabetic patients with ACS. Results: 14 studies and 1822 patients: 805 and 1017 in the ticagrelor and prasugrel on HTPR. Pooled estimates were calculated by using a random-effects model with 95% confidence intervals.

Conclusions: Our results suggest that ticagrelor allows a higher platelet reactivity inhibition as compared to prasugrel and leads to further decrease the rate of HTPR.

P1490 | 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 - cohort: aspirin and clopidogrel, but no VKA) and 100 patients on oral anticoagulation 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 (≥468 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

P1491 | BEDSIDE
Ticagrelor and prasugrel have shown superiority as compared to clopidogrel in the diabetic population due PCI for 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 8 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]).

Conclusions: Our results suggest that ticagrelor allows a higher platelet reactivity inhibition as compared to prasugrel and leads to further decrease the rate of HTPR.
Platelets and antiplatelets therapy IV

P1494 | BEDSIDE
Comparison of short-term clinical outcomes between new p2y12 receptor inhibitors and clopidogrel in patients with acute myocardial infarction: from the core cohort in Korea
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Background and objects: It has been well known that new P2Y12 receptor inhibitors (RIs; 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 RIs 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 (892 pairs) were performed in order to compare the in-hospital clinical outcomes between new P2Y12 RI and clopidogrel after adjusting for baseline clinical and procedural confounders.

Results: P2Y12 reactivity unit by the VerifyNow P2Y12 test was 77.5±74.50 in new P2Y12 RI and 212.5±80.72 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=0.106). On multivariate analysis, use of statin, TFI vs. IDR, and use of glycoprotein IIb/IIIa inhibitors were independent predictors of the composite of cardiac death, MI, stent thrombosis, stroke or TIMI major bleeding (odd ratio [OR]=0.187; 95% confidence interval [CI]=0.083–0.422, OR=10.811; 95% CI: 2.560–45.652, OR=2.174; 95% CI: 1.103–4.284).

Conclusions: Our study 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 (1.72–4.20), 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. In the multivariate analysis adjusted also for HCPR, HAPR was confirmed as an independent risk factor for cardiac death [HR 1.88 (1.21–2.93), p<0.005, p<0.001] and stent thrombosis [HR 1.91 (1.12–3.28), p=0.018]. Adding HAPR to the model including clinical and procedural risk factors, and HCPR, NRI improved significantly and was 39% for cardiac death and 34.7% for stent thrombosis. HAPR was found to be an independent risk factor for cardiac death and stent thrombosis in ACS patients undergoing PCI.

P1497 | BEDSIDE
Characteristics of dyspnoea and associated clinical outcomes in the CHAMPION PHOENIX study
R.F. Storey1, D.L. Bhatt2, P.G. Steg2, G.W. Stone3, H.D. White3, C.M. Gibson4, C.W. Hamm5, J. Prat6, K.W. Mahaffey7, R.A. Harrington8 on behalf of The CHAMPION PHOENIX investigators. 1Department of Cardiovascular Science, University of Sheffield, Sheffield, United Kingdom; 2Brigham and Women’s Hospital, Department of Medicine, Cardiovascular Division, TIMI Study Group, Boston, United States of America; 3University Paris Diderot, Paris, France; 4Columbia University Medical Center, New York, United States of America; 5Auckland City Hospital, Auckland, New Zealand; 6Harvard Medical School, Boston, United States of America; 7Kerckhoff Heart and Thorax Center, Bad Nauheim, Germany; 8The Medicines Company, Parsippany, United States of America; 9Stanford University Medical Center, Stanford, United States of America; 10School of Medicine, Stanford, United States of America

Background: Dyspnoea may be induced by some reversibly-binding P2Y12 inhibitors, including cangrelor and ticagrelor. The CHAMPION PHOENIX study compared initial treatment with cangrelor versus initial treatment with clopidogrel in patients undergoing PCI.

Purpose: To investigate the incidence, characteristics, and associated clinical outcomes in patients with dyspnoea in CHAMPION PHOENIX.

Methods: Adverse events (AEs) of dyspnoea were recorded in patients randomized to cangrelor or clopidogrel. The composite primary endpoint of death, MI, ischaemia-driven revascularization (IDR), or stent thrombosis (ST), as well as its individual components, were assessed in patients who did or did not report dyspnoea.

Results: 68 (1.2%) cangrelor-treated and 18 (0.3%) clopidogrel-treated patients reported dyspnoea (P=0.001). Most dyspnoea events in cangrelor-treated patients were transient (median 1.6 hours) and were considered mild (71%) or moderate (28%); 1 event was considered severe. No patient in either group discontinued study treatment due to dyspnoea. Rates of the primary outcome and its individual components in the modified intention-to-treat population are shown (Table).

Clinical outcomes by dyspnoea status

<table>
<thead>
<tr>
<th>With dyspnoea</th>
<th>Without dyspnoea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cangrelor</strong></td>
<td></td>
</tr>
<tr>
<td>N=68</td>
<td></td>
</tr>
<tr>
<td>N=17</td>
<td></td>
</tr>
<tr>
<td><strong>Clopidogrel</strong></td>
<td></td>
</tr>
<tr>
<td>N=5404</td>
<td></td>
</tr>
<tr>
<td>N=5453</td>
<td></td>
</tr>
<tr>
<td>Death/MI/IDR/ST</td>
<td></td>
</tr>
<tr>
<td>6 (8.8%)</td>
<td></td>
</tr>
<tr>
<td>2 (11.8%)</td>
<td></td>
</tr>
<tr>
<td>251 (4.6%)</td>
<td></td>
</tr>
<tr>
<td>320 (5.9%)</td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>18 (0.3%)</td>
<td></td>
</tr>
<tr>
<td>18 (0.3%)</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td></td>
</tr>
<tr>
<td>7 (5.4%)</td>
<td></td>
</tr>
<tr>
<td>1 (5.9%)</td>
<td></td>
</tr>
<tr>
<td>202 (3.7%)</td>
<td></td>
</tr>
<tr>
<td>254 (4.7%)</td>
<td></td>
</tr>
<tr>
<td>IDR</td>
<td></td>
</tr>
<tr>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>2 (11.8%)</td>
<td></td>
</tr>
<tr>
<td>28 (0.5%)</td>
<td></td>
</tr>
<tr>
<td>36 (0.7%)</td>
<td></td>
</tr>
<tr>
<td>ST</td>
<td></td>
</tr>
<tr>
<td>1 (1.5%)</td>
<td></td>
</tr>
<tr>
<td>2 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>45 (0.8%)</td>
<td></td>
</tr>
<tr>
<td>74 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>MI, myocardial infarction; IDR, ischaemia-driven revascularisation; ST, stent thrombosis.</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Cangrelor-related dyspnoea appears transient, is usually mild or moderate and does not seem to lead to therapy discontinuation. The occurrence of dyspnoea does not seem to be associated with any reduction in the efficacy of cangrelor compared with clopidogrel as initial therapy in PCI patients.

Acknowledgement/Funding: The Medicines Company

P1498 | BEDSIDE
Dual anti-platelet therapy after drug-eluting coronary stent implantation and risks associated with gastroscopy - a Danish registry study
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Background: Dual antiplatelet therapy (DAPT) is recommended for up to 12 month following percutaneous coronary intervention (PCI) with drug-eluting stent
implantation (DES) and increases the risk of upper gastrointestinal bleeding and need for gastroscopy. Real-life handling of DAPT in relation to gastroscopy varies and the associated risk of adverse cardiac events and bleeding complications is largely unknown.

**Purpose:** To quantify 1) the frequency of gastroscopy 2) the incidence of bleeding and cardiac events in relation to gastroscopy and 3) the association between DAPT discontinuation, cardiac events and bleeding within the first 12 months after DES implantation.

**Methods:** We studied the frequency of gastroscopy within 12 months and numbers of adverse cardiac events and hemostatic intervention in relation to gastroscopy among all-comers treated with DES by cross-linkage of Danish registries. In two nested case-control studies we evaluated hospital charts for the exposure to DAPT. In the adverse cardiac events nested case-control study, patients with cardiac death, myocardial infarction, or stent thrombosis were cases. In the hemostatic intervention study, patients with hemostatic intervention were cases, and patients with gastroscopy including biopsy were controls.

**Results:** In a cohort of 22,654 patients treated with DES, we identified 1497 patients (6.6%), who underwent gastroscopy within 12 month. Among these, 22 patients (1.5%) suffered from an adverse cardiac event within the first 30 days after the gastroscopy and 93 patients (6.2%) had hemostatic intervention during gastroscopy. The nested-case control studies showed heterogeneity in DAPT prescription; 74% received DAPT during gastroscopy. Discontinuation of both aspirin and the P2Y12-inhibitor was associated with a non-significant increased risk of adverse cardiac event (odds ratio 3.46, 95% confidence interval 0.49–24.7). Periprocedural DAPT was not associated with an increased risk of hemostatic intervention compared to no antiplatelet treatment (odds ratio 1.31, 95% CI: 0.37–4.70). No patients experienced bleeding complications as a consequence of gastroscopy with or without biopsy can safely be performed despite ongoing treatment with DAPT.

**Conclusion:** Gastroscopy is a frequent procedure within the first year of stent implantation. While adverse cardiac events were increased with discontinuation of DAPT, the risk of a hemostatic intervention was not demonstrated. Gastroscopy with or without biopsy can safely be performed despite ongoing treatment with DAPT.

**Acknowledgement/Funding:** TRYG. Knud and Edith Eriksen’s mefindet. Aarhus University Hospital. Department of Cardiology
an increased risk of bleedings (12.3% versus 9.9%) (OR [95% CI] = 1.37 [1.16–1.62], p=0.0002; phet = 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 stent implantation, requiring chronic oral anticoagulation, the use of a triple antithrombotic therapy is associated with a significant reduction in mortality that largely outweighed the risk of major bleeding complications associated with triple therapy.

P1502 | BEDSIDE
Comparison of in-hospital clinical outcomes between ticagrelor versus clopidogrel in patients with acute myocardial infarction undergoing successful revascularization

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Objectives: This study sought to determine the efficacy and safety of ticagrelor compared to clopidogrel in patients with acute myocardial infarction (AMI).

Background: It has been well known that ticagrelor could improve clinical outcomes in patients with AMI without increasing bleeding risk. However, the clinical impacts of ticagrelor in Korean patients with AMI have not been well established.

Methods: Between November 2011 and August 2014, a total of 4,029 patients (3,186 patients were prescribed clopidogrel and 843 patients ticagrelor) with AMI undergoing PCI were included. Patients 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±6.82 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; 8.4% 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 (odd ratio [OR]=3.807; 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: 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


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: In times of spectrum of ST 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.
P1505 | BEDSIDE
Access site versus non-access site bleeding in primary PCI: Incidence, impact on mortality and risk reduction according to antithrombin treatment. The EUROMAX trial
S. Kilic1, A.W.J. Van ‘t Hof1, J.M. Ten Berg2, A. Ayesta Lopez2, U. Zeymer4, M. Hamon5, L. Soulant6, D. Bernstein7, E.N. Deliargyris8, P.G. Steg1, A. Hoff, Twente, Netherlands; 2Antoni van Leeuwenhoek Hospital, Amsterdam, the Netherlands; 3University Hospital Gregorio Maranon, Madrid, Spain; 4Klinikum Ludwigsheiden, Ludwigsheiden Am Rhein, Germany; 5University Hospital of Caen, Caen, France; 6Hospital Center of Chateauroux, Chateauroux, France; 7Medicines Company, Parispary, United States of America; 8Hospital Bichat-Claude Bernard, Paris, France

Purpose: Impact of post-PCI bleeding on prognosis after STEMI may differ according to the site of bleeding. We determined the frequency and origin of bleeding, the associated risk for 30 day death and the impact of antithrombin choice in PPCI.

Methods: We blindly reviewed all case records of TIMI major or minor bleeds and assigned them in 4 groups: access only, non-access only, both locations and no location. Mortality at 30 days and impact of randomized treatment were assessed for each group.

Results: A total of 231 out of 2198 ITT patients suffered a TIMI major or minor bleed (10.5%). Mortality at 30 days was higher in patients who suffered a non-access site-related bleed (50/1967, 2.5%; \( p < 0.0001 \)) compared to patients who did not suffer a bleed (50/1967, 2.5%; \( p < 0.0001 \)). There was no difference in mortality for patients with an access related bleed (3/112, 2.7%; \( p = 0.76 \)) compared to patients who did not suffer a bleed (3/112, 2.7%; \( p = 0.76 \)) compared to patients who did not suffer a bleed (3/112, 2.7%; \( p = 0.76 \)) compared to patients who did not suffer a bleed (3/112, 2.7%; \( p = 0.76 \)) compared to patients who did not suffer a bleed (3/112, 2.7%; \( p = 0.76 \)) compared to patients who did not suffer a bleed (3/112, 2.7%; \( p = 0.76 \)).

Conclusion: In PPCI, bleeding is equally distributed between access and non-access related locations with a higher risk for 30 day death associated with non-access site bleeds. Bivalirudin reduces the risk of bleeding irrespective of origin.

Acknowledgement/Funding: Medicines Company

P1506 | BEDSIDE
Coronary index of microcirculatory resistance and echocardiographic parameters evolution in patients with ST-elevation acute myocardial infarction treated with primary angioplasty (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.

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 pa-

Abstract P1506 - Table 1

<table>
<thead>
<tr>
<th>Category</th>
<th>Total (%)</th>
<th>Bivalirudin (%)</th>
<th>UHPR/GPI (%)</th>
<th>Relative risk p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access only 112/2198</td>
<td>44/1099</td>
<td>68/1109</td>
<td>0.66</td>
<td>0.03</td>
</tr>
<tr>
<td>Non access only 72/2198</td>
<td>24/1099</td>
<td>48/1109</td>
<td>0.51</td>
<td>0.005</td>
</tr>
<tr>
<td>Both 18/2198</td>
<td>6/1099</td>
<td>12/1109</td>
<td>0.51</td>
<td>0.17</td>
</tr>
<tr>
<td>No location 29/2198</td>
<td>11/1099</td>
<td>18/1109</td>
<td>0.62</td>
<td>0.21</td>
</tr>
<tr>
<td>All bleeding excluding access 119/2198</td>
<td>41/1099</td>
<td>78/1109</td>
<td>0.54</td>
<td>0.0007</td>
</tr>
</tbody>
</table>

Conclusion: Coronary microcirculatory resistance and echocardiographic parameters evolution in STEMI patients are associated with worse short and long term LVF.

P1507 | BEDSIDE
Microvascular dysfunction following ST-segment elevation myocardial infarction is associated with short and long term cardiac function assessed by cardiac magnetic resonance imaging
M.E.C.J. Hassell, R. Delewi, M.A. Laverien, R. Nijveldt, A. Hirsch, L. Robbers, K.M. Marques, F. Zijlstra, A.C. Van Rossum, J.J. Piek, Academic Medical Center of Amsterdam, cardiology department, Amsterdam, Netherlands

Background: Despite restoration of epicardial blood flow, compromised myocardial tissue perfusion due to microvascular dysfunction has been described in 30–40% of reperfused ST-segment elevation myocardial infarction (STEMI) patients. Analysis of the time course of microvascular dysfunction and its implications on long term left ventricular function is lacking.

Purpose: We investigated the relationship of microvascular dysfunction following STEMI on long term left ventricular function (LVF) as assessed by cardiac magnetic resonance imaging (CMR).

Methods: In 62 patients, Coronary Flow Velocity Reserve (CFVR) in the infarct related artery (IRA) was assessed with intracoronary Doppler flow measurements within 1 week and 4 months after STEMI. CMR was performed within one week, at 4 months and 2 years.

Results: CFVR at baseline in the IRA is associated with left ventricular ejection fraction (LVEF) and wall thickening in the affected segments at both 4 months (\( \beta = 4.66, \text{SE}=2.10; \text{P}=0.03 \) and \( \beta = 9.37, \text{SE}=4.42; \text{P}=0.04 \)) and 2 years follow-up (\( \beta = 5.84, \text{SE}=2.45; \text{P}=0.026 \)) and \( \beta = 12.36, \text{SE}=5.88; \text{P}=0.04 \)). In patients with an initial CFVR <2, the absolute increase in CFVR was the only variable associated with LVEF improvement in the first 4 months (\( \beta = 4.33, \text{SE}=1.65; \text{P}=0.045 \)). 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 (\( > \text{median} \) of 3 CFVR) had an increased LVEF 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 LVEF at 4 months, underlining its clinical significance.

P1508 | BEDSIDE
Association of SDF-1 polymorphisms with differential platelet CXCR4 expression in patients with coronary artery disease
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1University Hospital Tubingen, cardiology department, Tubingen, Germany; 2Dr Margarete Fischer-Bosch Institute of Clinical Pharmacology, Stuttgart, Germany

Background: Surface expression of SDF-1 on platelets is enhanced during ischemia and to a higher degree in patients with coronary artery disease (CAD) when compared with healthy controls. In this study we investigated a possible influence of distinct SDF-1 polymorphisms rs266085, rs266087 and rs1065297 on platelet expression in patients with coronary artery disease.

Methods: IMR was evaluated immediately after P-PCI in STEMI patients correlated with GLS. Absence of MD as evaluated invasively (IMR >26) is associated with a significantly higher recovery of the LVEF, WMSI, E/E' ratio and GLS, suggesting that IMR is an early marker of cardiac remodelling after acute myocardial infarction.
Methods and results: In a cohort study, platelet surface expression of CXCR4, CXCR7 and SDF-1 was measured by flow cytometry in 30 patients with symptomatic coronary artery disease (CAD) at the time of percutaneous coronary intervention (PCI). SDF-1 single-nucleotide polymorphism analysis was performed with MALDI-TOF mass spectrometry. Platelet CXCR4 levels were significantly elevated in the SDF polymorphisms rs266085 and rs266087 (CXCR4 median MFI 31.18; 25th/75th percentile 24.09/57.45 vs. 22.44; 25th/75th percentile 17.24/26.28, p < 0.019 and median MFI 31.18; 25th/75th percentile 24.09/57.45 vs. 22.44; 25th/75th percentile 17.24/26.28, p < 0.019) as compared to the wild type. Platelet CXCR4 levels were significantly decreased in the SDF polymorphism rs1065297 as compared to the wild type (median CXCR4 MFI 20.88; 25th/75th percentile 17.78/24.47 vs. 30.10; 25th/75th percentile 23.27/51.59, p < 0.032). We could not find any significant associations between any of these SDF-1 polymorphisms and platelet CXCR7 and SDF-1 expression.

Conclusions: In a prospective single 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.

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 were analyzed twice by three blinded examiners (2 CMR experts and 1 novice). On the first hand, an analysis was performed on cine MR and late gadolinium enhancement. On the second hand another analysis was performed following initial protocol combined to first pass perfusion sequences.

Results: On CMR at baseline, a thrombus was found in 29 of 331 (8.7%) patients. Thrombus formation was independently associated with lower LV ejection fraction (40.3±7.9% vs. 48±19.7%, p < 0.001), end-systolic volume (54.8±25.9 mm^3 vs. 43.4±18.0 mm^3, p < 0.001), peak creatine kinase (4076±2402 U/L vs. 2873±2122 U/L, p < 0.001), infarct size (33.6±19.6 g vs. 22.4±17.1 g, p < 0.001) and anterior wall infarct (median MFI 31.18; 25th/75th percentile 24.09/57.45 vs. 22.44; 25th/75th percentile 17.24/26.28, p < 0.019) as compared to the wild type. Platelet CXCR4 levels were significantly decreased in the SDF polymorphism rs1065297 as compared to the wild type (median CXCR4 MFI 20.88; 25th/75th percentile 17.78/24.47 vs. 30.10; 25th/75th percentile 23.27/51.59, p < 0.032). We could not find any significant associations between any of these SDF-1 polymorphisms and platelet CXCR7 and SDF-1 expression.

P1510 | BEDSIDE
Risk-treatment paradox in anticoagulation therapy selection: Insights from a single center PCI registry


Background: Novel oral anticoagulants (NOACs) have been proven both efficacious and safe in patients with atrial fibrillation (AF). However evidence describing the real world use of NOACs in patients with symptomatic coronary artery disease (CAD) at the time of percutaneous coronary intervention (PCI) is scarce.

Methods: We conducted a five-year (2010–2014), retrospective, single center study of 735 patients with AF undergoing PCI and discharged in either NOACs or coumadin. The patients’ ischemic (CHADS2) and bleeding risks (ATRIA) were calculated. We sought to examine differences in patients’ characteristics and anticoagulation therapy selection according to ischemic and bleeding risk scores.

Results: Overall, 205 (28%) patients were discharged on NOACs vs. 529 (72%) on coumadin. Patients on coumadin were more likely to have higher creatinine value, to be dialysis dependent, to present with unstable angina, have a higher mean of CHADS2 score and have more complex lesions. When stratified by incremental ischemic risk, NOAC discharge therapy decreased progressively over increasing score (P for trend=0.0045). Coumadin prescription showed an inverse trend. No trend was detected when anticoagulation therapy was plotted according to bleeding risk (P for trend=0.43) (Figure; NOAC in green; coumadin in red).

Conclusions: In a prospective single 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.
P1514 | BEDSIDE
Risk factors for major bleeding and efficacy of modified HAS-BLED score in patients on oral anticoagulation after coronary artery stenting

Background: Dual antiplatelet therapy is required for a long time after coronary artery stenting, and oral anticoagulation (OAC) is necessary for the prevention and treatment of thromboembolic events; however, increased risk of bleeding needs to be considered when deciding the initiation of triple oral antithrombotic therapy. The HAS-BLED score could be recommended to assess bleeding risk, but clinical usefulness of the score remains unclear.

Purpose: To compare the clinical implication of HAS-BLED score and modified HAS-BLED score.

Methods: Between January 2010 and December 2011, 1507 patients required dual antiplatelet therapy after coronary artery stenting. Until January 2015, 200 of them required OAC, and their backgrounds and major bleeding events (Bleeding Academic Research Consortium criteria ≥3) were analyzed. A modified HAS-BLED score comprised the following points: 2 points for bleeding/gastric ulcer and oldest old (<80 years); 1 point for a past history of hypertension, abnormal renal function (estimated glomerular filtration rate <30), stroke, labile international normalized ratio (INR), elderly (>66 to 79 years), and drug/alcohol consumption.

Results: At baseline, the mean age was 71.8 years, 75.5% were men. OAC was taken in 107 patients (54%) for atrial fibrillation/flutter, 53 (27%) for low cardiac output syndrome/intraventricular thrombus, 31 (16%) for postoperative cardiovascular surgery, and 6 (3%) for pulmonary embolism/deep vein thrombosis. During the follow-up period, 31 patients suffered from major bleeding, 130 survived without major bleeding, 36 died without major bleeding, and 3 dropped out. We show the distribution and the rate of major bleeding in patients classified into each scores by HAS-BLED score or modified HAS-BLED score in the table.

Table 1: Modified HAS-BLED N (%) 5 (3) 26 (17) 62 (39) 35 (22) 7 (4)
BARC ≥3 20% 44% 10% 10% 0% Modified Modified HAS-BLED N (%) 26 (17) 62 (39) 35 (22) 7 (4)
BARC ≥3 44% 20% 10% 6% 0% Conclusion: A modified HAS-BLED score could be more effective to assess and classify bleeding risk in patients taking triple oral antithrombotic therapy.

P1515 | BEDSIDE
D-dimer levels in patients with acute chest pain
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Current guideline of European Society of Cardiology recommended the measurement of d-dimers to rule out acute aortic dissection in patients presenting acute chest pain, however, the distribution of d-dimer levels in various diseases presenting acute chest pain is not sufficiently accessed.

We retrospectively reviewed 953 consecutive patients who admitted to the hospital for acute chest pain between January 2011 and April 2014. D-dimer levels were measured in 887 patients (acute aortic dissection 97, symptomatic aortic aneurysm 26, pulmonary embolism 29, acute
segment elevation myocardial infarction (STEMI) is a challenge with relevant implications in patients management. Cardiac magnetic resonance (CMR) has emerged as the gold standard for establishing this diagnosis. We aimed to characterize the incidence, predictors and dynamics of this finding using CMR. The ability of echocardiography to identify CMR-derived VTh was also addressed.

**Methods:** We enrolled 574 patients with a first reperfused STEMI. This study was performed within the first 6 months post-infarction. Additionally, echocardiography within 2 days prior to the first CMR was carried out in 411 patients.

**Results:** In 1-week CMR, VTh was detected in 24 patients (4%). Patients with VTh displayed a more depressed left ventricular (LV) ejection fraction (EF), more dilated LV volumes and LV mass and a larger % of LV mass with edema, MVO and necrosis (p < 0.001). Of 24 patients with VTh, 23 (96%) had an anterior infarction and 21 (87%) a depressed LV EF (0.67 ± 0.17) compared to those without RevRem (0.70 ± 0.06; p < 0.001). VTh occurred in 11/24 patients (46%) with preserved LVEF and preserved LVEF, in 2/21 (10%) with both anterior infarction or depressed LVEF and in 21/217 (10%) with both anterior and depressed LVEF (p < 0.001 for the trend). In the multivariate analysis, the presence of simultaneous depressed LVEF and anterior infarction independently predicted the occurrence of RevRem (OR 15 [2–114], p = 0.008). Out of 24 patients with VTh in the first CMR, 17 were re-studied with a second CMR within the following 6 months. VTh had vanished in 13 (76%) and persisted in 4 (24%). Of the 391 with a second CMR, a new VTh was detected in 9 cases (2%). All patients (9/9, 100%) with a newly developed VTh in the second CMR had a depressed LVEF and 8/9 (99%) had an anterior infarction. Of 411 patients studied with echocardiography within 2 days prior to the first CMR, VTh was detected in 11 (3%). A diagnosis of VTh by CMR was established in 22 (5%) of these 411. As compared with CMR, echocardiography correctly diagnosed VTh in 8 patients (38%) and 14 (68%) were undetected. VTh was discarded by CMR in 389 patients (95%). Echocardiography properly discarded VTh in 386 cases (99%) but inappropriately in 3 of them (1%).

**Conclusions:** CMR allows for a comprehensive characterization of the incidence, patterns and dynamics of VTh after a first reperfused STEMI. This finding occurs in around 4% of patients and associates with the presence of severe LV structural damage. The majority of cases occur in patients with anterior infarction and depressed EF.

**P1518 | BEDSIDE**

**Prediction of reverse remodeling by cardiac mr imaging soon after a first reperfused st-segment elevation myocardial infarction. Results of a large prospective registry**


**Purpose:** In ST-segment elevation myocardial infarction (STEMI) a specific approach to reverse remodeling (RevRem) using cardiac magnetic resonance (MR) has not been performed yet. We aimed to predict the occurrence of RevRem using cardiac MR soon after STEMI.

**Materials and methods:** We prospectively studied 507 patients with a first STEMI. 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 (LVESVI) > 10% from 1-week to 6-months.

**Results:** Patients with RevRem (n = 211, 42%) had a lesser extent of 1-week IS (p < 0.001), MVO (p < 0.001) and hemorrhage (p < 0.01) compared to those without RevRem (n = 296, 58%). 1-week LV ejection fraction (LVEF) and LVESVI 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 < 2.5% of LV mass); 3.2 [1.8–5.7], p < 0.001. From 1-week to 6-months, LVESVI diminished in patients with simultaneous non-extensive IS-MVO (355±15 vs. 313±13 mm², p < 0.001), did not vary in those with extensive MVO (42±11 vs. 41±11 mm², p = 0.7) or extensive IS (54±26 vs. 56±28 mm², p = 0.5) but did so in patients with simultaneous extensive IS-MVO (59±21 vs. 65±27 mm², p = 0.004).

**Conclusion:** Assessment of the extension of IS and MVO by cardiac MR imaging soon after STEMI is decisive in the prognostication of RevRem.
P1519 | BEDSIDE
Natural history and clinical significance of infarct zone volume and remodelling in survivors of acute STEMI

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Background: The natural history and clinical significance of extracellular volume (ECV) expansion in infarcted myocardium post-STEMI is unknown. Myocardial ECV can be estimated by cardiac magnetic resonance imaging (CMR) using T1 MOLLI before and after contrast. We aimed to measure infarct zone ECV post-STEMI and 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 (RI1=11/) for myocardium and LV blood pool before vs. after contrast, corrected for haemocrit (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. 52.8±9.6%, p<0.001) (n=161). Mean infarct size reduced from baseline to follow-up (17.5±12.8% vs. 12.7±10.2% of LV (P<0.001)) (n=161). ECV was correlated with infarct size at baseline (r=0.6, P<0.001) (n=124) and follow-up (r=0.6, P<0.001) (n=160). 87 (51%) patients had MVO at baseline. Mean LV EF reduced from baseline to follow-up (55±15.8% vs. 62±9.6% (P<0.001)) (n=160). The within-subject change in ECV varied markedly. For an ECV deviation of >1% from baseline, 67 (57%) patients had no change or decrease and 50 (43%) had an increase. An increase in infarct zone ECV at follow-up was associated with a lower troponin I, older age, presence of MVO at baseline, reduced LV ejection fraction (LVEF) and higher LV end systolic volume (LVESV) at follow-up (all P<0.05) (n=117).

Conclusion: Infarct zone ECV is increased at 6 months in approximately one half of STEMI patients. LVEF, LVESV at 6 months, MVO at baseline and peak troponin were associated with infarct zone remodelling. Infarct ECV represents a predictor of adverse cardiac events in acute STEMI survivors, 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.

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P1521 | BEDSIDE
Mitrail anular plane excursion measured during routine cine-cardiac magnetic resonance imaging is a predictor of adverse cardiac events in patients with known or suspected coronary artery disease

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Background: Longitudinal movement of the mitral annulus is a major component of normal left ventricular pump function, which involves the coordinated action of longitudinal, circumferential and radially oriented fibers. Longitudinal fiber dysfunction appears to be a very early marker of a number of pathological states, perhaps due to its subendocardial location. We therefore hypothesized that reduced mitral annular plane systolic excursion (MAPSE) measured during routine cine-Cardiac Magnetic Resonance (CMR) imaging reflects early changes in longitudinal fiber function and maybe associated with adverse cardiovascular outcomes.

Purpose: To assess the prognostic value of simple cine-CMR derived MAPSE for the prediction of adverse cardiac events.

Methods: 300 consecutive patients with known or suspected coronary artery disease undergoing CMR were prospectively enrolled. Lateral MAPSE was measured in the 4-chamber cine view by two independent observers. Patients were prospectively followed for major adverse cardiac events (MACE) - death, non-fatal myocardial infarction, hospitalization for heart failure or chest pain, and late revascularization.

Results: The mean age of the study population was 61±11 years, with a mean ejection fraction of 59±14%. 33% of the individuals had known coronary artery disease, and 35% were diabetic. 46 MACE occurred during a median follow-up of 15 months. By Kaplan-Meier analysis, patients with lateral MAPSE <11.3 (median) experienced higher incidence of MACE than patients with a MAPSE >11.3 (p=0.0399) (Figure).

Conclusions: Reduced longitudinal fiber function assessed with lateral MAPSE during routine cine-CMR is a predictor of MACE in patients with known or suspected coronary artery disease.

P1520 | BEDSIDE
The additive value of cardiovascular magnetic resonance first pass perfusion in diagnosis of microvascular disease in a population with chest pain and normal coronary arteries

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Introduction: Measurement of coronary flow velocity at rest and at peak hyperaemia allows calculation of coronary flow reserve (CFR). In patients with normal epicardial coronary arteries, a reduced CFR (typically <2) is considered diagnostic of microvascular dysfunction. Cardiovascular magnetic resonance (CMR) provides a non-invasive assessment of myocardial perfusion with high spatial resolution and no ionising radiation.

Purpose: We assessed the additive diagnostic value of CMR in the diagnosis of microcirculatory disease in a population of patients with suspected microvascular dysfunction.

Methods: Consecutive patients with a moderate-high pre-test probability of microvascular disease based on non-invasive testing, presenting with chest pain and angiographically normal epicardial coronary arteries were recruited. Patients underwent Doppler flow wire measurement of coronary flow and CFR in the proximal left anterior descending artery. They then underwent CMR assessment of first pass myocardial perfusion at rest and with adenosine stress perfusion on a 3T Skyra scanner (Siemens). Myocardial perfusion was assessed visually by two experienced observers blinded to the CFR result and quantified using a Fermi-constrained deconvolution algorithm.

Results: 37 patients (mean age 58±13, 70% male) were recruited. The mean CFR was 2.1±0.92. 22/37 (59%) patients had evidence of microvascular disease using the conventional criteria of a CFR<2. All of these patients had CMR evidence of microvascular dysfunction with a persistent circumferential subendocardial perfusion defect during adenosine stress. Four additional patients (11%) had CMR evidence of microvascular disease, despite a normal CFR (mean 2.4±0.16). There was no difference in age between these patients and the rest of the population (mean age 58±7, p=0.9).

Conclusions: CMR has additive diagnostic value in the assessment of coronary microvascular disease. A CFR greater than 2 does not rule out microvascular disease and further testing should be considered in patients with a history of chest pain suggestive of small vessel disease despite angiographically normal epicardial coronary arteries.

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P1522 | BEDSIDE
Temporal evolution and prognostic significance of infarct core pathology in ST-elevation myocardial infarction survivors revealed by serial quantitative T2-weighted cardiac magnetic resonance

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Background: Myocardial transverse relaxation time (T2, ms) is a fundamental magnetic property of tissue that is related to water content and mobility.

Purpose: 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 reperfusion in a serial imaging sub-set.

Methods: We performed a prospective single centre cohort study in reperfused STEMI patients who underwent CMR 2 days and 6 months post-MI. T2 (relaxation time, ms) was measured using quantitative T2-mapping. A sub-set of 30 STEMI patients underwent imaging at 4 time-points: 4–12 hours, 3 days, 10 days and 6–12 months post-MI. Inducible myocardial perfusion defect during adenosine stress (CER) was supported by the BHF. This study is supported by the BHF.

Results: 324 STEMI patients underwent CMR. 164 (51%) patients had microvascular obstruction (MVO) whereas 197 (61%) patients had an infarct core revealed
by T2 mapping. T2 core was present in all patients with late MVO. 33 patients had T2 core in the absence of late MVO. The presence of T2 infarct core was more closely related to early MVO (186 patients (57%) to late MVO. In multivariable regression, T2 in the infarct core was negatively associated with heart rate, Killip class, and peak neutrophil count at presentation (all p<0.05). An increasing T2-core value (ms) was associated with a reduced risk of all-cause death or heart failure hospitalisation (HR 0.786, 95% CI 0.658–0.939; p=0.008) after adjustment for baseline LVF (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 associated 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 infarct 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.

PI523 | BEDSIDE
Cardiac magnetic resonance findings in active rheumatoid arthritis
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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) techniques.

Methods: Fifty-eight consecutive patients (mean age of 50±12 years) with active RA underwent CMR. The study comprised with two female patient groups; patients with newly diagnosed RA starting treatment with conventional RA medication and patients with long-lasting active RA starting treatment with biological therapy. All patients with previously known cardiovascular disease or smoking were excluded.

CMR was performed to analyze native T1 mapping and LGE of the myocardium. Myocardial T1 mapping was performed in a mid-ventricular short-axis slice using a shortened Modified Look-Locker Inversion-recovery (shMOLLI) sequence. CMR imaging analysis was performed using tool developed for this purpose. LGE images were acquired after 15 min. after contrast agent. The location and pattern of LGE were visually estimated according to AHA 17-segment model.

Results: Mean native T1 relaxation times showed slightly elevated values compared to reference values: 1002±46 ms septum, 975±48 ms lateral wall in 1.5T and 1166±34 ms septum 1150±50 ms lateral wall in 3T (reference values: 965±48 ms in 1.5T and 1166±60 ms in 3T). Out of 58 RA patients 38 (58%) exhibited myo- cardiac diffuse fibrosis and scarring were visualized. One patient exhibited lateral transmural LGE indicating infarction. A hypointense infarct core revealed by T2-mapping was common and independently associated with all-cause death or heart failure hospitalisation post-discharge. T2 core reflects, not only IMH from microvascular destruction, but also functional MVO secondary to reduced tissue water as a result of reversibly obstructed capillary flow. T2 values are dynamic in the early reperfusion period and inversely associated with IMH. T2/IMH are biomarkers that may reflect the efficacy of therapeutic interventions in STEMI patients.

PI524 | BEDSIDE
1.5 T MRI in patients with classical cardiac implantable electronic devices: previous uncomplicated MRI study does not guarantee safety but increases the risk of adverse events
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Magnetic resonance imaging (MRI) in subjects with cardiac devices (CIED), though approved in legitimate cases, is still the subject of awareness and investigation due to uncertain security profile.

Aim: To find the factors that contribute to the occurrence of serious (SAE) and minor (MAE) adverse events of 1.5 T MRI examination in patients with CIEDs not certified for MRI environment.

Results: Between September 2009 and December 2014 MRI examinations were performed in 24 patients with CIED, 33 studies were conducted and a total number of 43 different anatomical regions were scanned. No SAE were observed as the result of 6 sessions (18.2%) in 6 different patients, a total number of 8 MAE occurred: decrease of R wave on ventricular lead in DDD system; decrease of P wave/increase of pacing threshold on atrial lead in DDD system; increase of pacing threshold on atrial lead in DDD system; software reversible reset and decrease of impedance on atrial and ventricular electrodes in DDD system; increase of troponin level in 3pts with DDD and VVI systems. Statistical analysis showed that the highest relative risk was associated with: more-than one or ICD lead, with the next MRI examination performed in one patient or with the next examination or more than one region scanned during the same MRI examination. Statistical significance was achieved for the last two situations and with lower relative risk - for the age of the patients and the number of regions scanned during one study.

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 coexistence 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 (Uhrab IV > 50% and LA DEMRI < 40%) and the large group (Uhrab IV > 50% and LA DEMRI > 40%). Outcome after catheter ablation (CA)

Results: The large group was older, had higher level of serum NT pro-BNP, LA appendage size, LA appendage emptying velocity, AF was more persistent in this group (63.6% vs. 37.2%, p=0.043). More extensive ablation was required to achieve endpoint in the large group (40.9% vs. 9.3%, p=0.006), but the acute success rate was significantly lower (71.4% vs. 95.3%, p=0.012). During mean 209.8 days of follow-up, the recurrence rate was significantly higher in the large group (45.5% vs. 20.9%, p=0.040). No factors were remained as independent predictors of large extent of LA DEMRI in multivariate logistic regression analysis.

Conclusions: In addition to commonly recognized risk criteria - particular caution is suggested in patients with classical CIEDs when: performing consecutive 1.5 T MRI and/or more than one region is scanned and in subjects with more-than-one or defibrillation lead.
CARDIOVASCULAR MAGNETIC RESONANCE IN CLINICAL PRACTICE II

P1526 | BEDSIDE
The left ventricular apical aneurysms in Chinese hypertrophic cardiomyopathy
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Background: The formation of left ventricular apical aneurysm (LVAA) is a distinctive subset in hypertrophic cardiomyopathy (HCM), however, it is still unknown about the prevalence and clinical characteristics of LVAA in Chinese HCM.

Purpose: The study was carried out to assess the prevalence and clinical characteristics of LVAA in Chinese HCM.

Methods: Of 1551 HCM patients, 30 (24 M/6 F) were identified as HCM with LVAA. Left cardiac catheterization was performed and coronary artery disease was ruled out. In addition, the LVAA was evaluated with late gadolinium enhancement magnetic resonance imaging (LGE-MRI). Pathological findings of LVAA were obtained in 5 patients.

Results: The prevalence of LVAA was 1.93% in Chinese HCM. In addition, LVAA occurred in 23 patients with mid-ventricular obstructive HCM and 7 patients with apical HCM. Two patterns of LVAA were identified with LGE-MRI: 21 LVAA with LGE and 9 LVAA with non-LGE. In particular, the transition from non-LGE to LGE LVAA was recorded in one patient. Pathological findings confirmed that LGE corresponded well with the fibrous tissue in LVAA. 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).

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.

P1527 | BEDSIDE
Clinical impact and usefulness of native T1 mapping in patients with idiopathic dilated cardiomyopathy
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Background: Myocardial extracellular volume (ECV) using cardiac magnetic resonance (CMR) T1 mapping is a promising technique for quantifying diffuse interstitial fibrosis in idiopathic dilated cardiomyopathy (DCM). However, it is limited by using gadolinium contrast in patients with chronic renal insufficiency. Native T1 is another index of T1 mapping, which is obtained without gadolinium contrast.

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 in survivors (141±33 msec vs. 131±59 msec, p=0.020).

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

P1528 | BEDSIDE
Substrates and predictors of acute and late myocardial dysfunction in acute myocarditis: a study performed by contrast enhancement cardiac magnetic resonance
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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 current 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 both to identify ventricular dysfunction (LVEF<50%) population was divided in 2 groups: without (n=84) and with (n=19) ventricular dysfunction. Among all clinical parameters, only CMR parameters of extensive myocardial edema (more than 3 segments) and the presence of a LGE stria pattern in almost 3 segments were related to ventricular dysfunction in the acute phase. At follow up only the presence of a intra mural stria pattern and an extension of LGE in more than 3 segments were significantly associated with 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 ventricular 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 identified the substrate of acute cardiac dysfunction and to provide information about the disease progression toward dilated cardiomyopathy at the follow up.

P1529 | BEDSIDE
Significant improvement of survival by T2* CMR in thalassemia major
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Background: In 2004 seven Italian centers reported survival data for patients with thalassemia major (TM) and showed that heart disease due to iron overload was the most common cause of death (Borgna et al Haematologica 2004). In the same years the accurate and noninvasive assessment of cardiac siderosis was made possible in Italy by the introduction of the T2* cardiovascular magnetic resonance (CMR).

Purpose: We aimed to evaluate if the deployment of T2* CMR had an impact on the mortality rate.

Methods: Four centers contributed to the present study, updating the data of the enrolled patients until August 31, 2010. For the patients who died, the date of the diagnosis represented the end of the study. 577 patients (264 F) died before the year 2000. MRI was performed in 406 patients (70.4%) and no patient had been scanned before his/her death. Among the survivors, MRI was not performed in the 59% of the cases (P<0.0001). The absence of an MRI scan was a significant univariate prognosticator for death (HR=43.25, 95% CI: 11.32–165.33, P<0.0001).

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

Conclusions: The prevalence of LVAA in Chinese HCM approximates to that in Western world. Furthermore, LVAA with LGE tended to have worse prognosis in HCM, and non-LGE LVAA might develop into LGE-LVAA. Further research was required to reassess the mechanism, treatment considerations and prognosis of the disease.
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 decompen-sated 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 association of microvascular ischaemia with outcomes has not yet been demonstrated independently from LGE. We investigated the interaction between LGE and perfusion abnormalities using novel high-resolution perfusion analysis techniques in conjunction with LGE quantification.

Purpose: To apply high-resolution quantitative perfusion analysis with and without pixel-wise correction for LGE maps and to compare high-resolution and standard quantification by pixel-wise correction.

Methods: 30 patients with HCM underwent CMR with Fermi constrained quantitative perfusion analysis on segmental and high-resolution data. The latter were corrected for the presence of fibrosis on a pixel-by-pixel basis.

Results: High-resolution quantification proved more sensitive for the detection of microvascular ischaemia in comparison to segmental analysis (See table). Areas of LGE were associated with significant reduction of myocardial perfusion reserve (MPR) leading to an overestimation of the total ischaemic burden on non-corrected perfusion maps. Using a threshold MPR of 1.5, LGE caused an overestimation of the ischaemic burden of 28%. The ischaemic burden was more severe in patients with fibrosis, also after correction of the perfusion maps, in keeping with more severe disease in this subgroup of patients.

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

<table>
<thead>
<tr>
<th>Group</th>
<th>PA-LGE (N=12)</th>
<th>PA-LGE (N=7)</th>
<th>PA-LGE (N=9)</th>
<th>PA-LGE (N=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Segmental</td>
<td></td>
<td></td>
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<tr>
<td>PA-LGE&lt;0.3</td>
<td>2.1±0.5</td>
<td>2.3±0.5</td>
<td>2.4±0.5</td>
<td>2.6±0.6</td>
</tr>
<tr>
<td>PA-LGE&gt;0.7</td>
<td>1.8±0.7</td>
<td>2.1±1.1</td>
<td>2.0±0.8</td>
<td>2.5±0.9</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.0002</td>
<td>&lt;0.0004</td>
<td>&lt;0.001</td>
<td>1.05</td>
</tr>
</tbody>
</table>

Conclusions: LGE is an important confounder in the assessment of the ischaemic burden in patients with HCM. High-resolution quantitative analysis with LGE correction enables the independent evaluation of microvascular ischaemia and fibrosis and should be used when evaluating patients with HCM.

Acknowledgement/Funding: Wellcome Trust/EPSRC WT 088641/Z/08/Z; BHF RE/08/003

P1531 | BEDSIDE

Prospective changes of left ventricular iron and function by MR in pediatric thalassemia major patients treated with different chelators or not chelated

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Background: There are no prospective studies comparing the effectiveness of 3 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 not chelated.

Methods: Among the first 1611 TM patients enrolled in the MIOT (Myocardial Iron Overload in Thalassemia) network, we considered pediatric patients who had maintained the same chelation regimen between the two MRI scans. MIO was quantified by a multislice multiecho T2* sequence. Function parameters were evaluated by cine images.

Results: Four groups of patients were identified: 6 patients (3 F, 10±2.2 years) treated with desferrioxamine (DFO)–mean dosage 43.7±6.8 mg/kg/die, 7 patients (3 F, 15±1.7 years) treated with deferiprone (DFP–75.0±9.2 mg/kg/die), 39 patients (13 F, 13±3.4 years) treated with deferasirox (DFX–26.6±5.7 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 no-chelated groups no patient showed a global heart T2* value<20 ms. In all 4 groups all patients who showed no MIO at baseline maintained the FU the same status. At baseline in DFX group 5 patients had heart T2* values<20 ms. The 4 patients with intermediate cardiac iron (T2* 20–20 ms) and the other 3 heart T2* values<20 ms at the baseline showed no iron at the FU while the patient with severe MIO (T2*<10 ms) remained in the same status at the FU. Non chelated patients had higher global heart T2* values at baseline (non-chelated 37.7±0.5 ms > DFP 35.3±4.9 ms > DFX 32.7±9.6 ms > DFO 31.9±10.5 ms) while DFP patients had higher global heart T2* values than DFO 39.5±6.1 ms > DFX 34.2±7.3 ms DFO 33.6±7.6 ms< on-chelated 28.9±4.0 ms.

In the DFO group at baseline 1 patient showed pathological left ventricular ejection fraction (LVEF) and he recovered at the follow up. In the DFP group at baseline 2 patients showed pathological LVEF and both were 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: This young population, DFO and DFP 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) compared to the "MD carrier group" and were prospectively studied. All MD carriers underwent a complete CMR study comprising cine- and late gadolinium enhancement (LGE)-imaging. In 22 of these women ("female MD carrier comparison group"), 7 DMD and 15 BMD, at least one first degree male relative with a previously established diagnosis of MD underwent the same CMR protocol and was assigned to the "male MD comparison group" (N=24, 6 DMD and 18 BMD).

Results: In the total MD carrier group, 17 (47%) MD carriers had at least one pathological CMR finding (five (14%) with a reduced LV-EF and 16 (44%) with pathological LGE). All LGE-positive patients (N=16) showed non-ischemic LGE with subepicardial involvement of the LV lateral free wall 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±11 yrs vs. 50±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 DMDc/BMDc carriers. Those DMDc and BMDc with cardiac involvement demonstrate the same myocardial fibrosis pattern as their male counterparts with overt disease.
P1533 | BEDSIDE
A prospective CMR study of cardiac iron and function in non-transfusion-dependent thalassemia intermedia patients treated with desferrioxamine
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Background: In thalassemia intermedia (TI) patients no observational study prospectively evaluated in the real life the efficacy of the desferrioxamine (DFO) therapy in removing or preventing myocardial iron overload.

Purpose: The efficacy endpoint of this study is represented by the changes in cardiac T2* values and biventricular function parameters in non-transfusion dependent (NTD) TI patients after 18 months of desferrioxamine therapy.

Methods: Among the 325 TI patients enrolled in the MIOT (Myocardial Iron Overload in Thalassemia) network, we selected 129 TI patients NTD. We considered 29 patients who had been receiving DFO therapy alone between the two MRI scans. Cardiac iron overload was assessed by the multislice multi-echo T2* technique. Biventricular function parameters were quantified by cine SSFP sequences. Myocardial fibrosis was evaluated by late gadolinium enhancement (LGE) acquisitions.

Results: Mean age was 39.69±8.12 years and 14 (48.3%) patients were females. Patients starting DFO therapy at a mean age of 21.92±15.89 years. The mean administered dosage of DFO via subcutaneous route was 38.46±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%.

Conclusions: In this small population of sporadically or non transfused TI patients, the DFO therapy showed 100% efficacy in maintaining a normal global biventricular function. Three (14.3%) patients had myocardial fibrosis at baseline and FU MRIs, and this subgroup was considered. Three (14.3%) patients had myocardial fibrosis at baseline, all with a non ischemic pattern. At the FU two new occurrences of non-ischemic myocardial fibrosis were detected.

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 (ECG) is usually abnormal and up to 40% of patients may present with T-waves inversion (TWI). Cardiac magnetic resonance (CMR) has emerged as a non-invasive modality for the diagnosis of acute myocarditis by identifying in vivo regions with myocardial edema and necrosis (late gadolinium enhancement). Previous studies demonstrate by CMR a cause-effects relationship between myocardial edema and TWI in Takosu-Takubo cardiomyopathy. In the setting of inflammatory cardiomyopathy this relationship remain to be established.

Aim: To disclose the relationship between myocardial edema and TWI in patients with acute myocarditis.

Methods: We enrolled consecutive patients with suspected myocarditis as suggested by ECG discordant findings in which the diagnosis was confirmed by CMR fulfilling Lake Louise criteria. The ECGs were recorded the same day of the CMR. The presence of myocardial edema was quantified by both visual and semiquantitative analysis (using regional T2-ratio method analysis). The presence of LGE was assessed with an automated thresholding. Moreover a further ECG was collected after a 6 months follow up.

Results: 76 patients were enrolled. All patients had troponin I releasing (median peak 9.9 μg/L) and 62% had a preserved LV ejection fraction. In the setting of inflammatory cardiomyopathy this relationship remain to be established.

P1535 | BEDSIDE
Pre-contrast T1-mapping and extracellular volume mapping for the assessment of myocardial fibrosis: A validation with histologic sample
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Introduction: Contrast enhanced T1 mapping allows for the detection of increased extracellular volume (ECV) in myocardial fibrosis. However, increased tissue collagen is also associated with prolonged pre-contrast T1. We investigated the value of pre-contrast T1 mapping for assessing increased collagen in dilated cardiomyopathy (DCM) by using histologic sample as a reference.

Methods: Twenty DCM subjects (18 men, 57±16 years old) underwent pre- and post-contrast T1-mapping as well as late gadolinium enhanced (LGE) MRI using a modified Look-Locker inversion recovery sequence at 3. T1 values were quantified within the septal myocardium and LV blood pool with a heart rate correction. ECV was quantified from pre- and post-contrast T1 values of the blood and myocardium with histogram fitting. Biopsy samples were used for quantification of collagen volume fraction (CVF) using picrosirius red staining.

Results: LGE was observed in 5 of the 20 patients on LGE MRI. While patients with non-ischemic LGE had significantly greater CVF than those without (27±15 vs. 13±8%, p<0.05), substantial overlap was found between patients with and without LGE. Both pre-contrast T1 and ECV were significantly associated with CVF (r=0.68, 0.71, p<0.05). Inter- and Intra- observer reproducibility for native T1 and ECV were 0.90, 0.98, 0.94 and 0.99, respectively.

Conclusion: The current results demonstrated that both native T1 and ECV have a good correlation with histological collagen fraction in DCM patients. Diffuse myocardial fibrosis in DCM may be reliably assessed by native T1 mapping without administration of gadolinium contrast agent.
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).

Conclusion: Increased resting levels of PRD predict development of exercise-induced TWA.

P1537 | BEDSIDE

Early repolarization pattern in patients with false tendons

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Background: Although early repolarization pattern (ERP) has been considered for long to be a normal electrocardiographic finding, it has been recently linked to sudden cardiac death. Exact mechanism underlying this electrocardiographic phenomenon is not well established. False tendons are (FT) fibromuscular bands that traverse the left ventricular cavity and often contain conduction tissue which has been associated in some case reports with ventricular tachycardias.

Objectives: To investigate the electrocardiographic characteristics of patients with FT and their association with ERP.

Methods: We studied 60 non-cardiac subjects with FTs and another 60 non-cardiac subjects with ERP. Patients were classified according to presence of ERP and FTs to: ERP+FT (Group 1, n=62), isolated ERP (Group 2, n=37) and isolated FT (Group 3, n=31). ERP was defined as J point elevation manifested either as QRS slurring (transition from the QRS segment to the ST segment) or notching (positive deflection on terminal S wave), upper concavity ST segment elevation for more than 0.1mV and prominent T waves in at least 2 contiguous leads. False tendons were defined (by 2D TTE) as bands stretching across the left ventricle for more than 0.1mV and prominent T waves in at least 2 contiguous leads. False tendons were identified 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. PFR, 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 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: Echocardiography and 12-lead resting ECGs were performed in 326 hospitalized, otherwise normal African cardiac subjects with echocardiographic LVH in a native Tanzanian population.

Methods: Echocardiography and 12-lead resting ECGs were performed in 326 hospitalized, otherwise normal African cardiac subjects with echocardiographic LVH in a native Tanzanian population.

Results:

<table>
<thead>
<tr>
<th>Risk Variable</th>
<th>Standardized coefficients</th>
<th>p-value</th>
<th>Standardized coefficients</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.11 (0.04–0.18)</td>
<td>0.001</td>
<td>0.06 (−0.02–0.15)</td>
<td>0.162</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.05 (0.02–0.15)</td>
<td>0.01</td>
<td>0.07 (0.00–0.13)</td>
<td>0.544</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.02 (−0.14–0.10)</td>
<td>0.932</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>−0.06 (−0.13–0.01)</td>
<td>0.117</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max HR</td>
<td>0.02 (−0.09–0.04)</td>
<td>0.399</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline heart rate</td>
<td>0.03 (−0.04–0.01)</td>
<td>0.252</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta blockers</td>
<td>0.11 (0.04–0.18)</td>
<td>0.003</td>
<td>0.10 (0.01–0.19)</td>
<td>0.038</td>
</tr>
<tr>
<td>History of MI</td>
<td>0.05 (−0.02–0.11)</td>
<td>0.183</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PRD at rest</td>
<td>0.22 (0.16–0.29)</td>
<td>&lt;0.0001</td>
<td>0.20 (0.14–0.26)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion: The ECG sensitivity detected in this study is much higher than that respectively for Sorkollow-Lyon, Cornell-product and for either criterion. The ECG sensitivity detected in this study is much higher than that respectively for Sorkollow-Lyon, Cornell-product and for either criterion.

P1540 | BEDSIDE

Heart rate variability in patients with false tendons


Background: Ventricular arrhythmia (VA) is one of the electrical myocardial instability (EMI) markers. It is important to study other markers, such as fragmentation of QRS (QRS) complex, microvolt T-wave alternans (mTWA), heart rate turbulence (HRT) and heart rate variability (HRV).

Methods: To study the markers of EMI (VA, QRS 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 VEChour without any therapy. Structural abnormality in the heart was excluded by an ECG, echocardiogram, stress ECG and cardiac MRI. EMI markers were analyzed using Holter ECG and ETT (protocol Bruce). ETT was performed up to submaximal heart rate 85% or more.

Results: During Holter ECG 59% of VA was monomorphic. Night type of arrhythmia was determined (387±152 VEChour during the day vs. 2003 VEChour at night, P<0.05). Nonsustained VT was in 8% of patients. QRS in sinus complex was not found. QRS in VEC was registered in 7% in the II, III, aVF leads. mTWA was positive in 59%. Pathological turbulence onset was in 3.7%, while turbulence slope was in the normal range in all patients.

Conclusions: HR participates in the HRV predictive value, however this impact depends on the prognostic power of HR and is different for different indices and outcomes. DC reveals the strongest predictive power with the least dependence on HR.
At the peak ETT VA persisted in 44%, mean 3.4 SVE/m2. At the recovery period (RP) VA gradually returned to the pretest values. At the 1 min of RP VA was in 44% (3.5 SVE/m2), at the 3 min of RP - 48% (5.4 SVE/m2), at the 5 min of RP - 53% (7.9 SVE/m2).

**Conclusion:** We found no abnormal markers that could indicate structural changes of the myocardium. However, we observed the pathological changes due to autonomic nervous system modulation (the abnormal mTWA in LV in 289% 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 of 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. QTcF was performed 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±7.3bpm and QRSd 99.8±25.3ms. Sinus rhythm (SR) represents 87.9%, 7.5% AF/AFL, 4% ventricular pacing and 0.6% other. All patients were included in the analysis.

Overall, QTcB (435±38ms) was significantly longer than QTcF (421±35ms) and QTcR (422±26ms) p<0.001. Risk classification based on QTcF considered 41.5% less patients at risk vs QTcB (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 withdrew following parameters as significant predictors of early mortality: Hazard ratios: absence of SR 2.34 (1.65–3.31); age 1.06 (1.05–1.08); HR 1.033 (1.027–1.038); 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 2.8 (0.9–3.9), QTcF 2.9 (2.0–4.1), QTcR 3.3 (2.3–4.7).

**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 or without structural heart disease and patients with CAD.

**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 (fQRS) 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 VECday (28 males) were divided into 2 groups.

Group I: 27 patients without structural heart disease, mean age 42±15years, 436±196 VEC/hour, ejection fraction (EF) 65±6% by Simpson. Structural abnormality of the heart was excluded using an ECG, ecoCG, in some cases stress ECG and cardiac MRI.

**Results:** Group II: 25 patients after myocardial infarction (mean age 59±11 years), VA (208±103 VE/hour), EF 47±8% by Simpson. EMI markers were analyzed using Holter ECG in both groups.

**Conclusion:** Group with LVH had monomorphic, typical type of arrhythmia was dominant (387±152 VE/hour during the day, 495±203 VE/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. MTWA 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 VE/hour during the day, 140±84 VE/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. MTWA 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 an imbalance of autonomic nervous system impacts on the maintenance of EMI in this group. While the daily type of arrhythmia, nonsustained VT, QRS fragmentation, pathological MTWA and HRT indicate the presence of EMI in patients with coronary artery disease, even when EF is preserved. ECG markers combination requires further studies.

P1543 | BEDSIDE

**The electrocardiogram (ECG) is a poor diagnostic tool for the detection of left ventricular hypertrophy (LVH) in elderly patients with aortic stenosis**

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**Royal Brompton Hospital, London, United Kingdom.

**Background and introduction:** Several current scoring systems exist for assessing the presence of left ventricular hypertrophy (LVH) on the electrocardiogram (ECG). However, whether these scoring systems remain accurate in the setting of severe aortic stenosis has not been previously 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±9.5 years, 49% Female) with severe aortic stenosis underwent CMR. The Romhilt-Estes LVH point score system was used to ascertain the presence of LVH on ECG. LVH on CMR was diagnosed using criteria of LV mass index ≥112 g/m² for men and ≥92 g/m² for females. The Marquette criteria were used to determine the presence of poor R wave progression.

**Results:** Overall 34/92 (36.9%) patients had confirmed left ventricular hypertrophy on CMR, 23/34 (67.6%) of these patients met ECG criteria for LVH. Of patients who did not have CMR evidence of LVH, 39/58 (67%) 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**


1 University Hospital of Fort de France, Department of Cardiology, Fort de France, France; 2 CHU Martinique, Centre Integre de la Drepanocytose, Lamentin, Martinique.

**Background:** Ventricular arrhythmias have been previously observed during acute crisis among patients with sickle cell disease (scd). No data lacking is available for patients in stable conditions.

In the present study, we examined the frequency and clinical correlates of ventricular arrhythmias in 125 consecutive patients with homozygous sickle cell disease referred to our centre for routine cardiac evaluation, and compared them with 116 controls. All participants completed a 24-hour Holter ECG monitoring, 6 min walking test distance (6MWT), echocardiogram, and standard blood tests.

The incidence of ventricular ectopy was significantly higher in the scd patients than in controls (195±341 vs. 24±39, p<0.001). Also, non sustained ventricular
ECG, arrhythmia analysis, signal processing / e-Cardiology other 251

tachycardia occurred in 15% of the patients with SCD, but none of the controls (p=0.03). Ventricular arrhythmias were significantly associated with older age, creatinine levels, left atrial indexed volume, velocity of tricuspid regurgitation, and not with left ventricular size or ejection fraction. They were also associated with higher ProBNP levels, and reduced 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 (± SD)</td>
<td>13.1±1.4</td>
<td>8.2±1.5</td>
</tr>
<tr>
<td>Creatinine level, μmoll (± mean SD)</td>
<td>73.5±13.9</td>
<td>56.2±26.3</td>
</tr>
<tr>
<td>Heart rate, beats/min (mean ± SD)</td>
<td>71.8±9.7</td>
<td>79.5±8.8</td>
</tr>
<tr>
<td>Total VPC, n (%)</td>
<td>24.9</td>
<td>195.2±431</td>
</tr>
<tr>
<td>NSVT, n (%)</td>
<td>0</td>
<td>14 (9.7)</td>
</tr>
<tr>
<td>Complex ventricular arrhythmias, n (%)</td>
<td>0</td>
<td>29 (20.0)</td>
</tr>
</tbody>
</table>

P1545 | BEDSIDE Evaluation of changes in T-wave alternans induced by 21-days of bedridden immobilization by head-down bed-rest

1Politecnico di Milano, Electronics, Information and Bioengineering Dpt., Milan, Italy; 2Università di Aragona, Aragon Institute of Engineering Research, Zaragoza; 3San José University, School of Computer Science, Zaragoza, Spain

Introduction: Cardiovascular deconditioning induced by microgravity exposure and reports on ventricular arrhythmias during space flight raise the question of whether reduced gravitational stimuli or immobilization could increase potential lifetime vulnerability to 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 scheme, and was normalized by the corresponding T wave amplitude (expressed as %TWA). Then, the normalized TWA amplitude of all ECG segments was averaged, yielding the average night normalized T-alterations index (ANNAI), which was computed, together with the heart rate–restricted indices (ANNAIX), considering only those ECG segments with average HR ≤ X=60,70,80,90 beats/min.

Results: Compared to PRE, HDT21 normalized ANNAI showed a trend to increase (median (25th,75thpercentile) from 0.29 (0.19,0.47) to 0.40 (0.31,0.52)), p=0.084. Interestingly, when considering heart rate–restricted indices, ANNAIX showed a significant increase after 21 days of HDBR (p=0.05) for ANNAI60 (0.28 (0.19,0.43) vs 0.42 (0.31,0.52)) and with p=0.062 and p=0.055 for ANNAI70 and ANNAI80, 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=119) or computerized tomography angiography (CTA) (n=119). The data were collected in three populations (see table). Population 1 and 3 were obtained at Aarhus University Hospital, Denmark and population 2 was collected at Copenhagen University Hospital, Denmark. The recordings were used for improvement, calibration and validation of the CAD-score algorithm. The algorithm automatically validates the suitability of the recordings and thus excluded 28 (9.4%) subjects (arrhythmias, excess noise or poor recording quality), providing a quantitative acoustic CAD-score in suitable subjects based on diastolic sound characteristics.

Quantitative coronary analysis (QCA) was performed after CAG. CAD was defined by at least one >50% diameter stenosis (DS). Non-CAD was defined as either: no coronary stenosis exceeding 30% DS in QCA or a negative CTA (no CAG performed). Subjects with a maximal CAG stenosis in the 30–50% DS interval and subjects with a stenosis identified by CTA, which was not confirmed by CAG, were defined as having insignificant-CAD.

Results: The CAD-score was higher in subjects with than subjects without CAD in all three populations (see table). Using CAD-score for classification of CAD and non-CAD cases gave areas under the receiver operating curves (AUC) from 63.3% to 84.0%.

Population Number of subjects CAD-score (mean ± std) AUC (95% CI)

<table>
<thead>
<tr>
<th>Population</th>
<th>non-CAD</th>
<th>Insign. CAD</th>
<th>CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population 1</td>
<td>25±13</td>
<td>29</td>
<td>21</td>
</tr>
<tr>
<td>Population 2</td>
<td>15</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>Population 3</td>
<td>38</td>
<td>13</td>
<td>12</td>
</tr>
</tbody>
</table>

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

Acknowledgement/Funding: Acarix a/s

P1547 | BEDSIDE Continuous monitoring with an implantable loop recorder improves outpatient heart failure care

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Introduction: Heart failure (HF) patients have an increased risk of future adverse events. Little is known about the incidence of (sub)clinical arrhythmia’s in stable ambulatory HF patients. Timely detection of relevant events could improve patient management. Implantable loop recorders (ILR) allow for continuous intensive monitoring of HF patients in an ambulatory setting by implementation of home-monitoring, however no studies are available whether an ILR can impact HF care. We investigated whether ILR diagnostic data could change HF patient management in 3 large community hospitals.

Methods: Eligible patients were in stable ambulatory condition (NYHA II or III), had systolic or diastolic HF with EF <35%, a virtual CHADS2 score <2, no device indication, no antiocoagulant use and no previous AF documentation. After ILR insertion (Medtronic Reveal XT), all patients were put on home-monitoring and seen every 3 months up to one year at the outpatient clinic by their cardiologist. Relevant pre-specified ILR data (pauses ≤3 sec, patient registered pauses, AF or SVT >6 min, NSVT ≤3 beats, 2nd or 3rd degree AV block) were shared with their cardiologist. Subsequent therapeutic decisions were documented.

Results: Between July 2011 and May 2013, 30 patients were implanted with an ILR. At baseline, patients were aged of 72±9 and in NYHA II (25) or III (5). 24 patients had systolic HF and 66% had an HF history of >6 months. Mean EF was 44±7.8, 83% were on beta blockers and 90% on ACE-inhibitors. The ILR had excellent sensing throughout the study (R wave amplitude 0.54±0.19 mV). During FU 4 ILR were removed. Mean time to a pre-specified event was 5.8±3.4 months. In 15 patients (50%) pre-specified events were detected: 5 pauses ≤3 sec, 2 NSVT, 7 AF ≤6 min, 1 SVT ≤160 bpm). Based on the ILR data the following therapeutic changes were executed: 1 pacemaker implant, 7 initiations of (N) OAC, and 6 adjustments beta-blocker dose. Of the pre-specified ILR events detected in the study, none were detected by the routine outpatient clinic visits.

Conclusion: Ambulatory HF patients have a high incidence of subclinical but relevant arrhythmias. Intensive continuous monitoring with an ILR significantly changed patients management in 47% of patients.

Acknowledgement/Funding: unrestricted research grant Medtronic
acknowledgement/funding: Japanese and Swedish healthcare context.

Monitoring has not been implemented for HF patients in Japan and Sweden. Only N.K from the Japan Society for the Promotion Science (e.g., cannot envisage how it works, and lack of equipment), healthcare professionals (low-high expectations) were to reduce hospitalizations (8.3 in Japan and 7.5 in Sweden). The highest expectations of telemonitoring rated on a scale from 0–10 (by 35% p < 0.047). PKP-2 mutation did not have any influence on the distribution of QRS notching did not differ between PKP2 positive and negative documents 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, bothsided. Only the distribution of the disease based on task force criteria as well as in the assessment of the distribution area for the right anterior side and on the duration of the amplitude. PKP-2 mutation seems to have no influence on it. BSPM can quantitatively characterize EW and should be applied for follow-up-investigation in order to document progressive changes.

Methods: Clinical data: In 28 AF patients (left atria 43±5 mm; n=13 persistent), we measured atrial conduction at 64-pole catheters (Constellation, BSCI) while pacing into AF, using custom software to identify AF rotors as phase singularities. Computer models: Monodomain simulations used isotropic sheets and the Fenton-Karma (FK) model. Conduction slowing was coded by spatially varying FK parameters of excitability. AF was initiated and ablation lesions were modeled as 4 mm radius disks of inexcitable tissue.

Results: In patients, conduction showed rate-dependent slowing at AF rotor sites (by 35% p < 0.001), that varied throughout atria (p<0.05). In computer models, several mechanisms enabled ablation to terminate AF. 1. For rotors anchored in low excitability (slowly conducting) regions (fig. 1A, circle), lesions enabled the wave front and back to meet, de-anchoring the rotor to terminate AF (fig 1B,C). Ablation can also 2. Create an excitable gap that can be invaded by fibrillatory waves to terminate reentry (figure 2A–D); 3. Anchor a rotor, converting AF to flutter.

Results: To patients with AF exhibit marked spatial gradients in atrial conduc-
tion velocity that provide several mechanisms by which localized ablation can terminate an AF rotor. Clinical studies should define if AF sources or regions of disorganization co-localize with sites of fiber anisotropy.

Methods: Noninvasive measurement of stroke volume using impedance cardio
graphy

Introduction: Stroke volume is an important measure in the clinical evaluation of cardiac patients. Impedance cardiography can be used to noninvasively measure cardiac performance. Classically, three points are derived from the impedance cardiogram (ICG): 1. The “B point” represents the moment of opening of the aortic valves 2. The “C point” the moment of maximal flow of blood through the thoracic aorta and 3. The “X point” depicts the moment of closing of the aortic valves. Stroke volume is computed using the product of the amplitude of the C point and ejection time, weighing for blood resistivity, baseline thorax impedance and the total volume enclosed by the measuring electrodes.

Objectives: This study aims to validate systolic time intervals and stroke volume measured by impedance cardiography.

Methods: 77 Healthy volunteers (41 girls, 36 boys) with an average age of 11.5 y (range 1–18) were recruited to undergo simultaneous recording of both impedance- and echocardiography. Impedance cardiography was measured using the VU Ambulatory Monitoring System (VU-AMS). In the echocardiogram, the 3 systolic time intervals of interest were mapped using a pulsed wave Doppler flow signal over the left ventricular outflow tract in a parasternal 5 chamber view. Stroke volume was assessed using velocity time integral, Bland-Altman plots and Intra Class Correlations were used for analysis of the agreement between TTE and ICG.
P1552 | 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-invasive 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. Differentely, 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 synergy 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) was developed for the specific task of distinguishing the noise of the echo image from the presence of cardiac tissue. Therefore the KNN has the goal of highly precision segment 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).

The 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 performed 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 EndDiasstolic (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 78±14 mL; LVEF of 56±13% and area of the LV M was calculated to 174±12 mm² 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.

P1554 | INTERVENTIONAL
Interobserver and intraobserver validation of a novel echocardiographic 3D automated software for the assessment of mitral valve anatomy
University Hospital Ramon y Cajal de Madrid, Cardiac Imaging, Madrid, Spain

Background: The increasing number of interventional procedures demands non-invasive techniques to be not only accurate but also reproducible for its use in clinical practice. In this regard, the future of 3D echocardiography requires not only superb image quality with high temporal and spatial resolution but also ease of use, reliable and accurate quantification. For this reason new technological developments need to prove their accuracy with higher reproducibility before they can be used in clinical practice replacing the available conventional methods.

Purpose: Thus, the aim of our study was to evaluate the inter- and intra-observer reproducibility of a novel full-automated software in the evaluation of MV anatomy compared to routine clinical manual 3D assessment.

Methods: 36 out of 56 screened patients referred to our Cardiac Imaging Unit for TEE were included.3D TEE analysis was performed both manually and with the automated software. Same volume dataset and frame were used for both manual and software analysis, which included the following parameters: intercommissural distance, the area of annular mitral and the leaflets length. 3D mitral valve images were imported for analysis into the software eSie Valves (Autovalve prototype version 1.22.).Manual measurements of the MV were performed using QLab 11; Philips Medical System. To test interobserver variability between both methods, all images were analysed by 2 cardiologists that independently reviewed the 3D images. One observer repeated the measurements in 15 randomly selected cases to assess intraobserver variability. At both time points the intraobserver test was repeated by the second observer and intraobserver variability were analysed using the Bland-Altman method. Interobserver and intraobserver agreements for qualitative analysis score by 3D Echo manual and software assessments were calculated using intraclass correlation coefficient.

Results: Interobserver variability assessed by the intraclass correlation coefficient was superior for the automatic software: intercommissural distance 0.997 vs. 0.76; mitral annular area 0.957 vs. 0.858; anterior leaflet length 0.963 vs. 0.734 and posterior leaflet length 0.936 vs. 0.838. Interobserver variability was good for both methods with a better level of agreement with the automatic software.

Conclusions: The novel 3D automated software is more reproducible in MV anatomy assessment compared to 3D manual evaluation. For this reason new technological developments with higher reproducibility can be used in clinical practice replacing the available conventional methods.

P1555 | SPOTLIGHT
Ritmo project (real time continuous web monitoring) a model of a multidisciplinary approach for safely managing of new therapies
S. Nodari1, M. Triggiani1, L. Lupi1, A. Manerba1, E. Rocco1, C. Villa1, N. Dasseni1, G. Milesi1, N. Berlinghieri1, F. Gilisenti1, 2University of Brescia, Department of Clinical and Surgical Specialties, Cardiology section, Brescia, Italy; 3Health Telematic Network srL, Brescia, Italy

Introduction: According to the decision of the Committee for Medicinal Products for Human use (CHMP), first dose administration of tigloholm must comply with the following conditions: 1) 12-lead electrocardiogram (ECG) and blood pressure (BP) measurement prior to administration of the first dose and thereafter 6 hours later; 2) Measurement of BP and heart rate every hour for 6 hours after first dose administration; 3) Continuous ECG monitoring (CEM) during the first 6 hours of treatment.

Aim of the study: To evaluate the effectiveness of our virtual intensive care unit connected with neurological departments for the continuous cardiology web
monitoring during the first fingolimod dose administration in patients (pts) with multiple sclerosis (MS).

Materials and methods: Health Telematic Network (HTN), in cooperation with the Cardiology Department of the our University Hospital, has installed in a selected number of Neurology Departments, the web-connected information center IntelVue Philips M315D. Every of treated with fingolimod was remotely monitored during the first 6 hours thereafter the administration of the first dose. Reporting of ECG outcomes was carried out by HTN with 24 hour availability of a remote cardiology call-center, with either external reporting service (remote MS sites where the cardiologist was not available for consultation), or with the support of internal cardiology service where available (local MS sites).

Results: One hundred and eleven sites with active ECG and 61 sites with remote reading system have actively participated in the RITMO project and 845 pts were read. The following events were reported: atrioventricular block (AVB) in 30 pts, 2nd degree AVB Mobitz I in 20 pts, 2nd degree AVB Mobitz II in 8 pts, prolongation of QTc interval in 55 pts, ventricular arrhythmias (singles or couples) in 75 pts and only 1 case of non-sustained ventricular tachycardia.

Conclusion: The RITMO project based on real-time web-based telemetry has represented an optimal solution for the first fingolimod dose administration, according to CHMP indications. RITMO project is the first example of telemonitoring in a network of neurology departments, and could pave the way for using a 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 a 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 angiogenic, arteriogenic and vasculogenic. Thus, we assumed that CST might exert beneficial effects in experimental MI.

Methods and results: To test the effect of CST on cardiac angiogenesis in vitro, matrigel assays with human coronary artery endothelial cells (HCAEC) were performed. CST significantly mediated capillary like tube formation comparable to basic fibroblast growth factor (bFGF), which was used as positive control (rel. tube formation vs. ctn: CST 1.2±0.1, p<0.05). Immediately, blockade of bFGF either by a bFGF-antibody (Ab) or a specific receptor blocker (PD173074) resulted in abrogation of effects suggesting a bFGF-dependent mechanism.

Moreover, C1T induced proliferation of HCAEC and human coronary artery smooth muscle cells (HCSMC) as determined by BrdU-incorporation. Similar to the matrigel assay blockade of bFGF attenuated the effect (HCAEC: rel. proliferation CST 1.1±0.1, p<0.001; CST+bFGF-Ab 1.0±0.1, p<0.001 vs. CST; CST+PD173074 0.7±0.1, p<0.001 vs. CST; HCSMC: relative proliferation vs. ctn: CST 1.1±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 detection of hypoxia inducible factor (HIF) and angiogenesis related signal regulated kinase 1/2 by CST in these cell lines. To evaluate the effect of CST on cardiomyocyte apoptosis in vivo the mouse myocardial infarction/reperfusion model was performed. After reversible ligation of the left anterior descending artery an intra-myocardial injection of CST or saline 0.9% (control) was performed. In this animal model CST-treatment was associated with a significant reduction of cardiomyocyte apoptosis (apoptotic cardiomyocytes/HPF: CST 9.1±0.95 vs. ctr. 19.36±1.74, n=8/group, P<0.01).

Conclusion: Due to its favorable effects on cardiac vascular cells CST might qualify as potential candidate for therapeutic angiogenesis in MI.

P1557 | BENCH
Protein phosphatase 1 beta is modulated by chronic hypoxia and involved in the angiogenic endothelial cell migration
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Background and aim: Endothelial cell migration is required in the physiological angiogenic process, but also contributes to various pathological conditions, including tumor vascularization. Protein phosphatase 1 (PP1) is the major serine/threonine specific protein phosphatase and the expression of PP1cβ, the beta isoform of the catalytic subunit of PP1, has been shown to be upregulated in certain cancers, as well as in chronic hypoxia, one of the major regulator in angiogenesis and vascular remodeling.

The finding that PP1cβ is overexpressed in several cancers, and that angiogenesis is a hallmark of cancer development, with certain tumors developing a hypoxic microenvironment to further potentiate its vascularization and growth, suggest that PP1cβ might play an essential role in angiogenesis. Hence, the potential role of PP1cβ in angiogenesis is investigated in the present study.

Methods: We examined PP1cβ protein level in pediatric heart following chronic hypoxia and found PP1cβ upregulation in cyanotic compared with acyanotic myocardium. By treating HUVEC cells with hypoxia mimicking agent, PP1cβ protein level increased with maximum at 8 hours. The effect of PP1cβ pharmacological inhibition, in addition to knocking down and overexpressing PP1cβ, on endothelial cell migration and morphogenesis was examined in vitro wound healing scratch assay and endothelial tube formation assay. The PP1cβ knockdown effect on focal adhesion formation (vinculin) was evaluated by immunocytochemical staining with specific antibodies.

Results: PP1cβ knockdown significantly reduces endothelial cell migration, but not proliferation. PP1cβ knockdown has no significant effect on endothelial tube formation. Endothelial cell migration in the knockdown group is restored to the control level upon consecutive transfection with PP1cβ CDS. Furthermore, PP1cβ knockdown induces a profound cytoshkeletal reorganization, loss of focal adhesion sites and impairment of focal adhesion kinases (FAK) activation.

Conclusions: PP1cβ is regulator of endothelial cell migration, which is critical in the angiogenic process. PP1cβ inhibition reduces endothelial cell migration through focal adhesion turnover and actin polymerization pathways.

P1558 | BENCH
Glucagon-like peptide-1 (GLP-1) directly promotes angiogenesis via PKA/AMPK-dependent autophagy in endothelial cells
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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 autophagy in myocardium; however, it remains unclear whether GLP-1 may modulates angiogenesis in heart.

Purpose: To evaluate the impact of GLP-1 on angiogenesis and its link to endothelial function.

Methods: T2DM was treated with Ex4 (24 nmol/kg/day for 4 weeks). Cardiac capillary density was measured by CD31 immunohistochemical staining Cultured human umbilical venous endothelial cells (HUVECs) were used for in vitro experiments. Analyses for the changes in activities of autophagy (LC3-turnover assay and protein levels of p62 and Beclin1), and angiogenesis (tube formation assay and Akt/AMPK/eNOS activity), were evaluated. Role of PKA was assessed by CREB phosphorylation and RNA interference (siRNA). Effect of autophagy was assessed by use of pharmacological inhibitor 3MA and siRNA of autophagy-related gene (ATG) 5, ATG7, and p62.

Results: Immunohistochemical analyses revealed that T2DM exhibited reduced cardiac capillary density, which was reversed by Ex-4 treatment with concomitant amelioration of systemic diabetic condition. The Ex-4 treated heart exhibited increase in myocardial cyclic AMP concentration. We thus observed direct impact of Ex-4 and cyclic AMP elevation on ECs, in which GLP-1 receptor expression was confirmed by immunoblot and QPCR. In vitro angiogenesis assay revealed that Ex-4 and PKA enhanced angiogenesis. Activated PKA was facilitated angiogenesis and autophagy in HUVECs and the PKA/AMPK/eNOS phosphorylation levels of Ex-4 treated HUVECs were enhanced. Of note, each Akt activity remained unchanged. PKA inhibitors (H89, Rp-AMP; and siRNA for catalytic subunit of PKA) reduced Ex-4 and autophagy. H89 and ATG5 knockdown significantly reduced angiogenesis. Autophagy was impaired by 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 ischemia-mediated angiogenesis by ppar alpha independent modulation of thioecdin inducing protein
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Background: Fenofibrate, a peroxisome proliferator activated receptor alpha (PPARα) agonist, reduced amputation events in the Fenofibrate Intervention and Event Lowering in Diabetes study. However, the mechanisms for the vascular benefits of fenofibrate in diabetes mellitus (DM) are largely unknown.

Purpose: To investigate the effects and mechanisms of fenofibrate on impaired ischemia-mediated angiogenesis in diabetes in vitro and in vivo.

Methods: In vitro angiogenic events (tube formation) and in vivo angiogenic events (tibialis anterior ischemia-reperfusion injury) were assessed in primary human endothelial cells (ECs) under normal (5mM) or high (25mM) glucose with/without fenofibric acid (50mM). PPARα independent mechanisms of fenofibrate were investigated by use of PPARα antagonist and PPARα KO
murine endothelial cells. Hindlimb ischemia (HLI) was induced in a murine model of DM in wildtype (WT) and PPARs knockout (KO) mice with/without fenofibrate. Ischaemic recovery was assessed by laser Doppler (LDI) and capillary density analysis.

**Results:** Fenofibrate (FA), the active component of fenofibrate, rescued high glucose-induced impairment in EC migration (82.5±1.1% vs. 52.8±0.4% of control, P<0.05) and tubulogenesis (89.5±2.0% 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 thioredoxin-interacting protein (TXNIP) (P<0.05), an exquisitely glucose-sensitive regulator of angiogenesis. Interestingly, overexpression of TXNIP abrogated the protective effects of FA on tubulogenesis under high glucose (P<0.05). In vivo, fenofibrate rescued diabetes-related impairment in ischaemic blood flow recovery and angiogenesis in both WT (LDPl: P<0.05, Capillary density: p<0.001) and PPARα KO mice (LDPl: P<0.01; Capillary density: p<0.001), consistent with a PPARα-independent effect. Fenofibrate also reversed diabetes-related overexpression of TXNIP in WT (P<0.01) and PPARα KO mice (P<0.01), a finding associated with restoration of diabetes-related impairment in VEGF production to non-diabetic levels (0.94±0.12% vs. 56.5±1.4% of control, P<0.05).

**Conclusion:** Fenofibrate rescues diabetic impairment in ischaemia-mediated angiogenesis, in large part, by PPARα. Improved chaemic blood flow recovery and angiogenesis, in large part, by PPARα- independent reversal of high glucose-induced expression of thioredoxin-interacting protein (TXNIP) (P<0.05), an exquisitely glucose-sensitive regulator of angiogenesis. Interestingly, overexpression of TXNIP abrogated the protective effects of FA on tubulogenesis under high glucose (P<0.05). In vivo, fenofibrate rescued diabetes-related impairment in ischaemic blood flow recovery and angiogenesis in both WT (LDPl: P<0.05, Capillary density: p<0.001) and PPARα KO mice (LDPl: P<0.01; Capillary density: p<0.001), consistent with a PPARα-independent effect. Fenofibrate also reversed diabetes-related overexpression of TXNIP in WT (P<0.01) and PPARα KO mice (P<0.01), a finding associated with restoration of diabetes-related impairment in VEGF production to non-diabetic levels (0.94±0.12% vs. 56.5±1.4% of control, P<0.05).

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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 univariate (OR 1.445 (1.106–1.889), p=0.007) and multivariable (OR 1.643 (1.166–2.314), p=0.005) binary logistic regression analysis when adjusted for multiple cardiovascular risk factors and biomarkers. Receiver-operating-characteristic analysis demonstrated that anxA5 predicted thickened IMT with a positive predictive value 77.4%, specificity 65.8%, positive predictive value 76.4%, negative predictive value 61.0% at the optimal cutoff.

**Conclusions:** Circulating anxA5 plasma levels are related to carotid IMT but not coronary plaque composition in high-risk patients with type 2 diabetes.

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**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 marker 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 200 and Hba1c > 6.5%), who had a fasting plasma glucose of 110mg/dl or higher, or who took oral diabetic agents, we measured FMD and EndoPAT-RHI at the same time. The scatter diagram showed no significant correlation between FMD value and EndoPAT-RHI. While FMD value was significantly associated with the number of conventional risks of CVD, such as age (over 75 years old), DM, hypertension (systolic blood pressure (SBP)<135mmHg), dyslipidemia (High LDL cholesterol, triglycerides, and HDL cholesterol), current smoking, obesity (Body Mass Index>25kg/m2), uric protein (albuminuria > 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: P=0.002, r=-0.14, albuminuria; P=0.0005, r=-0.17), EndoPAT-RHI was positively associated with these values (SBP: P≤0.0001, r=0.24, albuminuria; P=0.005, r=0.10). On the other hands, although there was no correlation between FMD and HOMA-R, insulin resistance index which calculated fasting plasma glucose/insulin (405), EndoPAT-RHI was negatively correlated with HOMA-R (P=0.002, r=-0.17).

**Conclusions:** Although both FMD and EndoPAT-RHI is same kind of examination which evaluates endothelial function, they each may evaluate different state of endothelial dysfunction. FMD and EndoPAT-RHI may indicate opposite reaction in patients with high SBP and albuminuria. Meanwhile, EndoPAT-RHI may be able to show endothelial dysfunction in IGM patient with insulin resistance which FMD could not catch in the early stages.

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**P1565 | BEDSIDE**

Usefulness of brachial flow-mediated dilation and platelet function to predict long-term adverse clinical events in subjects with heart disease

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

**Methods:** 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 <12 hours FMD and endothelium-independent, nitroglycerin-mediated vasoresponse (NTG) were assessed. Platelet aggregation was assessed by conventional aggregometry, and platelet adhesion and aggregation under flow conditions by cone-and-plate(let) technology (Impact-R).

**Results:** After a mean follow-up of 7±2 years there were 29 total adverse clinical events, of which 11 were CV end points. Subjects with CV events had significantly lower FMD compared to those without CV events (10.4±8.0% vs 17.5±9.7%, p=0.02), while NTG was similar in both groups. Furthermore, 73% with and 37% without CV events had FMD ≤ the median (p=0.02). Additionally, subjects with the highest (FMD>16.8%) compared to the lowest baseline FMD tertile (FMD<9.6%) had significantly the less CV events compared to the associated with low CV events (p=0.01) (Figure). ADP+ and arachidonic acid-induced platelet aggregation were significantly higher in subjects with compared to those without CV events (p=0.01). In addition, platelet adhesion which reflects platelet reactivity, as seen by surface coverage (SC) under flow conditions, was greater in those with than without CV events (14±8% vs 9±6%, p=0.05). Furthermore, more subjects without compared with CV events had SC < the median (62% vs 27%, p=0.02).

**Conclusion:** Tissue accumulation of AGEs is increased in patients with an Abdominal Aortic Anomaly but does not predict all-cause mortality during 7 year follow-up

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**Background:** Accelerated accumulation of tissue advanced glycation endproducts (AGEs) has been linked to cardiovascular disease and is 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 2013. AGEs were measured with the AGE-receptor, 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 was predictive after adjustment for age, gender, diabetes, smoking and history of coronary or cerebrovascular disease.
and myocardin protein expression induced by balloon injury and improved vascular endothelial function after short-term resistance training in healthy elderly people

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**Background:** Moderate- or high-intensity exercise training is well known to activate endothelial nitric oxide synthase (eNOS), resulting in the improvement of vascular endothelial function. Although asymmetric dimethylarginine (ADMA), endogenous NOS inhibitor, is reported to decrease NO production, it is still unknown whether ADMA affects the improvement of vascular endothelial function in exercise training. This study aimed to investigate the effect of serum ADMA on vascular endothelial function after short-term resistance training in healthy elderly people.

**Methods:** We recruited 20 healthy elderly people (71 ± 4 years, 17 males and 3 females) who had no habit of regular exercise. We measured serum ADMA and divided subjects into two groups based on the median of ADMA level: high ADMA and low ADMA groups. All subjects performed resistance training for 20 minutes a day for 4 weeks. We measured serum trombomandinol (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 0.53 μM, and the median was 0.42 μM. The TM and tPAIC decreased significantly after the training period in the high ADMA group (P < 0.05, respectively). There were no significant changes in TM and tPAIC before and after the training period in the high ADMA group. The RHI measured after the training period was significantly higher in the low ADMA group than in the high ADMA group (P < 0.1).

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

**P1568 | BENCH Angiotensin II downregulates microrna-145 to regulate kruppel-like factor 4 and myocardin expression in human coronary arterial smooth muscle cells under high glucose conditions**

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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-inflammatory response which mediates the expression of miR-145 in VSMCs. We investigated whether miR-145 serves as a critical regulator to regulate the downstream proliferation factor (such as Kruppel-like factor 4 [KLF4] and myocardin) in VSMCs under hyperglycemic condition.

**Methods and results:** Human coronary artery smooth muscle cells (HCASMCs) were cultured under high glucose conditions. Sustained high glucose at 25 mM significantly decreased the expression of miR-145 in HCASMCs. High glucose significantly increased angiotensin II (Ang II) secretion from HCASMCs and Ang II suppressed miR-145 expression in HCASMCs. Exogenous addition of valsartan, enalaprilat dehydrate, and antagonim-145 before high glucose stimulation reversed KLF4 and myocardin expression induced by high glucose stimulation, indicating the involvement of autocrine Ang II loop in the regulation of miR-145 in the regulation of KLF4 and myocardin expression. Ang II mediated the KLF4 and myocardin expression in high glucose state. MIR-145 significantly decreased KLF4 and increased myocardin expression in high glucose state. High glucose stimulation for 4 h and Ang II alone for 4 h without high glucose stimulation significantly increased KLF4 promoter activity in control cells. Overexpression of miR-145, addition of valsartan and enalaprilat significantly attenuated the promoter activity induced by high glucose. When the conserved site of miR-145 in the promoter area of KLF4 was mutated, the increased promoter activity induced by high glucose and Ang II was abolished.

**Conclusion:** Our study reveals that Ang II downregulates miR-145 to regulate KLF4 and myocardin expression in HCASMCs under high glucose conditions. Ang II plays a critical role in the regulation of miR-145 under hyperglycemia conditions.
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 ischaemia, a mechanism that may be impaired during hyperglycaemia. We therefore hypothesized that endothelial dysfunction during prolonged ischaemia followed by reperfusion can be reversed in persons without diabetes but not in persons with diabetes during postprandial hyperglycaemia. In our preliminary studies, post-prandial endothelial dysfunction was not apparent in younger control persons. Therefore, we investigated the effect of an OGTT on vascular function in younger and older healthy individuals.

Methods and results: Seven younger (median 25, range 23–28) and seven older (median 65, range 54–70) healthy persons underwent forearm blood flow (FFB) 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, glycaemia did not differ in younger and older persons while 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.

P1571 | BEDSIDE
Vascular ageing is apparent during an oral glucose challenge in healthy persons

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 (7.4±0.4 vs. 7.2±0.6, P=0.242), AIx(75) (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 in the annual absolute changes of PWV, FMD, AIx75 and cIMT. However, when a subgroup of patients ≤60 years with more rapid progression of endothelial aging was investigated, metabolic syndrome was associated with almost 7 times higher annual change of FMD (−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 correlation with standard, Tissue Doppler and Speckle tracking echocardiography, and a right heart catheterization (RHC). A blood sample was collected during the RHC in the distal peripheral circulation of the pulmonary arteries to perform the metabolic analysis. Samples were analysed with a 1H-NMR 500MHz spectrometer. An Orthogonal Signal Correlation (OSC) and a Projection on Latent Structures Discriminant Analysis (PLS-DA) were applied.

Results: Based on PVR we divided the population in Group A (N=8; PVR<1.6 uW; meanSD = 1.16±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 (25±5 vs 20±4 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 was related to a metabolic fingerprint depending on a limited set of metabolites: Group B was characterized by higher values of Lactate, Glucol, fatty acids, Acetocetate, Valine, Leucine, Isoleucine and VLDL/LDL, whereas Group A showed higher values of Choline, Betaine, Alanine, Glycine, Taurine, Arginine and 3-OH-butyrate; worthy of note is that all the compounds higher in Group A were related to the NO metabolism and endothelial function.

Conclusions: Increased PVR appear to be related to the presence of specific metabolites, in turn closely connected with endothelial dysfunction. Additionally, MBS was able to accurately identify the metabolic imbalance of vasoactive factors, able to determine and maintain the increased PVR. This approach could be useful for a better understanding of the pathophysiology of this severe complication of SSc.
Cardiovascular function is assessed 1.5 and 3 hours post-randomization to LMWH or saline placebo (30mg IV bolus and 1mg/kg subcutaneous dose). High-risk women are then randomized (FMD), and uterine artery Doppler. High-risk pregnant women exhibit abnormalities in baseline cardiovascular function. Acute improvements in endothelial function in response to LMWH suggest that this drug may prevent sPE via direct cardiovascular actions.

Results: 20 high-risk women and 10 controls have participated in the study. Gestational delivery was significantly easier in the high-risk group when compared to controls (34±0.6 vs 39±0.6 weeks; p<0.003), with 58% of the high-risk women developing PE vs 0% of the healthy controls. At baseline, HR was higher in the high-risk group as compared to controls (74±3 vs 73±2 bpm; p=0.01). Systolic and diastolic BP were higher in the high-risk group, although the difference was not significant (117±3 vs 109±3 mmHg; p=0.107, 68±3 vs 62±1 mmHg; p<0.01). Despite their higher HR, CO was significantly lower in the high-risk group as compared to controls (5.9±0.4 vs 7.5±0.3 L/min; p<0.0001). Systemic vascular resistance was also lower in the high-risk group (900±45 vs 1017±65 dyne·sec·cm⁻², p<0.003), consistent with the phenotype of established sPE. There was no significant difference in FMD between high-risk and control groups (6.4±1 vs 9.2±2%, p=0.07). Uterine artery Doppler-based pulsatility index was significantly higher in the high-risk group, although the difference was not significant (117±3 vs 109±3 mmHg; p=0.107, 68±3 vs 62±1 mmHg; p<0.01).

Women at high-risk of developing sPE exhibit abnormalities in baseline cardiovascular function. Acute improvements in endothelial function in response to LMWH suggest that this drug may prevent sPE via direct cardiovascular actions.

**P1576 | BEDSIDE**

**Impaired endothelial function and arterial stiffness in patients with pseudoexfoliative glaucoma**

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**Background:** Primary open-angle glaucoma (POAG) is one of the most prevalent causes of irreversible blindness and is associated with endothelial dysfunction and arterial stiffness. Pseudoexfoliative glaucoma (PEG) is another type of glaucoma observed in pseudoexfoliation syndrome. It is characterized by the deposition of pseudoexfoliative material not only to the anterior segment of the eye, but also to the vessels, heart and other organs.

**Purpose:** We evaluated the association of endothelial function and arterial stiffness with POAG and PEG.

**Methods:** Forty four POAG patients, 22 PEG and 38 healthy subjects (Cl) were included in this study. All subjects were free of cardiovascular or inflammatory diseases. Endothelial function was evaluated by flow-mediated dilatation (FMD). Carotid-femoral pulse wave velocity (PWV) was measured as an index of arterial stiffness and augmentation index (Aix) as a measure of arterial wave reflections.

**Results:** Between the three study groups CL, POAG, PEG there was no difference in age (67±10 years vs. 70±9 years vs. 66±12 years; p=0.12) or prevalence of male sex (70% vs. 57% vs. 50%, p=0.21). Importantly, there was a linear impairment of FMD (7.35±2.77 vs. 6.58±1.18 vs. 4.8±3.29, p=0.006), PWV (7.98±1.56 vs. 9.2±1.84 and 9.2±2.16/sec; p=0.004) and Aix (21.9±8.77 vs. 25.1±5.71 vs. 28.2±10.75; p=0.002) from CL to POAG and PEG. Interestingly post hoc test after Scheffe correction revealed also that PEG subjects had not only significantly impaired FMD, compared to control subjects, but also compared to POAG subjects (4.8±3.29 vs. 6.58±3.18; p=0.02).

**Conclusion:** Endothelial function and arterial stiffness is significantly impaired in patients with pseudoexfoliative glaucoma. These findings add weight to the pathophysiology of pseudoexfoliative glaucoma and support the theory that pseudoexfoliative fibrils may also accumulate and damage the arterial wall.

**LIPIDS IN ATHEROSCLEROSIS**

**P1578 | BENCH**

**Modulation of cardiac structure by epicardial adipokines**

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**Background:** 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 and adipokine-like substances secreted by the epicardium can act in a paracrine manner directly on the myocardium and influence its 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 media. After incubation, organotypic cultures were prepared for functional experiments. Epicardial adipocytes were prepared by enzymatic 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.
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 therapy, an unfavorable feature has been the considerable response 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 microRNAs in vitro in 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-30c-5p, miR-429-5p and miR-454-3p) were downregulated after atorvastatin treatment (P<0.05). Regulatory pathway examination showed that deregulated microRNAs interact with key genes of lipid metabolism (HMGCGR, LDLR, ABCA1, SCAP, INS1G1, LPL and SREBP1). Moreover, after sub grouping LDL-C reduction into quartiles of response according to specific lipid-lowering therapy, quartile 1 - poor response to atorvastatin - showed reduced expression of miR-106b-5p, miR-17-3p and miR-590-5p, whereas in the quartile 4 - enhanced response to simvastatin- miR-106b-5p, miR-17-3p and miR-183-5p were overexpressed.

Conclusions: Our results show, for the very first time worldwide, that statins modulate the microRNA expression pattern in vivo. Also, microRNAs miR-106b-5p and miR-17-3p, together with miR-590-5p and miR-183-5p, can be markers of decreased response to atorvastatin and high response to simvastatin therapy, respectively.

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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 vitamin D (25(OH)D) level. However, vitamin D deficiency and VDR gene polymorphisms (BsmI, ApaI, TaqI polymorphisms) and their associations with lipid levels need to be fully explored.

Materials and methods: We studied 449 women, aged 30 to 52 years old (mean age 35.8±5.7 years) determined by measurements of serum 25(OH)D level on Abbott Architect 8000 (USA), lipids level on COBAS INTEGRA 400/700/800 (Germany), VDR gene (Apal, BsmI, TaqI polymorphisms) - 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 (R=0.27, p<0.0008). Analysis showed that women with vitamin D deficiency (serum 25(OH)D level lower than 50 nMol/l) had high risk comparing to normal levels of HDL (OR 2.3, [1.04-4.59]) (p<0.05). HDL level was negatively associated with ApaI polymorphism. VDR genotype carriers of BsmI, ApaI, TaqI VDR gene polymorphisms were not significant difference (p>0.05). Women-carriers of BB and Bb genotypes (BsmI polymorphism) had lower triglyceride level compared with BB genotype carriers (1.32±0.5 and 1.54±0.09 mmol/l, respectively; p>0.05). Women-carriers of AA and Aa genotypes (Apal polymorphism) had higher total cholesterol and LDL than those with aa genotype (5.52±0.07 mmol/l and 5.14±0.15 mmol/l, respectively; p<0.05). LDL levels in women-carries of different genotypes of VDR gene TaqI polymorphism were the same (p>0.05).

Conclusions: The study showed that vitamin D deficiency and carriage of VDR gene polymorphisms (AA/AA genotypes and BB genotype) in women might possibly be a risk factor for dyslipidemia.

P1582 | BENCH
Local production of fatty acid-binding protein 4 in the extracellular 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 aortic root (Ao-FABP4) bloods were determined in 34 male patients with suspected or known coronary artery disease.

Results: FABP4 was expressed in adipocytes and macrophages within coronary atherosclerotic plaques, epicardial/perivascular fats and coronary thrombi. FABP4 was secreted from both adipocytes and macrophages into the conditioned medium. 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
dentitate its signaling. Hence, we added the HSPP27-auto-antibody complex to macrophages pre-treated with NBD cholesterol and found a 30% increase of secreted cholesterol-NBD into the medium (p<0.0001). Moreover, using an exo- osomal capture ELISA we show that exosome secretion is promoted (p<0.05). After treatment with the HSPP27-auto-antibody complex, finally, compared to the same concentration of HSPP27 without auto-antibodies, the HSPP27 auto-antibody complex increased the abundance of cholesterol-NBD positive exosomal particles by approximately 70%, as measured by flow cytometry.

Conclusion: HSPP27 has a dual action on cholesterol efflux. First, it promotes the upregulated expression of proteins participating in reverse cholesterol and is associated with increased HDL formation. Second, HSPP27 enhances cholesterol efflux via a novel exosomal pathway. Taken together, these data provide potential mechanistic explanations for the stabilization/regressive effects of HSPP27 on coronary atherosclerotic lesions.

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

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 (HSPP27) are predictive of reduced cardiovascular clinical events (MI, CVA, death). Moreover, attenuation of experimental atherogenesis, characterized by reduced cholesterol accumulation in the artery wall and serum can be achieved by augmenting serum HSPP27 levels. While the reduced influx of cholesterol into lesion may occur because HSPP27 binds to and reduces the expression of Scar-related Regulator A, this indirectly explains the stabilization/regression of established atherosclerotic lesions that we have also observed.

Hypothesis: Exogenous HSPP27 enhances cholesterol efflux from lesions by enhancing a) conventional and b) novel (exosomal) reverse cholesterol transport pathways.

Methods and results: a) THP-1 macrophages pre-treated with oxLDL and incubated with HSPP27 for 24h showed enhanced mRNA and protein expression levels for the reverse cholesterol proteins ABCA1 and ABCG1, as well as the upstream transcriptional factor LXRF, whereas treatment with a truncated (inactive C-terminus) form of HSPP27 (rC1) did not. As well, when THP-1 macrophages were labeled with NBD-cholesterol, treated with HSPP27 for 24h and then incubated with 40 ug/mL apoA1 or 100 ug/mL HDL for 1h there was a marked increase in cholesterol efflux to apoA1 and HDL-cholesterol. b) NBD-cholesterol and the exosome biomarker CD61 co-localized in exosome particles (as detected by FPLL and flow cytometry). In separate studies we demonstrated that HSPP27 auto-antibodies are generated in vivo and po-
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.

**P1585 | 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 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 perform pathological analysis of FABP5 expression in atherosclerotic lesions and compared the results against FABP4, a conventional biomarker of atherosclerosis. Furthermore, we evaluated their expression levels in macrophage cells under polarized states.

Methods: Serial cross-sections of aorta were exposed to 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 lesion possessing the vulnerable-like characteristics, and preferentially localized in macrophage infiltration areas (the correlation rate: r=0.75, P<0.05), but not in the smooth muscle cells and other connective tissues. The similar result was also seen in the FABP4 study. As for the outside tissues of aorta such as connective tissues, FABP4 but not FABP5 highly expressed. Furthermore, M1 polarized RAW264.7 cells showed significant higher expression levels of FABP5 and FABP4 (12.9±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

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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 search 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 error 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); there was a significant reduction in fibrous PV (SMD: −0.193 mm³, 95% CI: −0.255, −0.053; 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=0.882) tissue volumes were not statistically significant.

Conclusions: This meta-analysis indicates a significant effect of statin therapy on plaque and external elastic membrane volumes and fibrous and dense calcium volumes. There was no effect on lumen volume, fibro-fatty and necrotic tissue volumes.

**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...
P1587 | BENCH
Gold nano particles, conjugated to HDL reduces Lp-PLA2 level in human macrophages
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Background: Inflammation leads to macrophage accumulation in unstable atherosclerotic plaques, which eventually weakens the extracellular matrix and causes plaque rupture. Lipoprotein-associated phospholipase A2 (Lp-PLA2) is an enzyme produced by inflammatory cells, co-travels with circulating low-density lipoprotein (LDL), and hydrolyzes oxidized phospholipids in LDL. The product of Lp-PLA2 is bioactive lipids that are involved in the formation of foam cells and macrophage accumulation in lesion-prone vasculature, and are known to elicit inflammatory responses. HDL is known for its anti-atherosclerotic properties through various mechanisms, including inhibition of Lp-PLA2. We hypothesized that gold nano-particles which are scavenged by macrophages, can be used in order to deliver HDL to inflammatory plaques and thereby reduce inflammatory activity.

Methods: Human peripheral blood mononuclear cells (PBMCs) were isolated from healthy donors. The cells were allowed to differentiate into macrophages (validated by immunostaining) and were then incubated with GNPs and GNP conjugated to HDL. Lp-PLA2 levels were measured in the supernatant using ELISA. The hypothesis was tested in an in-vivo model of injured carotid artery in Sprague-Dawley (SD) rats. Rats were scanned using diffusion-reflection molecular imaging with near-infrared calcium tracer. In addition, CD14+ cells isolated from healthy donors were treated with either recombinant human IFNg or IFNg from conditioned medium (CM) derived from stimulated hVSMC-foam cells. Interestingly, it has been proposed that intracellular Hsp60: 3.8±1.2-fold, p=0.01. Further, mRNA levels for osteoclast markers, including RANKL: 6.4-±1.9-fold, p=0.01; and TRAP: 8.3±2.9-fold, p=0.01 increased significantly in patient fingertips. FH is a treatable disease. If premature development of cardiovascular disease can be assessed during childhood, the disease might be prevented.

Purpose: The purpose of this study is to evaluate vascular health using peripheral artery tonometry and specific biochemical markers in children with FH and compare results with healthy controls (HC).

Materials and methods: Following approval by the institutional review board 41 eligible participants were enrolled in the study. Group of 24 children with FH (13.9±2.4yrs) matched with 17 HC (15.2±2.2yrs). EndoPAT recorder was used for the determination of RHI as well as specific biochemical markers of endothelial function were assessed (hsCRP, ADMA, e-selectin, VCAM). RHI was evaluated in all children with FH and further compared with HC. Results: Significantly lower RHI were revealed in children with FH in comparison with HC (1.63±0.50 and 2.03±0.54 respectively; p<0.05). In addition, E-selectin (p<0.01) were also significantly increased in the FH subjects compared with the control group, but not levels of vascular cells adhesive molecule-1, asymmetric dimethylarginine neither high sensitive CRP. Conclusions: In the present study, we showed lower RHI and elevated E-selectin in FH when compared with FH. These findings suggest that children with FH and further the attainment of early ED detection when the atherosclerotic process is still reversible. This combined method might be a useful tool for cardiovascular risk stratification in children with FH.

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MITRAL VALVE DISEASE

P1589 | BENCH
Release of interferon-gamma by activated CD8-positive T cells in human calcified aortic valves fosters formation of osteoclasts with enhanced calcium resorptive potential
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Purpose: The release of interferon-gamma from activated CD8+ T cells could be involved in the calcification process in human aortic valve disease. We hypothesized that the release of interferon-gamma from activated CD8+ T cells could promote aortic valve calcifications.

Methods: Primary cultures of human aortic valve fibroblasts were stimulated with interferon-gamma and CD8+ T cells were isolated from healthy donors and cultured in the presence of these stimulants. Gene expression patterns were confirmed by immunohistochemistry and ELISA. To recapitulate a CAVD environment with high interferon (IFN) expression, calcified paraffin sections were stimulated with phorbol 12-myristate 13-acetate and ionomycin. qPCR detected signature molecules of CD8+ cells activation and their association with osteoclasts, the cells with specialized calcium resorptive potential, remains unknown in CAVD.

Results: To test the hypothesis that CD8+ T cells promote calcification in CAVD. Methods: CAVD valves (n=46) from valve replacement surgeries were dissected into ends, root, and leaflets and identified and calibrated parts followed by mRNA extraction and quantitative qPCR. Gene expression patterns were confirmed by immunohistochemistry and ELISA. To recapitulate a CAVD environment with high interferon (IFN) expression, calcified parts were stimulated with phorbol 12-myristate 13-acetate and ionomycin. qPCR detected signature molecules of CD8+ cells activation and their association with osteoclasts, the cells with specialized calcium resorptive potential, remains unknown in CAVD.

Conclusion: The release of interferon-gamma from activated CD8+ T cells in human calcified aortic valves fosters formation of osteoclasts with enhanced calcium resorptive potential.
fold, \(p<0.01\) and qPCR (44.3±24.8-fold, \(p<0.001\)) reduced mRNA levels of RANKL (0.03±0.01, \(p<0.01\)) and Cathepsin K (0.013±0.01, \(p<0.001\)), whereas TRAP did not change (0.4±0.2, \(p=0.6\)) compared to unstimulated regions. In addition, calcium signal intensity was increased in stimulated vs. unstimulated calcified parts (\(p<0.001\)). Moreover, IFNg reduced transcripts for Cathepsin K, TRAP, RANK, and TRAF6, whereas CD80 and CD86 increased in parallel with reduced osteoclast resorptive function, which was restored by neutralizing anti-IFNg antibody.

**Conclusion:** Our results indicate that CD8+ cells highly expressing IFNg in CAVD mediate osteoclastogenesis, and thus promote valvular calcification.

**Acknowledgement/Funding:** Dr E Nagy: Swedish Research Council (grant no: 537-2013-484), Swedish Heart and Lung Foundation; Dr E. Aikawa: NIH R01 HL 109506.

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**P1590 | BEDSIDE**

Clinical use of the cardiovascular medicine heart failure (CVM-HF) index in mitraclip population

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**Background:** The CardioVascular Medicine Heart Failure (CVM-HF) index is a prognostic model to predict outcomes in stable heart failure patients. Aim of our study is to validate the feasibility of the score in HF patients undergoing MitraClip procedure.

**Methods:** We performed a prospective study in patients with left ventricular dysfunction and functional mitral regurgitation, who underwent MitraClip 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 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-II (100%) and no adverse events were observed; in group B one patient died for HF (3%) and one patient was admitted in hospital (3%) for percutaneous closure of the residual interatrial communication after MitraClip intervention; in group C two patients were in NYHA III (14%) and two rehospitalizations valve-related were observed (14%); 2 no-cardiac (14%) and 2 cardiac-deaths were observed. Although the incidence of adverse event was not statistically significant between the three groups, the Logistic EuroSCORE was significantly higher in group C, when compared to group A (37.7±25.1 vs. 5.1±2.9, \(p=0.044\)) and group B (37.7±25.1 vs. 17.1±14.8, \(p=0.001\)).

**Conclusion:** CVM-HF index is a not invasive and practical tool, which can be easily used to assess the clinical risk of HF patients undergoing MitraClip procedure. Poor 6-months outcomes have been observed in patients belonging to the high-risk Group.

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**P1591 | BEDSIDE**

Differential effects of percutaneous edge-to-edge mitral valve repair on endothelial function based on left ventricular function

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**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 assessment of flow-mediated dilation (FMD) as a measure of endothelial function at baseline and a mean of 3.7±1.4 days and 170.3±27.1 days after PMVR. Using ANOVA for repeated measurements FMD improved significantly from baseline (7.1±3.4 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 mm; \(F=3.49\); \(p=0.044\)). These changes were more pronounced in patients with an left-ventricular ejection fraction (LVEF) >35% -35% with significant improvements in FMD (3.5±0.5 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 mm; \(F=3.49\); \(p=0.044\)).

**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 overexpressed compensatory mechanisms in these patients translating to more direct effects of MR reduction on systemic vascular function.

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**P1592 | BEDSIDE**

Morphometric differences between primary and secondary mitral regurgitation evaluated by 3D transoesophageal echocardiography

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Real-time 3D imaging of the mitral valve offers the possibility of advanced quantification of the mitral valve complex, however the clinical significance of the 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 1.79 [1.75–2.89], \(p=0.001\), 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).

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**P1593 | BEDSIDE**

Mitral valve area obtained by the novel 3D PISA method has a statistically significant correlation with pulmonary artery systolic pressure in mitral stenosis

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**Introduction:** Two-dimensional (2D) proximal isovelocity surface area (PISA) method has important technical limitations for mitral valve orifice area (MVA) assessment in mitral stenosis (MS), mainly the geometric assumptions of PISA shape and the requirement of an angle correction factor. Recently developed single-beat real-time three-dimensional (3D) color Doppler imaging allows direct measurement of PISA without geometric assumptions nor the requirement of an angle correction factor. Our aim is to assess the correlation be-
**P1594 | BEDSIDE**

**Impaired radial and circumferential myocardial contraction assessed by speckle tracking echocardiography accounts for ischemic mitral regurgitation in acute interposterior 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 MR.

**Methods:** 69 patients with first acute inferior MI treated with percutaneous coronary intervention, and no structural cardiac valve abnormalities and 45 healthy individuals (age 49.3±10.9 years, 48.9% females) 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 group. (grade ≥2 MR, N=35, age 61.86±12.02 years, 54.3% males). 2D STE was performed within 48 h of presentation and reperfusion therapy. 2D STE analysis was performed offline (GE EchoPAC software). Statistical analysis was carried out with SPSS 21.0.

**Results:** LV ejection fraction (EF) and longitudinal deformation parameters were significantly better in healthy subjects, but did not differ between the study groups. All circumferential deformation parameters were significantly worse in IMR group compared to control and NMR groups. Radial strains did not differ between control and NMR groups neither globally nor regionally. Global, basal and mid-ventricular strain was significantly lower in IMR group compared to both – healthy subjects and NMR group.

**Myocardial function parameters**

<table>
<thead>
<tr>
<th>Controls, A</th>
<th>NMR group, B</th>
<th>IMR group, C</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLS (%)</td>
<td>−21.3±1.9</td>
<td>−17.9±2.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GCS (%)</td>
<td>−17.6±3.0</td>
<td>−17.6±7.9</td>
<td>0.9</td>
</tr>
<tr>
<td>BCS (%)</td>
<td>−14.5±3.9</td>
<td>−27.1±7.9</td>
<td>0.01</td>
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<tr>
<td>MRS (%)</td>
<td>−19.1±3.5</td>
<td>−19.3±9.9</td>
<td>0.2</td>
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<tr>
<td>AGS (%)</td>
<td>−18.1±4.5</td>
<td>−18.9±9.4</td>
<td>0.4</td>
</tr>
<tr>
<td>GRS (%)</td>
<td>37.1±12.1</td>
<td>28.1±12.9</td>
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<tr>
<td>BRS (%)</td>
<td>34.3±1.0</td>
<td>35.9±1.3</td>
<td>0.6</td>
</tr>
<tr>
<td>MRS (%)</td>
<td>44.2±2.0</td>
<td>40.9±1.8</td>
<td>0.5</td>
</tr>
</tbody>
</table>

**Conclusions:** Ischemic MR in acute inferior MI is associated with worse radial and circumferential LV deformation parameters assessed by 2D STE.
of the Kaplan-Meier curves and the log-rank test revealed that the all-cause mortality was significantly different between the four groups (p<0.001). Furthermore, Cox regression analysis revealed that NYHA class IV (HR 1.889, 95% CI 1.086–3.286, p=0.024) and NT-proBNP >5000 pg/mL (HR 2.638, 95% CI 1.503–4.630, p<0.001) independently associated with the mortality after mitricle.

Conclusion: NYHA class and NT-proBNP levels are not always correlated and independently have a predictive value in mitricle patients. Since the baseline HF status is strongly associated with the survival after mitricle, we may need to evaluate the HF status of mitricle patients carefully by using both objective and subjective parameters.

Acknowledgement/Funding: Japan Society for the Promotion of Science

P1599 | BEDSIDE
Survival and clinical outcome in functional mitral regurgitation: percutaneous mitral valve repair 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 conservative and interventional treatment.

Purpose: The aim of the present study was to assess survival rates and clinical outcome of patients with severe functional MVR treated conservatively compared with those who received PMVR with MitraClip.

Methods: Between December 2009 and February 2015, 237 consecutive patients were referred to our center for assessment. 83 underwent PMVR and 154 patients were male, p=0.35. The surgical risk was comparable as assessed by Logistic EuroSCORE and EuroSCORE II (24.3±12.8 vs 27.5±20.2, p=0.10; 8.1±6.5 vs 10.8±8.5, p=0.09). Mean creatinine and hemoglobin values were 1.43±0.5 vs 1.32±0.4 mg/dl, p=0.31, and 12.9±1.9 vs 12.0±1.8 g/dl, p=0.10, respectively, and glomerular filtration rate was 49.5±21.1 vs 50.1±17.8 ml/min/1.73 m², p=0.89. The echocardiographic assessment showed comparable volumes and biventricular function between the two groups in terms of left ventricle end-diastolic and end-systolic volumes (185±155.4 vs 202±170.8 ml, p=0.23; 119±55.9 vs 132±52.9 ml, p=0.37, respectively, left ventricle ejection fraction (35±12.7 vs 34.6±11.4%, p=0.89), left atrium area (30±5.7 vs 31±8.7 cm², p=0.43), systolic pulmonary artery pressure (49.9±14 vs 49.9±7.9, p=0.69) and tricuspid annular plane systolic excursion (19±6.5 vs 16±6.4, 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±8%, 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.

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 late-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±6.6 vs 8.2±2.4; p<0.01). Conversely, women had a higher rate of VARC-vascular complications (9% vs. 5%), life-threatening bleeding (10% vs. 5.5%), and in-hospital cardiac death (8% vs. 4%) (p=0.05 for all). After adjusting for confounders no gender-independent effect was shown considering the entire cohort and after excluding vascular complications and transfusion (Table).
Conclusion: Pre-existing moderate or severe mitral regurgitation is associated with an 84% higher mortality at 30 days, a 35% higher mortality at one year and a 38% higher mortality at two years as compared to patients with no or mild MR. Further studies are necessary to investigate whether additional treatment of MR in patients with concomitant moderate to severe MR will improve the prognosis in a TAVR population.

P1601 | BEDSIDE
Peak aortic velocity correlates with serum leukotriene B4, metalloproteinase-2 and IFN gamma in calcified aortic valve disease
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Background: An increment of the peak aortic valve jet flow velocity (PAJV) is associated with a progression of aortic valve sclerosis (AVS) to stenosis (AS). Increased serum concentrations of leukotriene (LT) B4 have been associated with fibrosis of connective tissue through regulating the synthesis, secretion and activation of matrix metalloproteinases (MMPs). IFN-g is a marker of inflammation. We assessed the association of these surrogate markers of inflammation and fibrosis with PAJV in patients with AVS and AS.

Methods: 826 patients from 398 (BAV=20; N=18) (BAV=50; N=72) (BAV=32; N=59) (BAV=83; N=81) patients were included from 398 (AS) (0.5–2%). It is well accepted that the disease involves not only the valve function but also the aorta, with the development of the so-called BAV aortopathy. However, few studies have addressed to the onset of aortic dilation and the determinants of aortic growth. We postulate that the aortopathy in a subset of BAV pts is caused by a defect in the early development of the aorta and thus is detectable in early stages of life.

Purpose: To identify the onset of the aortic dilation and which part of the aortic root is primarily involved in BAV pts.

Methods: Serial retrospective echocardiographical data on 191 consecutive pts with BAV were included. Aortic diameters were measured. ANNUS, sinus, sinoutubular junction and ascending tract were considered. Valve morphology was defined according to cusp fusion pattern in right-left coronary (RL) and right-non-coronary (RN). All data were compared with a series of 230 matched normal subjects (182 males, mean age 18y) with a tricuspid aortic valve (N). Both pts and controls were divided into 4 age groups (see Table). All data were normalized to body surface area (BSA).

Results: RL was present in 85% of BAV pts, RN cusp fusion in 15%. Valvular dysfunction of any degree was observed in 72% of BAV pts. Aortic dimensions were significantly greater in BAV pts than controls in all aortic regions considered (p<0.001). This significant difference was present from early age.

Conclusion: BAV is a complex condition and BAV aortopathy begins early in childhood and progresses during adolescence till adult age. According to this data, it is necessary to start medical therapy with betablocker or sartans still in pediatric age?

P1602 | BEDSIDE
Transcatheter aortic valve replacement improves functional mitral regurgitation
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Background: Severe aortic stenosis (AS) is commonly associated with mitral regurgitation (MR) in patients undergoing transcatheter aortic valve replacement (TAVR). The progression of such MR after TAVR has not been well defined.

Purpose: To examine the effects of TAVR on functional MR.

Methods: Echocardiograms (at baseline and 1 year) were evaluated in consecutively operated patients undergoing TAVR for AS between 2007 and 2011. MR was classified/predominantly calcified/predominantly non-calcified/completely non-calcified, calcium score and positive remodeling demonstrated the following. Increasing TPL (p=0.02, 95% CI: +0.01, +0.03 p<0.001), hs-CRP (p=0.07, 95% CI: +0.01, +0.14 p=0.02), ET (p=0.66, 95% CI: +0.07, +1.24 p=0.028), male sex (p=0.73, 95% CI: +0.08, +1.38 p=0.028), age (p=0.04, 95% CI: +0.07, +0.08), calcified cusp (p=0.01, 95% CI: +0.07, +0.24, p=0.027), stenotic coronary artery (p=1.80, 95% CI: +0.98, +2.62 p<0.001), and decreasing LDL (p=2.12, 95% CI: +2.97, +1.26 p<0.001) were all independent predictors of increasing AVC. This model explained 45% of the variance in AVC.

Conclusions: This study highlights the importance of pre-existing AS and its impact on the progression of pre-existing mitral valve regurgitation, and the markers of inflammation, hs-CRP and ET-1, and the need for additional interventions.

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P1603 | BEDSIDE
The influence of endothelin-1, hs-CRP, coronary artery plaque burden and plaque morphology on calcific aortic valve disease
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Background: Calcific aortic valve disease (CAVD) affects 1 in 4 of the population -65 years. Subsequent progression to severe aortic valve stenosis has a high morbidity and mortality. The pathophysiology of CAVD is poorly understood. Understanding the processes involved is important if successful non-surgical treatments are to be developed. Both systemic levels of inflammation and coronary atherosclerotic valve disease – itself an inflammatory process - are predictors of CAVD. However, whether their effects are independent of each other is unknown. Furthermore, the specific influences of plaque burden, differing coronary plaque morphology and systemic levels of the inflammatory mediator endothelin-1 (ET-1), on CAVD are unknown.

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

Methods: Patients undergoing CT coronary angiography (CTCA) for investigation of chest pain were recruited. Those with significant CAD (~50% luminal stenosis) and significant valvular dysfunction were excluded (aortic valve velocity >2.0 m/s). Coronary artery plaque burden, plaque morphology, and AVC were assessed with CTCA. Inflammatory markers were obtained from venous sampling.

Results: 183 patients, 53% male, mean age 59.8 (+9.6) years were recruited. AVC was present in 111 (61%) patients and stenotic coronary artery in 111 (61%) patients. Multivariable linear regression modeling including demographic data, AVC, total plaque length (TPL) (mm), inflammatory markers (hs-CRP mg/L and ET-1 pg/mL) and different plaque morphologies (completely calcified/predominantly calcified/predominantly non-calcified/completely non-calcified, calcium score and positive remodeling) demonstrated the following. Increasing TPL (p=0.02, 95% CI: +0.01, +0.03 p<0.001), hs-CRP (p=0.07, 95% CI: +0.01, +0.14 p=0.02), ET (p=0.66, 95% CI: +0.07, +1.24 p=0.028), male sex (p=0.73, 95% CI: +0.08, +1.38 p=0.028), age (p=0.04, 95% CI: +0.07, +0.08), calcified cusp (p=0.01, 95% CI: +0.07, +0.24, p=0.027), stenotic coronary artery (p=1.80, 95% CI: +0.98, +2.62 p<0.001), and decreasing LDL (p=2.12, 95% CI: +2.97, +1.26 p<0.001) were all independent predictors of increasing AVC. This model explained 45% of the variance in AVC.

Conclusions: This study highlights the importance of pre-existing AS and its impact on the progression of pre-existing mitral valve regurgitation, and the markers of inflammation, hs-CRP and ET-1, and the need for additional interventions. Both systemic levels of inflammation and coronary atherosclerotic valve disease – itself an inflammatory process - are predictors of CAVD. However, whether their effects are independent of each other is unknown. Furthermore, the specific influences of plaque burden, differing coronary plaque morphology and systemic levels of the inflammatory mediator endothelin-1 (ET-1), on CAVD 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 I-III/VI, 67.6%), with low risk of operative mortality (Euroscore I 1.5±1.0), and mean EF was 63.7±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≥15.4% had lower survival (37.5% vs 97.0%, p=0.001) and survival free of the combined endpoint (0 vs 91.2%, p=0.001). On Cox regression analysis, CVF was the only independent predictor of all-cause death (HR1.88; 95% CI: 1.08–3.29 for 10% increase; p=0.026) and survival free of the combined endpoint (0 vs 91.2%, p=0.001) and survival free of the combined endpoint (0 vs 91.2%, p=0.001).

Conclusions: Prognostic implications of myocardial fibrosis on clinical events after AVR in low risk severe AS patients 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±7.5 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 calcification and an AVA ≤0.5 cm². In the following 46 patients (Group B) underwent pre-implant balloon valvuloplasty if presenting with severe asymmetric calcification and an AVA ≤0.5 cm². The remain patients (48 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 in-hospital pacemaker implantation due to postprocedural AV block 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 chronic aortic regurgitation (AR). We have experienced late recurrent LV dysfunction despite ejection fraction (EF) was once normalized early after AVR, but there are few reports about chronological changes of LV function during long-term follow-up.

Purpose: The purpose of this study is to clarify chronological changes of LV function and predictors of recurrent LV dysfunction late after AVR.

Methods: Among 80 consecutive patients with AR for severe chronic AR between 1995 and 2010, we retrospectively investigated 55 patients who were followed up with echocardiography more than 5 years after AVR. 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 LVIDd before (77.6±6.6mm vs 67.6±7.7mm, p=0.001), and early after AVR (54.1±13 vs. 49.6±6mm, p=0.03), larger LVIDd before (62.6±7 vs. 49.5±6mm, p=0.01) and early after AVR (37.5± vs. 31.6±mm, p=0.04), 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±27.7 vs. 110.2±26.5g/m², p=0.02), and a higher incidence of postoperative AF (22% vs. 7%, p=0.01). There were no significant differences in the ages at AVR (p=0.24), laboratory data, medications, clinical background, and echocardiographic data were evaluated.

Results: The mean follow-up period was 10.7±4.4 years. LVIDd, LVIDs, and EF before, early and late after AVR were as follows: LVIDd: 69±7, 50±26 and 52±26mm, LVIDs: 47±9, 32±26 and 33±27mm, 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 LVIDd before (77.6±6.6mm vs 67.6±7.7mm, p=0.001) and early after AVR (54.1±13 vs. 49.6±6mm, p=0.03), larger LVIDd before (62.6±7 vs. 49.5±6mm, p=0.01) and early after AVR (37.5± vs. 31.6±mm, p=0.01), lower EF before (36.7±% vs. 57±13%, p=0.01) and early after AVR (59±9 vs. 66±10%, p=0.04), greater LVMi early after AVR (134.7±27.7 vs. 110.2±26.5g/m², p=0.02), and a higher incidence of postoperative AF (22% vs. 7%, 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 LVIDd 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.

Table 1. Echocardiographic outcomes

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Baseline</th>
<th>1 year</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitrval regurgitation class I–III (median)</td>
<td>II</td>
<td>I</td>
<td>0.0065</td>
</tr>
<tr>
<td>Tricuspid regurgitation class I–III (median)</td>
<td>I</td>
<td>I</td>
<td>0.6072</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>42.7</td>
<td>48.8</td>
<td>0.0342</td>
</tr>
<tr>
<td>PASP (mm Hg)</td>
<td>50.7</td>
<td>43.1</td>
<td>0.0225</td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>47.9</td>
<td>47.4</td>
<td>0.1383</td>
</tr>
<tr>
<td>LVESD (mm)</td>
<td>37.8</td>
<td>36.2</td>
<td>0.0134</td>
</tr>
</tbody>
</table>

CVF and 8 years event-free survival

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.
P1609 | 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 (72.2 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 MCE and the size of the prostheses (21 mm, 27 mm and 29 mm) was chosen. All prostheses were successfully implanted. During the procedure, there were 2 pull-throughs in 1 pt and 3 in another pt with the valve successfully retrieved. The individual AR was: 1 pt in 3 pts, trivial paravalvular in 1 pt, and mild paravalvular in 1 pt. In 1 pt, 3 days post procedure, the valve embolized into the left ventricular outflow tract. Posthoc analysis revealed an oversizing of the prostheses of only 2 mm. The pt underwent surgical conversion under stable condition and the valve was eventually recovered from surgery. No other 30 day MACCE’s occurred and the rate of new pacemaker was zero.

Conclusions: In high-risk pts with severe non-calcified pure aortic regurgitation, 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 the EuroScore I and II logistic models

Background and aims: The European System for Cardiac Operation Risk Evaluation (EuroSCORE) has been established as a tool for assessing 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 original version and the recently developed EuroSCORE II (ES-II); 2) to compare their performances and 3) to identify new variables that could further improve the performance of previous models.

Methods: Data from all (n=128) patients undergoing surgery for active IE between January 2007 and November 2014 was retrieved from a single center prospective registry and accordingly, the ES-I and ES-II were calculated for each individual case. The discriminative power of each score was assessed by determining the area under the Receiver Operating Characteristic (ROC) curve. Relative performances of the scores were compared using the DeLong method and calibration was assessed by the Hosmer-Lemeshow goodness-of-fit method and calibration curves.

Results: One hundred and twenty-eight patients were analyzed. The observed perioperative mortality was 16.4%. The mean ES-I and ES-II were 13.8% IQ [7.0–35.0] and 6.6% IQ [3.5–18.2] respectively. Discriminative power was higher for ES-II (AUC of 0.82, 95% CI, 0.74–0.88) than for ES-I (AUC of 0.73, 95% CI, 0.65–0.81), although the difference was not statistically significant (p<0.1). The Hosmer-Lemeshow test showed good calibration, however ES-I tended to over predict and ES II to under predict. Among variables known to be associated with greater IE severity, only prosthetic valve IE and elevated white blood cell count were independent mortality predictors (OR 8.0; 95% CI: 2.6–20.0; p<0.001 and an OR 3.5; 95% CI: 1.2–10.0; p=0.02, respectively). The new model including the ES-II variables and the independent predictors of mortality showed an AUC of 0.85, 0.77–0.93, and did not differ significantly from ES-II (p=0.65).

Conclusions: Both ES-I and ES-II adequately strictly ratify 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 validity.

P1611 | BEDSIDE
Evolution of 18F-FDG PET/CT findings under therapy in patients with infective endocarditis: first description
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Introduction: Infective endocarditis (IE) is associated with difficult and delayed diagnosis, high mortality, and risk of recurrence during the first year following diagnosis. 18F-fluorodeoxyglucose positron emission tomography-computed tomography (18F-FDG PET/CT) has recently proved useful for the diagnosis of IE and has been proposed as a new major diagnostic criterion for prosthetic valve IE. However, repeat 18F-FDG PET/CT has never been performed in IE, and the significance of a persistent positive 18F-FDG uptake remains unknown.

Purpose: First description of the evolution of a positive 18F-FDG PET/CT after treatment of IE and its correlation with patient outcome.

Methods: During the first week of their admission, 235 patients with definite IE (177 men, aged 24 to 91) underwent 18F-FDG PET/CT. Among them, 98 (42%) presented with a positive 18F-FDG PET/CT and were scheduled for 1 month follow-up PET-CT after the end of the antibiotic therapy. Patients treated by early surgery were excluded, to avoid false positive uptake related to the postoperative inflammatory process. After exclusion of operated patients, 1-month repeat18F-FDG PET CT was obtained in 33 patients. These 33 patients underwent repeat, clinical, biological and echocardiographic follow-up at 1, 3, 6 months and 1 year. Primary end point was mortality and/or recurrence of IE at 1 year.

Results: The 33 patients in which repeat 18F-FDG PET/CT was obtained included 22 (66%) men, 22 (66%) prosthetic valves, and 15 (45%) aortic IE. Repeat 18F-FDG PET/CT remained positive in 26 (78%) patients and became negative in 7 (22%) at one year, there were 3 deaths and 3 recurrences. All patients with recurrences had persistent positive 18F-FDG PET/CT at 1 month. No event (death or recurrence) was observed in patients with a negative 18F-FDG PET/CT at 1 month.

Conclusion: A persistent positive 18F-FDG PET/CT is frequently observed despite an apparently healed IE, when performed 1 month after the end of antibiotic therapy, irrespective of the clinical evolution. Negative follow-up 18F-FDG PET/CT after antibiotic therapy predicts the absence of recurrence of IE or death. Repeat 18F-FDG PET/CT under therapy is potentially useful for the follow-up of patients with IE under antibiotic therapy and may help optimizing patient management.
P1614 | BEDSIDE
Factors associated with progression or regression 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 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. These factors were independently associated with deterioration: Borderline RHD of the MV (A or B) (OR 4.6, 95% CI 1.8–12.1), NSVAs 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 (OR 95% CI 9.2–110.7), NYAS of a combined AV (OR 8.4, 95% CI 2.5–28.0), receiving secondary prophylaxis (OR 0.07, 95% CI 0.01–0.6), and Borderline RHD of the AV (C) (OR 62.0, 95% CI 14.9–258.7).

Conclusions: Some children with Borderline RHD or NSVAs progressed but this was not invariably and a proportion improved. AV changes were not independently associated with progression, and were more likely to improve, suggesting more intensive follow-up should focus on MV changes. The counter-intuitive effect of secondary prophylaxis on the odds of progression and regression is likely to reflect the selective use of this in those deemed by clinicians to be at highest risk of RHD.

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P1613 | 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 endemic. All patients admitted with newly diagnosed RHD according to World Heart Federation echocardiographic criteria were enrolled (2005–2013). Cross-sectional follow-up was carried out in 2014. Factors associated with adverse outcomes were analysed using a Cox proportional hazard model.

Results: Of 396 patients, 106 experienced major cardiovascular events (MACE) at inclusion (26.9%). 187 events were then performed in groups with none/mild (estimated glomerular filtration rate [eGFR] ≥30ml/min/1.73m2) versus 6 patients (10%) exhibiting an eGFR <30ml/min/1.73m2. On the basis of other risk factors, the early safety endpoint was defined as a combined early safety endpoint at 30 days according to the valve academic pilot consortium-2 (VARC-2) criteria. Post-procedural transthoracic echocardiography was performed in each patient and AR was classified as none/mild versus moderate/severe. Univariable 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%), with 60 patients (12%) having an eGFR ≥30ml/min/1.73m2 versus 6 patients (10%) exhibiting an eGFR <30ml/min/1.73m2. In patients with eGFR ≥30ml/min/1.73m2, hemoglobin [per 1 g/L increase: OR (odds ratio) 0.993, 95% CI (confidence interval) 0.988–0.999; p=0.016] and NT-proBNP (per 1000 ng increase: OR 1.005, 95% CI 1.000–1.000; p=0.016) were independent predictors of the early safety endpoint at multivariable 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 7.091, 95% CI 1.144–43.982). 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
Progression 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 success and (CUSUM) failure analysis of combined 30-day safety endpoints 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 30-day adverse events with an improvement after the initial 86 cases were analysed using a Cox proportional hazard model. We divided the Edwards valve cases and CoreValve cases into two groups (early experience: Cases 87 to 312). The rate of 30-day mortality and 1-year mortality was calculated. The purpose was to reflect the selective use of this in those deemed by clinicians to be at highest risk of RHD.

P1611 | 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 pilot consortium-2 (VARC-2) criteria. Post-procedural transthoracic echocardiography was performed in each patient and AR was classified as none/mild versus moderate/severe. Univariable 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) 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 increase: OR 1.005, 95% CI 1.000–1.000; p=0.016) were independent predictors of the early safety endpoint at multivariable 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 7.091, 95% CI 1.144–43.982). 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=0.0046). 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 3.05–38, p=0.0016 and OR 8.46, 95% CI 1.69–42.17, p=0.0092, respectively).

Conclusion: Independent predictors of bleeding event

Adjusted* odds ratio (CI) P value
Major/life-threatening bleeding
MPV 10.76 (3.05–37.99) 0.0002
PDW 8.46 (1.69–42.17) 0.0039
Any bleeding
MPV 4.08 (1.66–10.07) 0.0022
PDW 3.82 (1.41–10.36) 0.0084
Need for transfusion
MPV 4.11 (1.71–9.86) 0.0016
Logistic EuroScore 2.54 (1.06–6.09) 0.0362

*Adjusted for age, sex, logistic EuroScore, BMI, hemoglobin, diabetes mellitus, atrial fibrillation, chronic kidney disease, LVEF, non-femoral access, the use of oral anticoagulants, ASA or clopidogrel.

P1617 | BEDSIDE
Balloon aortic valvuloplasty is not required for safe and effective transcatheter 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.

Methods: We retrospectively evaluated all first-time TAVIs performed for predominant aortic stenosis using the balloon-expandable Edwards Sapien XT and Sapien 3 devices from March 2012 to July 2014. 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) counts. The emboli were assessed using 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 definite adverse events (93.4% in Group 1 vs 94.9% in Group 2) or early safety (80.3% in Group 1 vs 84.6% in Group 2). There was also no difference in the rate of post-deployment balloon dilation (2.6% in Group 1 and 2.6% in Group 2). In three cases there was difficulty in crossing the valve without BAV, partial inflation of the distal balloon tip within the TAVI valve enabled crossing of the native aortic valve without significant patient complications. There was a significant reduction in total procedure time in patients in Group 2 vs Group 1 (104.9 vs 125.5 mins, p=0.012) and fluoroscopic time (12.9 vs 18.4 mins, p<0.001). There were no differences between the 2 groups in terms of the number of solid, gaseous or total emboli on TCD (all p>0.05).

Conclusion: Balloon-expandable TAVI valves can be implanted transfemorally without BAV, with no reduction in VARC-2 defined success or safety. Without performing a BAV there is a significant reduction in the total procedure time and fluoroscopic time. There is no significant difference in the rate of embolisation on TCD.

P1618 | BEDSIDE
Conventional vs. transapical vs. transfemoral aortic valve replacement - Real world comparison of 3751 patients in propensity score matched groups
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Background: Transcatheter aortic valve implantation (TAVI) is an established method in high-risk patients. The objectives of this procedure are currently under discussion: 1) Do the data acquired from randomized studies and registers justify expansion of the procedure to include younger and healthier patients? 2.) Is the transfemoral approach superior to the transapical approach with regard to mortality and peri-procedural complications? Against this background we examined the mortality and morbidity of all patients who received an isolated conventional, transapical or transfemoral aortic valve replacement in accordance with the criteria of the Valve Academic Research Consortium (VARC)-2.

Methods: A prospective register was taken from a single center recording all conventional (CONV, n=2,881), transapical (TAVI-TA, n=363) and transfemoral (TAVI-TF, n=570) aortic valve implantations during the period from 07/2009 to 10/2014. Using propensity score (PS) matching, first CONV and TAVI (TA+TF) and then TAVI-TA and TAVI-TF were paired on the basis of 21 risk variables, creating comparable groups.

Results: 393 pairs CONV vs TAVI within a moderate risk could be created (EuroSCORE 18.7 vs 18.5; STS 5.0 vs 5.4). Comparison revealed no difference for 30d mortality (4.6% CONV vs 5.1% TAVI, p=0.74), stroke (2.8% vs. 2.0%, p=0.48) or myocardial infarction (0.0 vs. 0.3%, p=1.00). Bleeding complications were significantly more frequent in the CONV, 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. 4.2% TAVI, p=0.48; stroke 3.1% vs. 2.8%, p=0.8; myocardial infarction 0.4% vs. 0.4%, 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 transfemoral, produce comparable results. Randomized studies are required in order to clarify the superiority or inferiority of the procedures for specific risk collectives.

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-cTnT) 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).

Methods: We studied serum hs-cTnT values in 166 consecutive HCM patients in whom subsequent echocardiographic data were obtained for more than one year period.

Results: Serum hs-cTnT 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-cTnT: abnormal hs-cTnT group and normal hs-cTnT group (≤0.014 ng/ml).

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tients with abnormal hs-cTnT values (n=85), interventricular septal wall thickness (IVSWT) and maximum LV wall thickness (MLVWT) at baseline were thicker than in patients with normal hs-cTnT values. On the other hand, age at evaluation, LV end-diastolic diameter (LVEDD) and fractional shortening were not different between the two groups. During follow-up periods of 6.4±2.6 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 46.6±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 (13.9% 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 atioventricular block as the first clinical manifestation
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Introduction: Atioventricular 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 CS feature. Data from PM implantation to CS diagnosis and start of steroid therapy varied from 0 to 129 months. The delay was ≥3 months in 27 patients (=late steroid treatment group) and <2 months in 18 patients (=early steroid treatment group). Adverse cardiac events were recorded until 1 start of steroids in the late treatment group and 2) 2014 in all patients.

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 and 2 had sustained VT 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, 918 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 characterization of patients with early SCD/MVAs and to identify possible reliable indicators of early SCD/MVAs in a large cohort of DCMs.

Methods and results: From 1988 to 2014 952 patients with DCM were consecutively included in the Heart Muscle Disease Registry of Trieste. Globally, 20 patients (2.1% of the overall population) experienced SCD/MVAs within the first 6 months after enrollment (primary end-point). At baseline, they showed a worse functional class (NYHA III-IV 42% vs 22%, p=0.038), a longer QRS complex duration (127±41msecvs 108±33msec, p=0.013) and a greater indexed left ventricular end-systolic volume (LVEFVI) (82±49 ml/m² vs 67±34 ml/m², p=0.049). The rate of betablockers administration was significantly lower compared to patients without early SCD/MVAs (59% vs 83%, p=0.008), mostly due to hemodynamic intolerance. At multivariate analysis, LVEFVI (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 LVEFVI, 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) None/psychotic stress as “primary forms” and 2) Physical factors (aesthesia, 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 complain chest pain (89.4% Vs. 50.7%, p<0.001) and a greater indexed left ventricular systolic volume (LVESVI) (82±49 ml/m² vs 67±34 ml/m², p=0.049). The rate of betablockers administration was significantly lower compared to patients with secondary-TKS (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).

Conclusion: Secondary Takotsubo syndrome could present or mark worse short and long term prognosis in terms of mortality, recurrences and readmissions. We propose a simple working-nomenclature on TKS.

P1623 | BEDSIDE
High prevalence of NGS in a galician cohort cause hypertrophic cardiomyopathy associated with a benign course
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Background: Hypertrophic Cardiomyopathy (HCM) is a genetically heteroge-
neus disease. N271I missense mutation in TNNT2 is highly prevalent in Galicia (Spain).

**Purpose:** To define the clinical spectrum of N271I mutation, and its prognosis compared with similar mutations in TNNT2 gene.

**Methods:** HCM probands were screened by NGS with a panel of 12 main genes related to the disease. 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 N271I 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 N271I mutation in TNNT2. The mutation co-segregated with the disease in all the families (29 relatives were 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 N271I was near 80%, but dependent on age. The degree of hypertrophy was moderate (mean 17.76 mm) and none of the patients had severe hypertrophy (range 13–27 mm). Survival curves showed a clearer better prognosis of N271I compared with other pathogenic missense mutations in TNNT2 (log rank test p = 0.001).

**Conclusion:** N271I mutation in TNNT2 gene is highly prevalent in Galician population, having a founder effect in this region. The clinical course of HCM is relatively benign, in contrast with other missense mutations in TNNT2. This illustrates the importance of evaluating every mutation one by one, and the need to be cautious when trying to generalize prognostic issues in a particular gene.

**P1624 | BEDSIDE**

**Arrhythmic risk assessment in family members with arrhythmogenic cardiomyopathy associated desmosomal mutations**

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**Purpose:** Arrhythmogenic Cardiomyopathy (ACM) is a genetically determined disorder, mostly caused by mutations in genes encoding desmosomal proteins. Following the identification of the causal gene mutation in the proband, cascade genetic screening of the family members commences, leading to the identification of mutation carriers. Arrhythmic risk assessment of these individuals is less well studied but crucial for clinical decision making. We aimed to identify characteristics associated with increased arrhythmic risk among family members in a cohort of consecutive ACM families harboring desmosomal mutations.

**Methods:** Thirty-nine consecutive ACM families harboring desmosomal mutations were studied. The families were 13 of PKP2, 14 of JUP, 6 of DSC2, and 6 of DSP; one of the DSP families presented digenic heterozygosity with PKP2 mutation. Cascade genetic screening identified 66 family members carrying the causal mutation. A clinical work-up including history, physical examination, 12-lead ECG, cardiac magnetic resonance imaging, and 24-hour Holter monitoring was performed in all family members. Although one patient was initially found to have RVH on echocardiogram, no other arrhythmias were detected, and the participant refused to undergo further evaluations.

**Results:** Of the 66 family members screened, 14 (21%) participants experienced the arrhythmic outcome at median age of 33 (21–69) years. The first event was sustained ventricular tachycardia in 11 and sudden cardiac death in 3. Definite diagnosis according to the 2010 Task Force criteria in 38% (25 of 66) was confirmed by 24-hour Holter monitoring in the majority of patients (18 of 25). In the remaining patients (7 of 25), the diagnosis was based on clinical and echocardiographic abnormalities (p = 0.016), RV dysfunction (p = 0.002) and LV dysfunction (p = 0.011) were associated with adverse arrhythmic outcome.

**Conclusions:** Family members experience major arrhythmic events at lower rates than the reported for probands. Individuals not fulfilling the 2010 TFC are at very low risk. The presence of right ventricular dysfunction independently predicts major arrhythmic events.
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 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 4.2%. 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 with 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 10 years. Demographic, clinical, electrocardiographic and echocardiographic data were analyzed 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 have had complete recovery of LV systolic function and complete recovery had occurred in 50.9% of cases at 15 days after hospital admission. In patients TC-18–TC-14, the following factors are associated with LV systolic function recovery in the first 15 days after admission: absence of history of angina (97.6% vs 81.5%, p<0.001), the presence of a physical precipitating factor (23.8% vs 11.1%, p=0.032), the absence of ST-segment depression (96.4% vs 87.7%, p=0.036) and the absence of Q-waves in the initial ECG (88.1% vs 74.1%, p=0.021).

In multivariate analysis, the absence of history of angina (p=0.028) was identified as an independent predictor of LV systolic function recovery in the first 15 days after 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 in patients with TC.

P1628 | BEDSIDE
Ethnic variation in hypertrophic cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is a genetic disorder with significant variability influenced by echocardiogram in 10% of individuals. Most clinical studies to date have enrolled predominantly Caucasian patients, but racial background may have an important effect on the disease course. In this study we have used a large single centre population to examine the effect of racial background on phenotype and clinical outcomes in HCM. The case records of sequential patients seen in our specialist clinic were reviewed. Patients identified their racial group using the UK Office of National Statistics classification. Patients underwent comprehensive cardiac assessment at their first visit, and were followed up for a mean of 7 years. Records were available for 2248 patients (95 Black/African/Caribbean/Black British (B), 216 Asian/Asian British (A), 1937 White (W)). At baseline assessment, there were differences in the morphological pattern of left ventricular hypertrophy on echo, with more B patients having apical and concentric hypertrophy, while W and A patients mostly had asymmetric septal hypertrophy (p<0.02). There were no significant differences in maximal wall thickness, fractional shortening, or left ventricular outflow tract gradient. On resting ECG, W patients were less likely to have abnormal T wave inversion than other groups (p<0.05), but there were no significant differences in PR or QRS prolongation. On cardiopulmonary exercise testing, there was no difference in blood pressure response, but W patients did have higher maximum oxygen uptake (p<0.05). During follow-up, there were significant differences between ethnic groups in a combined endpoint of all-cause mortality and cardiac transplant (Annual rates W 1.4%, B 1.7%, A 0.6%, p<0.02), but there were no significant differences in a secondary combined endpoint of sudden cardiac death, aborted sudden death, and appropriate ICD therapy (Annual rates W 0.4%, B 0.4%, A 0.2%, p<0.04). W and A patients were significantly more likely to receive a pacemaker (Annual rates W 1.8%, B 0.9%, A 0.8%, p<0.02). B patients had a trend to fewer ICDs (Annual rates W 3.5%, B 2.5%, A 4.3%, p=0.18). Rates of septal reduction therapy were similar across groups (Annual rates W 3.0%, B 3.1%, A 2.2% p<0.02). In this large single centre study of hypertrophic cardiomyopathy, there were significant differences between racial groups in terms of their clinical phenotype at presentation and their long term outcomes. Further work is required to try and understand the different genetic and social factors which lead to these different disease patterns.
Purpose: To identify independent predictors of ventricular arrhythmias and to assess their relationship with the new recommended HCM Risk-SCD Score. Methods: We have prospectively enrolled 91 pts (52±17 years, 39 men) with HCM: 15 pts with non-sustained ventricular tachycardia during ambulatory 24 hours ECG monitoring (NSVT+) and 76 pts without (NSVT-). A comprehensive echocardiogram was performed in all pts, including measurement of maximum LV wall thickness (LVTWT) and RV free wall thickness (RWTWT). Global longitudinal LV strain (GLS) was assessed by speckle tracking echocardiography. HCM Risk-SCD Score was calculated based on the ESC 2014 guidelines on HCM.

Results: Pts carrying a frameshift mutation had significantly higher values of LVTWT (23.6±6.5 vs 19.8±4.1 mm, p<0.005) and RVWTWT (8.4±2.6 vs 6.0±1.5 mm, p<0.001), lower values of GLS (−12.6±2.8 vs −14.4±3.2%, p=0.04), and tended to be younger (46±21 vs 54±16 years, p=0.1) than pts NSVT-. There were no significant differences between NSVT+ and NSVT− pts regarding: sex distribution, indexed LV mass (185±56 vs 172±64 g/m²), indexed LA volume (58±16 vs 61±29 ml/m²), E/e′ ratio (15±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, RVWTWT emerged as the only correlate of NSVT (OR=2.2, 95% CI 1.36 to 3.77, p<0.002). Mean value of Risk-SCD Score was 3.3±2.3% (limits 0.83–15.90). Twelve pts had an intermediate calculated 5-year risk of SCD (between 4 and 6%) and 9 pts had a high calculated 5-year risk of SCD (>6%). RVWTWT correlated with HCM Risk-SCD score independently of the parameters included in the risk score calculation (p=0.93, 95% CI 0.21 to 0.61, p<0.001).

Conclusions: In this cohort, RVWTWT 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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P1631 | BEDSIDE Mid-regional pro-atrial natriuretic peptide for predicting mortality and heart failure in hypertrophic cardiomyopathy: a comparison with N-terminal pro-brain natriuretic peptide

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Background: Hypertrophic cardiomyopathy (HCM) has a diverse clinical spectrum and prognostication can be challenging. N-terminal pro-brain natriuretic peptide (NT-proBNP) has been recently proposed for predicting death and heart failure in HCM. Mid-regional pro-atrial natriuretic peptide (MR-proANP) is a stable natriuretic peptide reflecting increased atrial wall tension, with potential advantages over conventional natriuretic peptides. 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 centres 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 defined as death, 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=0.0001) and log MR-proANP (HR=4.25, CI 95% [2.45–7.38], p=0.0001) were strongly associated with primary endpoint. However, in a multiple stepwise regression analysis, findings closer, a stronger echocardiographic and then natriuretic peptides, the best model for predicting outcome was NYHA 3–4 versus 1–2 (HR=3.1, CI 95% [1.43–6.75], p=0.004), 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=0.0002) were 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.

Conclusions: 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.

P1632 | BEDSIDE A comprehensive clinical evaluation of demographics ARVC carriers: does the type of mutation influence the phenotype?

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Background: Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC) is an inherited disease characterized by variable phenotypic expression and incomplete penetrance. To date, few genotypic-phenotypic correlations have been reported and desmosplasia (DSP) gene mutations have been associated with a predominant left ventricle phenotype or biventricular involvement. Truncating mutations have been mostly associated with a more aggressive phenotype.

Purpose: Our aim is to assess the role of DSP mutation type in age-related penetrance in ARVC.

Methods: 26 fulfilled criteria ARVC patients, 17 probands and 9 family members, carrying a mutation on DSP were included in the study. The assessment included clinical history, pedigree evaluation, ECG, SAECG, 2D-echocardiography, maximal exercise testing, 24 hour ambulatory ECG monitoring and CMR. Arrhythmic characterization included: syncpe, any arrhythmia recorded during 24 hour ambulatory ECG monitoring and/or exercise testing, CA, ICD events. Age of onset of arrhythmic symptoms was analyzed separately from the age at diagnosis and from the age of LV dysfunction onset. Phenotype was analyzed accordant to the type of mutation (stopgain, frameshifting, splicing, non-synonymous). The only splicing mutation found leads to a truncated allele and haplosufficiency, mechanism shared by many frameshiftings. Therefore it was analyzed together with the frameshift mutations.

Results: DSP mutation identified in probands were 5 stopgain, 8 frameshifting, 3 splicing and 3 non-synonymous mutations. Among the 9 ARVC fulfilled criteria family members 3 carried a stopgain mutation and 6 a frameshifting one. Probands with frameshift mutations had a younger age at diagnosis. All of them had arrhythmic events and at a younger age than other mutation type. Despite a preserved left ventricle systolic function at arrhythmic event, frameshift mutation carriers showed a significantly lower systolic function when first evaluated and diagnosed (p=0.004). Isolated LV involvement was present at cardiac MRI in frameshift mutation carriers, all the other mutations carriers had biventricular involvement. Between family members, an higher prevalence of arrhythmic events and LV dysfunctions at a younger age was observed between the frameshift mutation carriers compared to stopgain mutation carriers, confirming what observed in probands.

Conclusion: Our findings support a more severe arrhythmic phenotype in patients carrying a frameshift mutation. Moreover, patients with frameshift mutation show left-sided ARVC while patients carrying other type of mutation have a biventricular involvement.
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=0.001), 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: 3.99-29.43, p<0.0001).

Conclusions: In the database from our Network, patients with TC admitted with p-QRSd were more associated with poor in-hospital clinical outcomes. Aggressive intervention may be required to prevent further deterioration of clinical course in TC 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 1 to 5 individuals and all the cardiovascular structures can be affected by amyloid infiltration. Liver transplantation (LT) is still the standard of care in symptomatic patients, but recently a new oral drug, tafamidis, that acts as a TTR stabilizing agent has shown promising results. LT besides being much more invasive, is not always available and doesn’t effectively prevent the development of cardiac involvement.

Our aim was to evaluate the cardiovascular (CV) impact of tafamidis in patients with FAP.

Methods and results: We performed a retrospective study enrolling 700 patients with FAP from our center, 162 of which (23.1%) medicated with tafamidis. 51.2% were female with a mean age of 37.8±11 years and the mutation Val30Met predominated (98.1%).

Clinical presentation was, in the majority, with neurological (75%) symptoms and only 3% presented with cardiac signs or symptoms. The mean age of symptoms onset was 34.7±10.5 years and the drug was initiated, on average, 2.8±3.3 years after symptoms onset.

Before treatment, 29 patients had CV symptoms and 91% were in sinus rhythm (atrial fibrillation was found in 2%). The prevalence of rhythm disorders was: first-degree atrioventricular (AV) block in 20%; Mobitz I second-degree AV block in 26%, Mobitz II second-degree AV block and complete AV block in 12%. Left anterior fascicular block was found in 12%; left bundle branch block in 2% and right bundle branch block in 1.2%; finally poor R-wave progression was present in 10%, low QRS voltage in 14%, pseudo-infarct Q waves in 8% and left ventricular hypertrophy pattern in 2%.

The median follow-up under tafamidis was 12 months (IQR 6–15) with a survival rate of 99% (one death; two drop-outs, one for liver transplantation and one with end-stage kidney failure). After 1 year of treatment CV symptoms improved in 9% patients and deteriorated in 3%, 87% remained unchanged. AV conduction was 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.

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 myotomy-myectomy in patients with hypertrophic cardiomyopathy
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Objective: Surgical myotomy-myectomy 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 myectomy in DDD pacing in HOCM pts. The aim of this nonrandomized 15-yrs cohort study was to compare subjective and objective outcomes in HOCM pts undergoing surgical myotomy-myectomy, DDD pacing and alcohol septal ablation.

Methods: 194 consecutive pts with drug refractory HOCM were treated invasively (108 male and 76 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 echocardiographic left ventricular function (LVF) and patients with additive LVOT and FMR degree >35 mmHg (group1). In 46 pts with massive LV hypertrophy and its cavity obliteration extensive myotomy-myectomy was performed (group2). In 82 pts with appropriate coronary anatomy transcoronary septal alcohol ablation was performed (group3).

Initial peak LVOT gradient was 98±5.2 mm Hg in group1, 107±5.8 mm Hg in group 2 and 93.7±5.9 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±6.8 mm Hg and FMR degree (p<0.01). After extensive myectomy we observed reducing LVOT SPG to 26.1±3.6 mm Hg and degree FMR (p<0.01). Septal alcohol ablation in group 3 brings LVOT SPG decrease to 22.5±4.1 mmHg (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 176 to 12 month)) was 64.3±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 2 month)) was 28.7±4.6 mm Hg (p<0.01).

Conclusions: Short-term results of DDD pacing, alcohol ablation and surgical myotomy-myectomy are comparable. But hemodynamic results of alcohol septal ablation and surgical myotomy-myectomy have an advantage in long-term period. DDD pacing didn’t show significantly good, stable long-term results.
justing for LVEF (HR 11.1, 95% CI 2.19–201.4, p=0.001). The median value of LVEF was 43%; 39 patients were classified as preserved EF (≥43%) (mean EF 53%), and 39 patients were classified as reduced EF (<43%) (mean EF 32%). The presence of VAs at diagnosis was a significantly worse prognostic factor in patients with reduced EF (log-rank p=0.011), but not in those with preserved EF (Figure).

Conclusions: Ventricular tachyarrhythmia at diagnosis was an independent strong prognostic factor in CS patients with reduced EF after treatment of corticosteroid therapy. 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). Thirty-six procedures (57%) were performed in emergency. Abnormal electrocardiogram was found in 10 patients. A total of 17/23 coronary obstructions were successfully treated with no immediate residual post-intervention stenosis. Initial balloon angioplasty was performed for all lesions (mean balloon size 2.4±0.8 mm), with subsequent stent placement in 11 of 17 lesions (average stent diameter 2.7±0.3 mm). There were 3 peri-procedural deaths. After mean follow-up of 34 months (1 week - 9.6 years) 3 late deaths occurred.

Conclusion: PCI can be used in the paediatric population to restore normal coronary blood flow in a wide range of anatomic conditions and revascularization indications. It may be safe and effective in selected patients with coronary artery stenosis and/or occlusion, but remains technically challenging.

P1640 | BENCH Selective propensity of bovine jugular vein to bacterial adhesion and impact of percutaneous pulmonary valve implantation procedural steps in genesis of infective endocarditis: an in vitro study
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Background: Percutaneous pulmonary valve implantation (PPVI) using bovine jugular vein to bacterial adhesion and leaflet mechanical behaviour.

Methods: Three valved stents (BJV valved stent, homemade stents with bovine and porcine pericardium) were tested in vitro in 4 conditions: I) control group, II) crimping, III) crimping + inflation of low-pressure balloon and IV) condition III + post dilatation (high-pressure balloon). For each condition, valvular leaflets (and venous wall sample for BJV stents) were taken for histological analysis, bacterial adhesion using S. aureus and S. sanguinis strains and mechanical uniaxial tests of 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. Fig. 1 shows bacterial adhesion of S. sanguinis on Melody valve (white arrow).

Figure 1. S. sanguinis adhesion electron microscopy
P1641 | BEDSIDE
Cardiac troponin I release after transcatheter closure of the atrial septal defect are related with arrhythmias in the early follow-up
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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 M with a mean age of 46.9±21.2 (16–73) years with ASD who underwent transcatheter closure, were analyzed. The troponin I (Troponin I) and CK-MB level was measured at 0, 8, 16, and 24 hours after procedure. Holter monitoring was performed on all pts before procedure, 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. Peripherically, the increase of cardiac markers: TnI over 50% beyond reference level was observed in 61%, pts of two-folded increase of CK-MB levels in 3.4%. There was a significant correlation between SVE premature beats/24 hours 1 month after procedure and periprocedural increase of TnI (p < 0.0001, r = 0.1121). 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 TnI rise are: number of the peri-procedural supraventricular ectopy, elongated time of procedure and larger device size. Cardiac troponin release can be an expression of myocardium microdamages, which can also be a response for the transient supraventricular arrhythmias after transcatheter ASD closure.

P1642 | BEDSIDE
Percutaneous occlusion of vascular malformations in pediatric and adult patients: 20-year experience of a single center
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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 no or minimal residual flow. Predictors of procedural failure were determined by multivariate logistic regression.
Results: A total of 122 VM were intervened, corresponding to 71 procedures in a predominately pediatric sample of 46 patients: median (minimum-maximum) 13 years (25 days-74 years), 48 (1.9–80) kg, 57% female and 52% with structural heart disease. Overall, 111 (91%) VM were arterial and 11 (9%) were venous: 53 pulmonary arteriovenous fistulae, 41 aortopulmonary collaterals, 9 systemic venovenous collaterals, 6 peripheral arteriovenous fistulae, 5 Blalock-Taussig shunts, 4 coronary fistulae, 2 Fontan fenestrations and 2 renal artery aneurisms. Lower body weight was independently associated with procedural failure (OR 1.05, 95% CI 1.01–1.09).
Conclusion: Percutaneous occlusion was safe and effective for the treatment of different VM in children and adults, using a variety of devices.

P1643 | BENCH
Correlation between coronary artery stenosis and subclinical atherosclerosis measured by magnetic resonance imaging
Background: Subclinical atherosclerosis is a frequent finding in healthy individuals and has been reported to be associated with coronary artery disease. The aim of the study was to determine the correlation between the presence of coronary artery stenosis measured by magnetic resonance angiography and subclinical atherosclerosis detected by magnetic resonance imaging (MRI).
Methods: A total of 50 patients (27 men and 23 women, mean age 64.2 ± 8.9 years) were included in the study. All patients underwent coronary artery stenosis measurement by MRI and coronary artery stenosis detection by magnetic resonance angiography. Subclinical atherosclerosis was defined as the presence of high-signal intensity plaques in the carotid arteries on T1-weighted images. The degree of coronary artery stenosis was classified as: no stenosis (0%–24%), mild stenosis (25%–49%), moderate stenosis (50%–69%), and severe stenosis (70%–99%). The correlation between the presence of coronary artery stenosis and subclinical atherosclerosis was assessed using the Spearman correlation coefficient.
Results: The prevalence of subclinical atherosclerosis was 46% (23/50) in the entire study population. The prevalence of subclinical atherosclerosis was significantly higher in patients with moderate (62%) and severe (75%) coronary artery stenosis compared to patients with no stenosis (25%) and mild stenosis (33%). The degree of coronary artery stenosis was positively correlated with the prevalence of subclinical atherosclerosis (r = 0.4, p < 0.05).
Conclusion: Subclinical atherosclerosis is associated with the degree of coronary artery stenosis, suggesting a potential role for early intervention to prevent the progression of both conditions.

P1644 | BEDSIDE
The fetal intracardiac echogenic foci debate: is it over?
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Background: Intracardiac echogenic foci (ICEF), echogenic images inside the fetal left ventricle, have been associated to a number of anomalies that affect to that of the heart, not bigger than 7 mm, are often detected in the second trimester of pregnancy. Several studies demonstrate their benignity, few ones their association with congenital heart diseases; nevertheless the question remains unclear and gynecologists keep requiring fetal echocardiography after ICEF visualization.
Purpose: To evaluate if the identification of prenatal ICEF is associated with the development of CHD both prenatally and postnatally.
Methods: 1272 consecutive women underwent fetal echocardiography at a median gestation age of 22±3 weeks. We described localization (left ventricle, right ventricle, biventricular) and number (isolated/double or multiple) of the diagnosed ICEF. Infants with ICEF during fetal life underwent transthoracic echocardiography (TTE) at a median follow-up of 12±4 months.
Results: Out of 1272 pregnant women (212, 16,6% ICEF were detected. 188 ICEF were isolated or double, 24 multiple (3–8). 85% were typically located near or within mitral papillary muscles, 2% within tricuspid subvalvar apparatus, 5% close to the right ventricle apex and 8% biventricular (near mitral and tricuspid valve). Only 3 ICEF cases (1,4%) were associated with CHD: 1 tetralogy of Fallot with pulmonary trunk hypoplasia showed an isolated ICEF located near a mitral papillary muscle; 1 atrioventricular canal defect in a Down’s syndrome 3 ICEF within mitral papillary muscles and 3 within tricuspid subvalvar apparatus. These postnatal TTE demonstrated in all infants (except that affected by Down’s syndrome) a complete ICEF regression within 12 months of life, in absence of residual morphofunctional anomalies.
Conclusions: We reported no significant difference in the prevalence of CHD in the fetuses with ICEF and the ones without ICEF (1,4% ICEF and 6,6% no ICEF group). In spite of the high diagnostic suspicion for CHD suggested by multiple ICEF detection, their identification seems to be not associated with an increased risk for CHD in euploid fetuses. Hence, ICEF could be explained by...
temporary abnormal processes of myocardial excavation and endocardial tissue fenestration, contributing to the formation of papillary muscles and chordae tendineae. In support of this thesis, ICFE disappears when cardiac structures develop completely with no consequences on systo-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. Idiopathic constriction of the DA is a rare finding, and experience with this defect is poor, but it is associated with right heart failure and fetal hydrops, leading in some cases to fetal loss. The aim of this study is to summarize the fetal 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 thoracochractic echocardiography postnatal. Ductus arteriosus constriction related to maternal use of cyclooxgenase inhibitors, ductus arteriosus stenosis caused by congenital heart disease or absent ductus arteriosus were excluded.

Results: The incidence of idiopathic DA constriction is 0.20%. Mean gestation age was 34.6±2.9 (33–37) weeks and maternal age was 31.2±7.6 (24–37) years. The narrowed middle diameter of DA was seen in 7 fetuses with mean diameter was 2.5±0.97mm; normal middle diameter of DA was seen in 2 fetuses with the diameter of 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 2.3±0.47m/s, diastolic velocity 0.75±0.17m/s. And pulsatility index 1.23±0.61. Right heart dilatation 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 transathoracic 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 as indications for FE, have a real role in predicting CHD.

Methods: We did a retrospective analysis of indications and diagnosis of 1272 performed FE in the last 10 years at our department.

Results: 881 (69.2%) FE were requested in absence of risk factors: 24.2% for a suspected CHD, 27% for inadequate visualization of 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. The following validated risk factors were 6.8% for twins pregnancy, 1% for maternal reumathological diseases, 2.1% for maternal infections, 3% for maternal antibodies, 2.8% for teratogen exposure, 3.9% for fetal arrhythmias, 5.2% for familiar history (first-degree relatives) positive for CHD, 2% for abnormalities of amniotic fluid volume, 4% for fetal extracardiac and/or chromosomal anomalies, 2% for 21 diaplasia CHD, only 2 cases (ventricular septal defects) were associated with maternal infections, 1 case (ventricular septal defect with carnoamplparation exposure, 2 pulmonary valve stenosis) with abnormalities of amniotic fluid volume, 3 (2 tumors and 1 tetralogy of Fallot) with fetal arrhythmias. In case of parental history of CHD, probability of CHD recurrence was around 2.8% and recurrent defects were aortic coarctation and ventricular septal defect. In 10 cases (cardiac rhabdomyomas, aortic coarctation, interrupted aortic arch, tetralogy of Fallot, common arterial trunk, transposition of the great arteries) chromosomal and/or extracardiac anomalies were present.

Conclusions: 85% of prenatally detected CHD were not associated with any identified risk factor, therefore the indication for a detailed fetal heart scan should be carefully taken into account also in “low risk” pregnancies. No significant difference existed in the prevalence of CHD between the twin and the singleton pregnancies. Chromosomal and extracardiac anomalies, if compared to other risk factors, seem to be the major predictors of CHD (14%; p < 0.001) and, particularly, of complex CHD and CHD with an adverse prognosis. Moreover, most cases of CHD were the first clinical manifestation of chromosomal aneuploidies, thus suggesting the need for a further investigation on coexisting maternal and genetic disorders.

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 adults 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 recorded.

Results: 29 patients (86% males) with mean age at time of surgery of 10.5±3.5 yrs and median follow up of 14±3 yrs (range: 12 to 23 yrs) were reviewed. The mean age at latest follow up was 25.7±4.9 yrs. CMR findings revealed PV Vmax of 2.30±0.71 m/s, pulmonary 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, and systolic volume indexed [ESVI]31.6±19.6 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±9.9%. 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±4.6 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 preceding Ross operation.

Conclusion: Over a period of 15 years, our data suggests an excellent survival rate for Ross procedure in adulthood. 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 rate and strain parameters.

Results: Twenty HLHS fetuses were enrolled during second and third trimester ultrasound (20–35w), the control group were 1:1 paired. Clips with high frame rate 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-pulmonary artery (RV-PA) conduit, 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 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 and ventricular-pulmonary artery 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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Background: Inherited long QT syndrome (LQTS) is associated with risk of sudden death. Previous follow-up studies on pediatric LQTS patients have mainly consisted of ungenotyped patients. We assessed the clinical course, and efficacy and side effects of β-blocker treatment in molecularly defined pediatric LQTS type 1 and (LQT1) and type 2 (LQT2) patients.

Methods: The study population was drawn from the Finnish Inherited Cardiac Disorder Research Registry comprising 4000 molecularly tested subjects. The inclusion criteria were 1) genetically confirmed KCNQ1 or KCNH2 mutation, and 2) age <16 years at enrollment. A questionnaire was sent to the study subjects or their parents. Data of all deaths were obtained from Statistics Finland. Kaplan-Meier graphs, the log-rank test and time-dependent Cox regression model were used to evaluate the contribution of risk factors to cardiac event.

Results: A total of 457 subjects fulfilled the inclusion criteria. Three of them died during the follow-up, and 313 (69%) responded to the inquiry. The 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 including the retrospectively collected data from birth was 12.0±5.5 years.

No arrhythmic deaths occurred during the follow-up. LQT1 Finnish founder (FF) mutation carriers had fewer cardiac events by the age of 18 years than other LQT1 patients (cumulative probability [CP]= 11% vs 26%, p=0.008, and hazard ratio [HR]=0.38, p=0.04). Similar trend was observed in LQT2 FF and non-FF patients (CP= 4% vs 43%, p=0.002, and HR=0.17, p=0.02). QTc interval <500 ms increased the risk of cardiac events compared to QTc ≥470–499 ms (HR=2.76, p=0.03). Treatment with β-blocker medication was associated with reduced risk of first cardiac event (HR=0.27, p=0.005). Non-compliant LQT2 patients were more often symptomatic than compliant LQT2 patients (18% vs 0%, p=0.03). Side effects were encountered in 23% of β-blocker users.

Conclusions: Severe cardiac events are uncommon in molecularly defined and appropriately treated pediatric LQTS mutation carriers. β-blocker medication reduces the risk of cardiac events in this age group of LQTS patients.

P1650 | BEDSIDE
Right ventricle and left ventricle follow-up for double-outlet right ventricle with biventricular repair
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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 in 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), 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 for 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 ncVSC (p<0.001). In multivariate analyses, the factors that influenced reoperation were: left ventricular outflow tract obstruction (p<0.05), associated surgical procedures during main procedure (p<0.05), duration of cardiopulmonary bypass procedures (p<0.01). The factors that influenced survival were: restrictive VSD (p<0.01), coronary artery anomalies (p<0.05), duration of cardiopulmonary bypass procedures (p<0.01), early cardiac reoperation (p<0.01). The type of repair did not influence reoperation (p=0.20) or mortality (p=0.27).

Conclusions: Factors affecting the prognosis of DORV are anatomical and surgical factors. However, there is no difference between the main types of surgical strategy.

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
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Background: As the proportion of elderly in the Japanese population is increasing steeply 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) 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 = 27x10^3) 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/1.73m^2), 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/1.73m^2 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.
Results: Over a mean follow-up of 115 months and >10 million patient-years of follow-up, over 65,000 individuals had at least one AF event (incident AF rate 5.1% and 5.8% excluding or including prior CVD, respectively). Those who de-
veloped AF were older and had more risk factors for atherosclerosis. The mean eGFR of those who developed AF during follow-up in both cohorts was approxi-
ately 63 ml/min/1.73m² as compared to approximately 95 ml/min/1.73m² in those who did not develop AF. Adjusting for age, gender, hypertension and di-
babetes mellitus, a 10-unit increase in eGFR was independently associated with a mean decrease in incidence AF of 1.4% and 2.3% in the cohorts excluding or including prior CVD, respectively (p=0.001 for both), with a sharp decline in AF events in the eGFR ≥100 ml/min/1.73m² range (Figure). The association between eGFR and incident AF was more significant in middle aged (41–60 y) or elderly (≥61 y), as compared to youngers (22–40 y) (p interaction <0.001).

Conclusions: In the normal or mildly impaired range is independ-
ently associated with lesser incident non-valvular AF in adults with and without prior CVD.

P1653 | BEDSIDE
A cardiometabolic protective phenotype associated with the ANP
genetic variant rs5068 in African Americans: the Multi-Ethnic Study
of Atherosclerosis (MESA)


Methods:
We genotyped 1628 African Americans for rs5068. Differences be-
tween genotype groups were tested via logistic or linear regression. Continuous
variables were rank transformed, if necessary.

Results:
Genotype frequencies of rs5068 were AA (N=1518) 93%, AG (N=109) +
GG (N=1) 7%. All subsequent analyses were done by combining AG and GG
and comparing to AA. After adjusting for age and sex, the G allele was associated
with lower prevalence of metabolic syndrome (24% vs 36%, p=0.003). After
further adjustment for BMI, the minor allele was associated with lower prevalence
of diabetes mellitus (8% vs 17%, p=0.02), lower plasma values of triglycerides (78
vs 91 mg/dl, p=0.02) and higher HDL-cholesterol levels (54 vs 50 mg/dl, p=0.01).
Additionally, carriers of the G allele had significantly lower fasting glucose levels
(91 vs 97 mg/dl, p=0.04). Genotype was not associated with blood pressure
values or BMI.

Conclusions: The association between the minor allele of rs5068 and a favor-
able cardiometabolic phenotype that was previously reported in whites is now
shown in a cohort of African Americans. The rs5068 G allele is associated with
lower prevalence of metabolic syndrome, diabetes and levels of fasting glucose.
The G allele carriers have a healthier plasma lipid profile characterized by higher
HDL-cholesterol levels and lower triglyceride values. Our findings suggest that
ANP plays an important role in determining the cardiovascular and metabolic phe-
notype. These studies may also support a novel strategy of cardiometabolic risk
assessment and importantly, lay the foundation for future development of an ANP
or ANP-like therapy for metabolic syndrome.

P1654 | BEDSIDE
Unexpected High Prevalence of Possible and Probable FH in Clinical Practice
- Results of DYSIS I

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Background: The recent EAS consensus paper on familial hypercholesterolemia
(FH) indicated a higher prevalence of elevated low density lipoprotein cholesterol
(LDL-C) due to genetic reasons than previously estimated. On the basis of the
DYSIS I registry we aimed to determine the % of patients with very high LDL-C
levels.

Methods: The cross-sectional, observational study DYSIS I examined lipid goal
attainment among statin-treated patients in Canada, Europe, the Middle East,
Egypt and South Africa. We identified patients with possible genetic background
for high LDL-cholesterol using 3 approaches: [1] prevalence of LDL-C > 190mg/dl
despite statin therapy, [2] Dutch Advanced method for the identification of patients
with inherited hypercholesterolemia (using prevalence of cardiovascular disease,
age, gender, LDL-C levels and family history of premature CVD) [2.1], prevalence
of possible FH and [2.2.] prevalence of probable FH. However, 3 variables used
in the Dutch score “first degree relative cholesterol,” “xanthomas,” “arcs corneals”
were not recorded in DYSIS I and therefore this aggregate method might under-
estimate the % of patients with FH.

Results: A total of 35.451 patients with chronic statin treatment were included, of
whom 2.9% (range 0.4–8.8% per country) had LDL-C > 190 mg/dl despite statin
therapy, 6.0% (1.7–16.7%) had possible FH and 0.3% (0.0–1.4%) had probable FH
with large variations between the countries (see figure).

Conclusions: In DYSIS I, the prevalence of LDL-C > 190mg/dl despite statin treat-
ment was 2.9%, in some countries even nearly 9%. Genetic causes may explain
the very high LDL levels. As not all parameters of the Dutch score were collected
in DYSIS I, this might be an even too conservative estimate of the prevalence of
familial hypercholesterolemia in clinical practice.

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P1655 | BEDSIDE
Lipoprotein(a) in familial hypercholesterolemia with proprotein
convertase subtilisin kexin type 9 gain-of-function mutations:
Implication of residual risk in statin-era

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Background: Lipoprotein(a) [Lp(a)] is an established residual risk factor for car-
diovascular disease. Proprotein convertase subtilisin kexin type 9 (PCSK9) in-
hibitors have been reported to reduce Lp(a) up to ~30%, the mechanism of which
remains unclear. In addition, few data exist regarding the Lp(a) levels in patients
with familial hypercholesterolemia (FH) exhibiting gain-of-function PCSK9 muta-
tions, which could provide us an insight into the mechanism of reduction of Lp(a)
by PCSK9 inhibitor.

Objective: We aimed to determine whether the patients with FH due to the gain-
of-function mutations in PCSK9 gene exhibit higher Lp(a) level as well as higher
incidents of cardiovascular disease compared to those in patients with LDL re-
ception mutation or to those in normal controls.

Methods and results: Nineteen mutation-determined heterozygous FH pa-
tients with gain-of-function PCSK9 mutation (FH-PCSK9, mean age = 38yr,
male = 9, mean LDL cholesterol – 264±58mg/dl), 68 mutation-determined heterozygous
FH patients with LDLR mutations (FH-LDLR, mean age=49yr, male=37, mean
LDL cholesterol = 245mg/dl), and 34 controls (CONTROLS, mean age=62yr,
males=20, mean LDL cholesterol = 108mg/dl) were evaluated. We assessed their
total cholesterol, triglyceride, HDL cholesterol, LDL cholesterol, the presence
of coronary artery disease, and Lp(a) levels. There were no significant differ-
ces of Lp(a) levels of among those 3 groups (FH-PCSK9, FH-LDLR, and CON-
TROLS, median Lp(a)=20.7mg/dl [IQR: 11.0–37.6], 23.4 mg/dl [IQR: 15.1–40.0],
21.0mg/dl [IQR: 13.2–31.3], respectively, Mann–Whitney U test). Also there was
no difference between the presence of coronary artery disease in FH-PCSK9 and
that of FH-LDLR (15.8% vs. 17%, Chi-square test).

Conclusion: These data suggest that the mechanism of reduction in Lp(a)
through PCSK9 inhibitor might be independent of LDL receptor. Such unknown
pathway(s) could be new therapeutic target(s) for the residual risk in this statin-
era.
P1656 | BEDSIDE
The association between serum apolipoprotein B and acute myocardial infarction is modified by plasma glycerol
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Background: Hepatic cholesterol uptake and VLDL excretion depend on the availability of free glycerol.

Purpose: We investigated whether plasma glycerol 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 statin therapy.

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 glycerol.

Results: Median (IQG) serum apoB was 87 (73–104) mg/dL, and slightly higher among patients with low glycerol levels. After median 4.6 years, 344 patients (8.3%) experienced an AMI, with equal incidence rates in strata of glycerol 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 glycerol 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 glycerol. This suggests that the relationship between circulating apoB and cardiovascular risk might be influenced by decreased hepatic clearance, rather than increased secretion, of circulating apoB containing lipoproteins. Impaired turnover of VLDL remnant particles between the systemic and hepatic compartments may increase the life-span of circulating atherogenic lipoproteins, and making them more prone to oxidative damage.

P1657 | BEDSIDE
A variant in FLT1 is associated with long-term cardiovascular events in high-risk patients: replication of genome-wide association data
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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 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 GWASs were selected for candidate SNPs. Replication cohort was established by 2,814 that showed strong associations with coronary artery disease in prior GWASs. Replication cohort was established by 2,814 participants recruited from the general population of the Metropolitan area of Seoul.

Results: Median (IQR) serum apoB was 87 (73–104) mg/dL, and slightly higher among patients with low glycerol levels. After median 4.6 years, 344 patients (8.3%) experienced an AMI, with equal incidence rates in strata of glycerol 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 glycerol 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 glycerol. This suggests that the relationship between circulating apoB and cardiovascular risk might be influenced by decreased hepatic clearance, rather than increased secretion, of circulating apoB containing lipoproteins. Impaired turnover of VLDL remnant particles between the systemic and hepatic compartments may increase the life-span of circulating atherogenic lipoproteins, and making them more prone to oxidative damage.

P1658 | BEDSIDE
Ideal cardiovascular health and carotid stiffness, The Paris Prospective Study III
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Purpose: To explore the associations between ideal cardiovascular health (ICVH) and surrogate markers of vascular disease including carotid intima media thickness (c-IMT), carotid stiffness and carotid distensibility using the baseline data of the Paris Prospective Study III.

Methods: Mean common c-IMT, carotid stiffness (Young elastic modulus) and carotid distensibility were measured by high-precision echotracking device in 6163 participants attending a health check up in a large health center 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 2–3; 4–5 and 6–7 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 0.53 (0.12) mm. Mean cIMT was 0.53 (0.12) mm. Among 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 glycerol. This suggests that the relationship between circulating apoB and cardiovascular risk might be influenced by decreased hepatic clearance, rather than increased secretion, of circulating apoB containing lipoproteins. Impaired turnover of VLDL remnant particles between the systemic and hepatic compartments may increase the life-span of circulating atherogenic lipoproteins, and making them more prone to oxidative damage.

P1659 | BEDSIDE
Twenty-five years 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 Monica-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 infarcts 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 infarcts decreased 5% both in females (from 434/10000 inh. to 89/10000 inh.) and in males (from 1032/10000 to 210/10000 inh, aged 35–74 years). Over the same period, the number of diagnostic coronary angiographic procedures performed increased steadily and significantly, both in males (from 510 to 1072/10000 inh, p < 0.01) and females (from 143/10000 inh. in 1986 to 439/10000 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 20% of first coronary angiograms performed in males and 30% of females.
males in 2011. Consequently, the incidence of patients diagnosed with significant new CAD on first angiograms decreased from 592/100000 to 393/100000 male inh. from 1995 until 2011 and 171/100000 to 108/100000 female inh. aged 34–75 years. Also, rates of first revascularization by either PCI or CABG remained stable in females at about 125/100000 inh. aged 35–74 years, while it decreased significantly in males from a peak of 426/100000 inh. aged 34–75 years in 1996 to 358/100000 inh. in 2011. The proportion of first coronary angiograms resulting in revascularization decreased in females from 43% in 1995 to 30% in 2011 and remained stable in males around 48–53% since 1995.

Conclusions: 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.

P1660 | BEDSIDE
The impact of single nucleotide polymorphism of superoxide dismutase on cardiovascular and all-cause mortality in the general population
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Background: Oxidative stress is a major cause of cardiovascular disease. Superoxide dismutases (SOD) are antioxidant enzymes which keep cellular reactive oxygen species homeostasis against oxidative stress. Single nucleotide polymorphisms (SNP) within SOD genes were reported to be associated with the development of cardiovascular disease. However, it remains to be determined the impact of SNPs within SOD on cardiovascular and all-cause mortality in general population.

Methods and results: This longitudinal cohort study included 2611 subjects who were recruited in a community-based health check-up with 8-year follow-up. We genotyped 7 SNPs within the SOD genes (rs2070424, rs4998557, rs1041740, rs4817420 and rs17880487 within SOD1; rs4880 within SOD2; rs1799885 within SOD3) and found that rs1041740 was related to clinical outcomes. There were 147 deaths during the follow-up period, including 42 cardiovascular deaths. The homozygous T-allele, heterozygous and homozygous C-allele carriers of rs1041740 were identified in 286 (11%), 1179 (45%), and 1146 (44%), respectively. The homozygous T-allele of rs1041740 carriers showed elevated brain natriuretic peptide levels and kidney dysfunction. Multivariate Cox proportional hazard regression analysis revealed that the homozygous T-allele of rs1041740 was associated with all-cause and cardiovascular deaths after adjustments for confounding factors. Net reclassification index was significantly increased by addition of rs1041740 to conventional cardiovascular risk factors. Kaplan-Meier analysis revealed that the homozygous T-allele carriers had higher rate of all-cause and cardiovascular deaths compared to those without.

Conclusions: SNP within SOD rs1041740 was associated with all-cause and cardiovascular deaths in the general population.

P1661 | BEDSIDE
Whole exome sequencing identifies deleterious variants in ABCA6 and ABCA10 genes possibly associated with hyper HDL-cholesterolemia
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Background: Plasma high-density lipoprotein cholesterol (HDL-C) is a quantitative, heritable risk factor for coronary heart disease. Several genes are known to cause high HDL-C level in Mendelian manner, including (Cholesteryl ester transfer protein) CETP.

Objectives: This study aimed to identify the causal variant in a large family with hyper HDL-cholesterolemia of unknown pathogenesis through whole exome sequencing.

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 (rs7542907, 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 pharmaceutical target for ABCA6 and ABCA10.

P1662 | BEDSIDE
Serum apoB level is superior to non-HDL-C and LDL-C in the severity prediction assessed by Gensini Score among un-treated patients undergoing coronary angiography
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Background: Cardiovascular risk assessment commonly incorporates measurement of atherogenic lipids such as low-density lipoprotein cholesterol (LDL-C), non-high-density lipoprotein cholesterol (NHDL-C), and apolipoprotein B (apoB). However, which is most closely related to the severity of coronary atherosclerosis has not been assessed yet.

Methods: We studied 1763 consecutive subjects undergoing coronary angiography who were not received any lipid-lowering therapy. LDL-C was measured directly, NHDL-C was calculated, apoB was measured with immunosassay. The severity of coronary stenosis was determined using the Gensini Score (GS) system.

Results: In patients with coronary atherosclerosis (n=1103), apoB (OR=0.138, p<0.001) and NHDL-C (OR=0.134, p<0.001) were more closely related to GS than LDL-C (OR=0.110, p<0.001) tested by Spearman correlation analysis. In the overall population, LDL-C, NHDL-C, and apoB were all dramatically increased according to the quartiles of GS (p<0.001, all). Multivariate logistic analysis suggested that apoB (OR=2.384, 95% CI 1.597–3.560, p<0.001) was superior to NHDL-C (OR=1.323, 95% CI 1.163–1.505, p<0.001) and LDL-C (OR=1.285, 95% CI 1.129–1.462, p<0.001) in predicting high GS after adjusting for potential confounders. To exclude the potential confounder induced by diabetes mellitus (DM), we performed a subgroup analysis and found that apoB (OR=2.912, 95% CI 1.344–6.308, p<0.001) was more strongly associated with high GS than NHDL-C (OR=1.337, 95% CI 1.050–1.702, p=0.018), while LDL-C (OR=1.224, 95% CI 0.955–1.569, p=0.110) could not predict high GS in patients with DM.

Conclusion: Our results demonstrated that apoB was superior to non-HDL-C and LDL-C in predicting the severity of coronary atherosclerosis, especially in patients with DM.

PSYCHO-SOCIAL STRESS: THE RISK FACTOR OF THE MODERN ERA

P1663 | BEDSIDE
Validity and reliability of the HeartQoL questionnaire based on the EUROASPIRE IV study
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Background: Recently, the HeartQoL, a core health-related quality of life (HRQL)

instrument in patients with coronary heart disease (CHD), was developed for making between-diagnosis comparisons possible and to assess the change in HRQL after treatment. The HeartQoL consists of 14 items; 10 items focusing on physical HRQL and 4 items on emotional HRQL 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, excellent internal consistency was found on the global scale (α=0.92) and the physical subscale (α=0.91), and good internal consistency was seen on the emotional scale (α=0.87). Factor analyses confirmed the two-dimensional construct with factor loadings >0.5 with potential allocation problems on one item and fit indices which resulted in inconsistent outcomes. On country-specific level, Bosnia scored poorly, probably due to a mistranslation of the questionnaire. Discriminative validity was confirmed with females reporting poorer global, physical and emotional scores, older patients reporting poorer global and emotional scores and lower educated patients reporting poorer global, physical and emotional scores. Likewise convergent validity was confirmed with moderate to strong correlations among hypothesized constructs.

**Conclusion:** Overall, psychometric analyses of the HeartQoL instrument in a population of patients with stable CHD who had been hospitalised for a first or recurrent coronary event, showed good reliability and validity both at the European as well as on country-specific level. Further research should focus on respective language translation issues, construct validity and the ceiling effect of the emotional subscale.

**P1664 | BEDSIDE**

**Prevalence, predictors and protective factors of job-related distress in a hospital cardiac 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 medical staff to adopt new demands that may engender stress and affect work satisfaction. Physician distress impacts on the frequency of medical errors, patient’s compliance and health care costs.

**Purpose:** The IANUS survey was designed to determine the prevalence of job-related distress in a nationwide cardiologist sample and to assess the relationship between personal-professional characteristics and positive and negative experiences in cardiological practice.

**Methods:** Out of 7393 cardiologists of a national scientific cardiology society, 1064 completed a web-based 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 medical profession, 52% were satisfied with their job. Factor analysis revealed a meaningful underlying structure consisting in four factors characterized as personal-professional imbalance, positive meaning, emotional fatigue and relational difficulties. Subjects working in interventional areas reported significantly higher positive meaning than those in clinical inpatients and outpatient departments of hospitals 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 translation issues, construct validity and the ceiling effect of the emotional subscale.

**P1665 | BEDSIDE**

**Psychosocial consequences of venous thromboembolism in youth. Results from 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 control were 7.0% and 15.8%, respectively;95% confidence interval 3.9% to 5.5%; respectively;10.8%, 95% confidence interval 9.4% to 12.3%). Four main themes relating to the psychosocial impact of a VTE in youth was identified in the interview data 1) To be different and alone 2) Raising a red flag 3) Living with uncertainty and 4) To be serious about serious issues.

**Conclusion:** A VTE diagnosis in youth is associated with a poorer mental health prognosis: more than one in five patients will experience mental health issues requiring psychotropic medication within 5 years. A VTE diagnosis is accompanied by serious concern of being alone, which is 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.
**Effect of combined occupational tasks on cardiovascular events: Prime study**

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**Background:** Sedentary behaviour in leisure time or at home increases cardiovascular risk, but it is uncertain whether this is also the case for occupational activity.

**Purpose:** To investigate the qualitative and quantitative effects of different types of occupational tasks and how they interacted together on incidence of cardiovascular disease (CVD).

**Methods:** The study included 7796 active middle aged European men from the PRIME cohort. Using Cox proportional hazards analysis, and taking account of anthropometric and biomedical factors, energy expenditure during leisure time and commuting related physical activity, lifestyle habits and social factors, the effects of time spent sitting or standing still, carrying objects and walking at work were investigated 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 still at work showed a hazard ratio (HR) of 1.38 [1.19–1.59] for subjects who spent > 300–1200 and 1200–1800 mins/week spent 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:** 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.

**Comparative potential of the 2- and the 9-item patient health questionnaire to predict death or re-hospitalization in heart failure**

S.M. Piepenburg1, H. Faller2, S. Storkel3, G. Gelbrich4, B. Warrings4, G. Eri5, C. Angermann5, 1Medizinische Klinik und Poliklinik I, Universität Würzburg, Würzburg, Germany; 2Abteilung für Medizinische Psychologie und Psychotherapie, Universität Würzburg, Würzburg, Germany; 3Institut für klinische Epidemiologie und Biometrie, Universität Würzburg, Würzburg, Germany; 4Klinik und Poliklinik für Psychiatrie, Psychosomatik und Psychotherapie, Universität Würzburg, Würzburg, Germany

**Background and aims:** Heart failure (HF) prevalence is growing in high-income countries. Comorbid depression is common in HF and may impact adversely on outcomes. Thus screening becomes more and more important. We studied the comparative potential of the shorter 2-item Patient Health Questionnaire (PHQ-2) versus that of the 9-item version (PHQ-9) to predict death or re-hospitalization in participants of the Interdisciplinary Network for Heart Failure Study program.

**Methods and results:** Patients were eligible, if hospitalized for cardiac decompensation and if left ventricular ejection fraction (echocardiography) was ≤40% before discharge. Patients were selected when they had completed the PHQ-9 at baseline. PHQ-2 scores were extracted from the first 2 questions. To analyze associations of PHQ-2 and PHQ-9 with death and re-hospitalization, univariable Cox regression models were employed. To compare the effectiveness of PHQ-2 versus PHQ-9 screening, c-statistics were computed. The sample consisted of 852 patients, (67.6±12.1 years, 27.7% female, 42.3% New York Heart Association class III/IV). Follow-up was 18 months (100% complete). Both PHQ-2 and PHQ-9 predicted death in univariable analysis [hazard ratio [HR] 1.18, 95% confidence interval [CI] 1.09–1.29, p<0.001, and HR 1.07, 95% CI 1.04–1.09, p<0.001]. They also predicted re-hospitalization in univariable analysis (HR 1.07, 95% CI 1.01 to 1.21, p=0.02 and HR 1.03, 95% CI 1.01 to 1.04, p=0.001). These results were confirmed by c-statistics.

**Predictive value of PHQ-2 and PHQ-9**

Conclusions: In univariable models and confirmed by c-statistics the predictive potential of both PHQ-2 and PHQ-9 proved comparable. In clinical practice, PHQ-2 screening seems reliable and more feasible than the time-consuming PHQ-9 to identify patients at risk of adverse outcomes.

**Abrupt changes in heart rate of supporters during FIFA world cups**

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**Background:** Heart rate changes in supporters have been linked to aspects of emotional state and sports results. However, it is not known how the relative importance of the match as first round, last sixteen to semi finale, and finale. We investigated the relative importance of the match as first round, last sixteen to semi finale, and finale.

**Methods:** Data were prospectively collected in 102 patients between june 2006 and july 2014 during the last three FIFA world cup of football. Participants were 102 fans of different national football teams participate in a simple, non-binding study devoted to football supporters during the last three FIFA world cup. We studied changes occurring in heart rate during football matches, taking into account both the cardiovascular risk factors of the participants, and the relative importance of the match as first round, last sixteen to semi finale, and finale.

**Results:** Average heart rate significantly increased during the matches (mean change 30 beats per minutes, p=0.02). The maximum heart rate reached 95% or more during the semi-finals and the final. The maximum heart rate reached 95% or more during the semi-finals and the final.

**Conclusions:** Heart rate changes in supporters during FIFA world cups

**Maximal heart rate of supporters during the last three World Cups of football (percentage refers to maximal theoretical heart rate)**

<table>
<thead>
<tr>
<th>World Cup 2006</th>
<th>World Cup 2010</th>
<th>World Cup 2014</th>
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</thead>
<tbody>
<tr>
<td>N=30</td>
<td>N=95</td>
<td>N=50</td>
</tr>
<tr>
<td>Finals</td>
<td>190/min (94%)</td>
<td>180/min (90%)</td>
</tr>
<tr>
<td>Semi-final</td>
<td>170/min (85%)</td>
<td>162/min (84%)</td>
</tr>
<tr>
<td>Last sixteen to quarter</td>
<td>158/min (83%)</td>
<td>152/min (78%)</td>
</tr>
<tr>
<td>First round</td>
<td>130/min (70%)</td>
<td>140/min (82%)</td>
</tr>
</tbody>
</table>

**Comparative potential of the 2- and the 9-item patient health questionnaire to predict death or re-hospitalization in heart failure**

S.M. Piepenburg1, H. Faller2, S. Storkel3, G. Gelbrich4, B. Warrings4, G. Eri5, C. Angermann5, 1Medizinische Klinik und Poliklinik I, Universität Würzburg, Würzburg, Germany; 2Abteilung für Medizinische Psychologie und Psychotherapie, Universität Würzburg, Würzburg, Germany; 3Institut für klinische Epidemiologie und Biometrie, Universität Würzburg, Würzburg, Germany; 4Klinik und Poliklinik für Psychiatrie, Psychosomatik und Psychotherapie, Universität Würzburg, Würzburg, Germany

**Background and aims:** Heart failure (HF) prevalence is growing in high-income countries. Comorbid depression is common in HF and may impact adversely on outcomes. Thus screening becomes more and more important. We studied the comparative potential of the shorter 2-item Patient Health Questionnaire (PHQ-2) versus that of the 9-item version (PHQ-9) to predict death or re-hospitalization in participants of the Interdisciplinary Network for Heart Failure Study program.

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Conclusions: In univariable models and confirmed by c-statistics the predictive potential of both PHQ-2 and PHQ-9 proved comparable. In clinical practice, PHQ-2 screening seems reliable and more feasible than the time-consuming PHQ-9 to identify patients at risk of adverse outcomes.
more of the maximal heart rate for age in 80% of the 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 compare to changes expected in maximal
treadmill exercise tests, what should be taken into account, especially for those
with overt cardiac diseases, or high global cardiovascular risk.

P1671 | BEDSIDE
Spirituality and depression in patients with coronary artery disease
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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 in-
terest to evaluate spirituality in the context of coronary artery disease (CAD).

Purpose: Evaluate spirituality and depression in CAD patients.

Methods: Cross-sectional, single-center study including 507 patients, aged >18
years, with CAD diagnosed by means of coronary angiography in an tertiary hos-
pital. All patients answered a self-administered questionnaire about depression
(Depression, Anxiety and Stress Scales 21-items - DASS-21) and spirituality
(Functional Assessment of Chronic Illness Therapy – spiritual well being – FACIT -
SP12). For statistical analysis, 2 groups of depression were defined: Group A (no
or mild) and B (moderate, severe or very severe).

Results: 507 patients, 66% male gender and median age of 63 years. CAD man-
dagement was 32.7% CABG, 32% PCI, 11.8% both and 23.5% optimal medical
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
quintile patients (p-value 0.018).

Conclusion: Lower scores of spirituality were associated with higher severity of
depressive symptoms. Results should be seen as hypothesis-generating and fur-
ther studies should be conducted to test association of spirituality and depression
and its impact on cardiovascular outcomes.

P1672 | BEDSIDE
Influence of cognitive decline on 30-day outcomes in hospitalized
patients with acute heart failure
H. Kawanishi1, M. Oguri1, K. Yasuda1, T. Katagiri1, M. Shimano1, H. Kamijya1, H. Ishii2, T. Murohara2.
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Background: Previous reports have shown that contribution of social factors to
the prognosis of heart failure is increasing. However, the effect of cognitive decline
to 30-day outcomes have remained largely unknown.

Purpose: The purpose of the present study was to examine the association be-
tween cognitive decline and outcomes in hospitalized patients with acute heart
failure.

Methods: A total of 743 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 nutritional status was
assessed using the Controlling Nutritional Status (CONUT) score taking into ac-
count including serum albumin, total cholesterol level and total lymphocyte count,
and poor nutrition status was defined as the score ≥5. Cox proportional hazard
analysis was used.

Results: The prevalence of cognitive decline was 13.7%. Overall 30-day out-
comes was 8.6% and median length of stay was 17 days (interquartile range
11–26). Age, female gender, the prevalence of poor nutrition status, anemia, and
stroke were greater, whereas the prevalence of smoking, diabetes mellitus, and
dyslipidemia were lower in patients with cognitive decline than those with nor-
cmal cognitive function. In hospital treatments, including intravenous diuretics or
vasodilators, and non-invasive positive pressure ventilation, were similar between
the two groups. The incidence of 30-day outcomes was significantly greater in pa-
tients with higher cognitive decline (15.8% vs. 7.4%, P=0.050). The hospital length
of stay was not different between the two groups (P=0.5813). Univariate cox propor-
tional hazard analysis revealed that age, poor nutrition status, cardiogenic shock,
hyponatremia (serum sodium concentration <136 mEq/L), chronic kidney disease
(eGFR ≤ 60 ml/min/1.73 m²), etiology of acute myocardial infarction, and cognitive
decline significantly (P < 0.05) associated with 30-day outcomes. In multivariate
cox proportional hazard analysis with adjustments for covariates, cognitive de-
icline significantly and independently associated with 30-day outcomes (hazard
ratio 1.41, 95% confidence interval 1.01–1.91, P=0.0410).

Conclusions: This study suggested that cognitive decline conferred a significant
increase in the occurrence of 30-day outcomes in hospitalized patients with acute
heart failure.

TREATMENT STRATEGIES AND ADHERENCE:
CAN WE DECREASE RISK?

P1673 | BEDSIDE
Plant sterol supplementation on top of lipid-lowering therapies in
familial hypercholesterolemia
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Paulo, Sao Paulo, Brazil

Background: Familial hypercholesterolemia (FH) is the most common inherited
disorder of lipid metabolism, resulting in very high levels of LDL-cholesterol (LDL-
C) from birth and increased premature coronary disease. Underdiagnosed and
untreated, this condition often requires combined lipid-lowering therapy (LLT),
with room for further interventions. Plant sterols (PS) supplementation, by reduc-
ing intestinal cholesterol absorption, can further lower LDL-cholesterol in 10%, but
the combination of high-dose statin, ezetimibe and PS has not been additive
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
blinding fashion for 12 weeks. After this period, 2g of phytosterols, as free sterols
were 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
statin therapy alone. In addition to ezetimibe, PS can counterbalance the increased
sterols 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.

Acknowledgements/Funding: FAPESP (Foundation for the Research of the State
of Sao Paulo, Brazil), INCT-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-clinical” workflow 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 HTA-DLP reduced direct costs of 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).

Conclusions: A lipid clinical practice a specific CDSST 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 Observa-

tions in health.

P1675 | BEDSIDE

Are coronary patients on lipid-lowering therapy in Europe achieving the recommended LDL-C target? Results from the Dyslipidemia International Study (DYSII) II Europe

A.K. Gitt1, J. Ferrieres2, G. De Ferrari2, M. Elissaf3, M.P. Herman4, T. Kieran5, R. Oganes6, D. Lautsch7, V. Ashton8, B. Ambegaonkar8 on behalf of DYSII II Europe Investigators. 1Stiftung Institut für Herzinfarktforschung und Herzcentrum Ludwigshafen, Med. Klinik B, Cardiology, Ludwigshafen am Rhein, Germany; 2Toulouse University School of Medicine, Rangueil Hospital, Toulouse, France; 3Fondazione I.R.C.C.S. Policlinico San Matteo, Pavia, Italy; 4University of Ioannina School of Medicine, Ioannina, Greece; 5Cliniques Universitaires St Luc, Brussels, Belgium; 6University Hospital Limerick, Limerick, Ireland; 7State Research Centre for Preventive Medicine, Moscow, Russian Federation; 8Merk & 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 world lipid target achievement, including dis-
tance to target, among patients with stable coronary heart disease (CHD) and patients surviving an acute coronary syndrome (ACS) event in Europe.

Methods: DYSII II 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 in all patients for 6 months prior to enrollment for CHD patients. Patients were on lipid-lowering therapy (LLT) >3 months and not participating in clinical trials involving medication. Patient characteristics, risk factors, treatment patterns, and laboratory values were collected.

LDL-C target achievement was assessed based on ESC/ESA guidelines.

Results: 880 ACS and 2778 CHD patients currently on LLT 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>Mean lipid values and LDL</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±1.0</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>2.8±0.9</td>
</tr>
<tr>
<td>Atraveso equivalent dose (mg/day)</td>
<td>22±17</td>
<td>27±20</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 (fibates, 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>

Conclusions: Three out of four coronary patients did not achieve the recom-

mended LDL-C target, even while being treated with LLT, primarily statin monotherapy. Nearly 60% of patients with low LDL-C targets were found in both patient cohorts, despite the high risk of our patient population and the need for more intensive LLT (as stressed by our distance to target findings).

Acknowledgement/Funding: This study was funded by Merck & Co., Inc.
with suspected SI presented with muscle-related symptoms (range across countries [RAC] 50–87%). In these patients, clinicians took a range of steps to establish SI, including (1) discontinuation of statin (average 59%, RAC 48–67%); (2) statin re-challenge (average 74%; RAC 60–85%); and (3) modification of statin regimen (average 76%; RAC 65–85%); 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 may foster more defined therapeutic algorithms and be expected to more satisfactorily address CV risk management in these patients.

Acknowledgement/Funding: This study was sponsored by Amgen Inc.

P1678 | BEDSIDE

Real life adherence data to clinical practice guidelines for lipid management in chronic kidney disease: a multicenter cross-sectional survey

M. Arici on behalf of Turkish Society of Nephrology Working Group on Cardiological Syndrome, Hacettepe University, Nephrology, Ankara, Turkey

Background: The recent “Clinical Practice Guideline for Lipid Management in Chronic Kidney Disease (CKD)”, to our knowledge, is the only clinical guideline for lipid management in CKD patients. 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 tailored LLT and 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: (age ≥ 53, ≥10 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±29208.86 mg/day. Mean LDL level was 131±2978.15 mg/dl and 44.2% of the patients had levels above normal (LDL-L 130 mg/dl). Lipid profile was assessed at first admission in only 3.2% 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 state was checked according to age and CKD stages, in adults aged ≥50 years with eGFR 60 ml/min/1.73 m² and GFR categories G3a-G5 only also contribute to insulin resistance and atherosclerosis. Prior reports of the hepatic uptake of triglyceride (TG)-rich lipoproteins (such as lipoprotein A) contribute to insulin resistance and atherosclerosis. Prior reports of the ApoC-III levels in patients from the MARINE and ANCHOR studies (IPE 4 g/day and placebo)

Conclusion(s): 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.

P1680 | BEDSIDE

High prevalence of persistent lipid abnormalities among coronary patients: the Dyslipidemia International Study (DYSIS) II global results

A.K. Gitt, J. Ferrieres, V. Ashton, M. Horak, P. Brud, B. Ambegaokar on behalf of DYSIS II Study Investigators. 1Stiftung Institut für Herzinfarktforschung, and Herzzentrum Ludwigshafen, Med. Klinik B, Cardiology, Ludwigshafen am Rhein, Germany; 2Toulouse University School of Medicine, Toulouse, Toulouse, France; 3Merck & Co., Inc., Kenilworth, United States of America; 1Stiftung Institut für Herzinfarktforschung, Ludwigshafen am Rhein, Germany

Background: Prior observational trials have documented a gap between guideline recommendations and low density lipoprotein cholesterol (LDL-C) target achievement in clinical practice. Little is known if this might have changed after the release of the most recent ESC/EAS guidelines promoting an LDL-C <1.8 mmol/l in high risk patients.

Purpose: DYSIS II documents real world lipid target achievements and the prevalence of dyslipidemias among patients with stable CHD and patients surviving an ACS event.

Methods: DYSIS II is a multi-country, observational, cross-sectional study conducted in 21 countries from Asia/Pacific, Europe, and Middle East/Africa. General practitioners, internists, cardiologists and endocrinologists from 362 sites enrolled patients into two study cohorts (ACS and CHD). Eligible adult patients were hospitalized for an ACS event or had a documented history of CHD, full lipid profile available within 24 hours of hospital admission for ACS patients and 0–12 months prior to enrollment for CHD, on lipid lowering therapy (LLT) >3 months or not at all, and not participating in medical trials involving lipid-lowering agents. Patient clinical, lab values were collected. LDL-C target achievement was assessed based on ESC/EAS guidelines.

Results: 3872 ACS and 6803 CHD patients were enrolled between 2012 and 2014, with 65.2% and 93.8% currently on LLT, respectively. Among LLT treated patients, 25.6% ACS and 30.6% CHD patients achieved an LDL-C <1.8 mmol/l, with distance to target being 0.9 mmol/l (IQR 0.4, 1.6) and 0.6 mmol/l (IQR 0.3, 1.0), respectively. Mean atorvastatin equivalent dose was 22±17mg/day for ACS and 25±18mg/day for CHD patients. ACS and CHD patients LLT regimens were: statin monotherapy 90.3%, 82.4%; statin + ezetimibe 4.2%, 10.5%; statin + other 5.5%, 6.1%; and 25±18mg/day for CHD patients. ACS and CHD patients LLT regimens were: statin monotherapy 90.3%, 82.4%; statin + ezetimibe 4.2%, 10.5%; statin + other 5.5%, 6.1%; and
### P1681 | BEDSIDE

Prevalence of lipid abnormalities among coronary patients remains high in the Middle East/Africa region: the Dyslipidemia International Study (DYSIS) II MEA results

S.N. Al Stri1, W. Al Mahmeed2, R. Azar3, M. Sobby4, A.K. Citt6,5, M. Horack6, V. Ashton7, F. Brudi8, B. Aribegaonkar9, S. Wajih10 on behalf of DYSIS II Middle East/Africa Investigators. 1Al-Hada Military Hospital, Taif, Saudi Arabia; 2Heart and Vascular Institute, Cleveland Clinic, Abu Dhabi, United Arab Emirates; 3Hotel-Dieu de France Hospital, Beirut, Lebanon; 4International Cardiac Center Hospital, Alexandria, Egypt; 5Stiftung Institut für Herzinfarktforschung, and Herzzentrum Ludwigshafen, Med. Klinik B, Cardiology, 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 <1.8mmol/l.

**Purpose:** DYSIS 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:** DYSIS 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 enrolment (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 DYSIS 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 target of <1.8mmol/l (mean LDL-C 2.8±1.1 mmol/l and 2.2±1.3 mmol/l respectively). Mediane 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).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ACS (n=501)</th>
<th>CHD (n=1031)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.2±10.5</td>
<td>63.5±10.1</td>
</tr>
<tr>
<td>Male</td>
<td>77.4%</td>
<td>75.8%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>81.1%</td>
<td>94.1%</td>
</tr>
<tr>
<td>Hypertension (diabetes)</td>
<td>66.5%</td>
<td>78.7%</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>54.0%</td>
<td>50.3%</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
<td>52.1%</td>
<td>66.6%</td>
</tr>
<tr>
<td>Current smoker</td>
<td>35.9%</td>
<td>14.1%</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>19.7%</td>
<td>65.5%</td>
</tr>
<tr>
<td>Family history of CHD</td>
<td>18.2%</td>
<td>30.4%</td>
</tr>
<tr>
<td>Atorvastatin equivalent dose (mg/day)</td>
<td>25±14</td>
<td>30±18</td>
</tr>
<tr>
<td>Statin monotherapy</td>
<td>93.0%</td>
<td>79.6%</td>
</tr>
<tr>
<td>Statin + ezetimibe</td>
<td>4.2%</td>
<td>14.6%</td>
</tr>
<tr>
<td>Statin + other non-statin (fibates, omega 3 fatty acids)</td>
<td>2.0%</td>
<td>5.0%</td>
</tr>
<tr>
<td>Non-statin monotherapy</td>
<td>0.8%</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

**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 cohort

J. Ferrieres1, D.L. Steen2, R. Sanchez3, J. Chin4, K. Gorycza5, I. Khan5

1University Hospital of Toulouse - Rangueil Hospital, Toulouse, France; 2University of Cincinnati Medical Center, Cincinnati, Ohio, United States of America; 3Regeneron Pharmaceuticals, Tarrytown, New York, United States of America; 4Cegedim Strategic Data, Jersey City, New Jersey, United States of America; 5Sanoﬁ, Bridgewater, New Jersey, United States of America

**Background:** The ESC/EAS cholesterol guidelines recommend lowering low density lipoprotein cholesterol (LDL-C) to <1.8 mmol/l (70mg/dl) for very high cardiovascular (CV) risk patients.

**Purpose:** To summarize lipid-lowering treatment (LLT) and achieved LDL-C levels in patients with established CV disease and/or diabetes from a general practice cohort in France.

**Methods:** This analysis included patients from the Cegedim general practice database in France meeting the following criteria: a valid LDL-C in 2013 (index date); ≥20 years of age; continuous representation in the database for ≥2 years; and ≥1 very high risk CV condition. Patients were placed into one of six exclusive categories via the following hierarchy: acute coronary syndrome (ACS) within 12 months; other coronary heart disease (CHD); ischemic stroke; peripheral arterial disease (PAD); and type 2 diabetes mellitus. Patients were considered treated with a medication if covered by a filled LLT prescription on the index date (or within 30 days).

**Results:** A total of 29,565 patients met the inclusion criteria. Median age was 68 years, 61% were male, and the median LDL-C was 2.6 mmol/l (100mg/dl). Overall, statin use was 57% with 13% of these patients treated with high-intensity statins. The use of statins in combination with non-statin LDL-C was low, 9% and 10% among high-intensity and moderate-to-low intensity statins, respectively. Additionally, 37% were not being treated with any LLT. Achievement of LDL-C <1.8 mmol/l was only 15% and was associated with LLT intensity.

**Conclusion:** The SOLID-TIMI 52 trial enrolled 13,026 patients stabilized within 30 days of hospitalization for an ACS. The use of guideline-recommended therapies was strongly encouraged and performance reports were sent to sites, but the decision to treat with a statin and the dose were at the discretion of the treating physician. A high potency statin regimen was defined as ≥40mg atorvastatin, ≥20mg rosuvastatin or 80mg simvastatin daily. A logistic regression model with forward selection was used to identify independent predictors associated with the failure to administer a high potency statin.

**Results:** Of patients enrolled, 95.4% were on a statin at baseline after ACS, but only 41.9% were on a high potency statin. Multiple independent predictors of the failure to treat with a high potency statin were identified including: age: >75 years, non-white race, eGFR ~60ml/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.

**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.
**Purpose:** To determine the prevalence of increased BNP and Troponin T.

**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.

**Methods:** DYDIS II is a multicountry, observational cross-sectional study conducted in 87 sites throughout Hong Kong, India, Indonesia, Philippines, South Korea, Singapore, Taiwan, Thailand, and Vietnam. General practitioners, internists, cardiologists and endocrinologists enrolled patients in two distinct study cohorts: patients surviving an ACS event and patients diagnosed with stable CHD. Full lipid profile was available within 24 hours of hospital admission (ACS) or 0–12 months prior to enrollment (CHD). Patients were on lipid-lowering therapy (LLT) and were invited to participate in the study if they met the inclusion criteria. Lipids and lipoproteins were measured by standard methods, and low density lipoprotein cholesterol (LDL-C) target attainment was assessed based on 2011 ESC/EAS guidelines.

**Results:** Overall 1803 ACS and 2802 CHD patients were enrolled in 2013/2014, with 63.3% (n=1142) and 91.7% (n=2570) currently on LLT respectively. Only 31.0% (n=354) of treated ACS and 32.6% (n=838) of treated CHD patients at- tained recommended LDL-C <1.8mmol/l, with median distance to target be- ing 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%.

**Conclusion:** More than two-thirds of LLT treated patients did not attain the recommended LDL-C target, primarily being on moderate statin dose. Higher intensity LLT should be provided to these high risk patients.

**Acknowledgement/Funding:** This study was funded by Merck & Co., Inc.

**HOW DOES STRESS AFFECT CARDIOVASCULAR RISK?**

**P1685 | BEDSIDE**

LDL-C target attainment remains low among treated coronary patients in Asia-Pacific: the Dyslipidemia International Study (DYDIS) II AP results

J.P.S. Sawhney1, F.T. Chiang2, Y.S. Jang3, P.N. Vinh4, K.K. Poh5, W. Buddhari6, R. Sy7, M. Munawar8, B. Yan9, H.P. Balaji10 on behalf of DYDIS II Asia-Pacific Investigators, 1Banyan Hospital, Kuala Lumpur, Malaysia; 2National Taiwan University Hospital, Taipei City, Taiwan, ROC; 3Severance Cardiovascular Hospital, Seoul, Korea, Republic of; 4Tam Duc Heart Hospital, Ho Chi Minh City, Viet Nam; 5National University Heart Centre, Singapore, Singapore; 6King Chulalongkorn Memorial Hospital, Bangkok, Thailand; 7Cardinal Santos Medical Center, Manila, Philippines; 8Binaipravati Cardiovascular Center, Jakarta, Indonesia; 9The Chinese University of Hong Kong, 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 preva- lence of dyslipidemias among patients with stable CHD and patients surviving an ACS event in Asia-Pacific.

**Methods:** DYDIS II is a multicountry, observational cross-sectional study conducted in 87 sites throughout Hong Kong, India, Indonesia, Philippines, South Korea, Singapore, Taiwan, Thailand, and Vietnam. General practitioners, internists, cardiologists and endocrinologists enrolled patients in two distinct study cohorts: patients surviving an ACS event and patients diagnosed with stable CHD. Full lipid profile was available within 24 hours of hospital admission (ACS) or 0–12 months prior to enrollment (CHD). Patients were on lipid-lowering therapy (LLT) and were invited to participate in the study if they met the inclusion criteria. Lipids and lipoproteins were measured by standard methods, and low density lipoprotein cholesterol (LDL-C) target attainment was assessed based on 2011 ESC/EAS guidelines.

**Results:** Overall 1803 ACS and 2802 CHD patients were enrolled in 2013/2014, with 63.3% (n=1142) and 91.7% (n=2570) currently on LLT respectively. Only 31.0% (n=354) of treated ACS and 32.6% (n=838) of treated CHD patients attained recommended LDL-C <1.8mmol/l, with median distance to target being 0.8 mmol/l (IQR 0.4, 1.4) and 0.6 mmol/l (IQR 0.3, 1.0) respectively. Mean atorvastatin equivalent dose was 22±18 mg/day for ACS and 20±14 mg/day for CHD patients. LLT regimens for ACS and CHD patients were respectively: statin monotherapy 91.6%, 86.3%; statin + ezetimibe 2.5%, 7.7%; statin + other non-statin 4.4%, 5.3%; and non-statin monotherapy 1.6%, 0.8%.

**Conclusion(s):** More than two-thirds of LLT treated patients did not attain the recommended LDL-C target, primarily being on moderate statin dose. Higher intensity LLT should be provided to these high risk patients.

**Acknowledgement/Funding:** This study was funded by Merck & Co., Inc.

**HOW DOES STRESS AFFECT CARDIOVASCULAR RISK?**

**P1685 | BEDSIDE**

Clinical impact of psychological interventions to quality of life in Japanese patients with implantable cardioverter defibrillator

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**Background:** The implantable cardioverter-defibrillator (ICD) prevents sudden cardiac death and improves quality of life (QOL) in patients with high risk of life-threatening arrhythmias. However little is known about the psychological influence of ICD therapy and the intervention to shock anxiety.

**Objectives:** This study is designed to evaluate the psychological impact of intensive psychological intervention to patients with ICD.

**Methods:** We analysed the data of 2 studies (DEF-Chiba and DEF-Chiba2), which were prospective multicenter-studies investigating the psychological influence of ICD therapy in Japan. All patients completed the Florida Shock Anxiety Scale (FSAS), which was a tool designed to provide a quantitative measure of ICD shock-related distress. High FSAS scores reflect a patient’s individual anxiety. In the DEF-Chiba study, all patients were followed-up without psychological interventions. On the other hand, in the DEF-Chiba2 study, all patients underwent examinations by psychiatrists before and after ICD implantation. The FSAS score at 12 months was significantly lower in DEF-Chiba2 study than in DEF-Chiba study (17.6±8.5 vs 14.3±5.0, P<0.001).

**Conclusion:** Psychological interventions were effective in patients with ICD. Female, experience of shock therapy and secondary indication influenced psychological QOL. Therefore, these population should be considered to aggressive interventions by psychiatrists.

**P1687 | BEDSIDE**

Trigger and consequence of shock therapy in Japanese patients with implantable cardioverter defibrillator

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**Introduction:** Shock-related anxiety is particularly relevant to psychological con- cerns and quality of life for the implantable cardioverter defibrillator (ICD) popu- lation. Recently, the Florida Shock Anxiety Scale (FSAS), which was designed to provide a quantitative measure of ICD shock-related distress, has established trigger factors of device firing (e.g., scaring sexual activity) and consequence fac-
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 0 of trigger factors was significantly higher in the “appropriate shock group” (patients who have experienced shock therapies) compared to the “no shock group” (patients who have never experienced shock therapies), as demonstrated in Table. The score of consequence factors was not significantly different between two groups.

Table: 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>0.01</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

P1688 | BEDSIDE
The effect of synthetic cannabinoids on P-wave dispersion: an observational study

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Purpose: Synthetic cannabinoids (SC) consumption has become widespread, due to its availability that is cheaper than other cannabinoids and its popularity has been increased due to recent trials.

Methods: We analysed the data of DEF-Chiba study, investigating the relationship between SC consumption and cardiovascular risk in patients with SC consumption.

Results: Age and sex distribution were similar between two groups (26.9±7.3 years vs 26.2±6.4 years and 39 male vs 19 male, p=0.687, 0.611, respectively). Mean duration of SC consumption was 1.8±0.7 years. Mean BAPI score of patients who have experienced shock therapies was 13.8±2.8. Our study population had moderate BASI score in those patients. Our results demonstrated that SC consumption was correlated with BASI score. PD value was independent predictor of BASI score in those patients. Our results demonstrated that SC consumption was correlated with BASI score (r² of the model = 0.298; p=0.025).

Conclusions: BAPI score was significantly correlated with PD value (r=0.528, p=0.003). Among patients who have experienced shock therapies) compared to the “no shock group” (patients who have never experienced shock therapies), as demonstrated in Table. The score of consequence factors was not significantly different between two groups.

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P1690 | BEDSIDE
A continuum in cocaine cardiotoxicity. From myocardial strain alteration to left ventricular dysfunction. A cardiovascular magnetic resonance strain/stRAIN study

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Background: Cocaine is a highly addictive drug with potentially cardiovascular lethal effects. We have previously shown with cardiovascular magnetic resonance (CMR) decreased left ventricular ejection fraction (LVEF) in 35% of asymptomatic cocaine addicts, though dysplastic myocardial dysfunction might appear earlier. New analysis softwares allow for the accurate and reproduce 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. A 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 global longitudinal and radial strain rate (GLSR, GRSR), all showing a significant and progressive decrease along the groups (H vs P vs D).

Conclusions: 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 multi-center study of patients with ACS in Switzerland. We used a validated self-assessed questionnaire, the 20-items Center for Epidemiologic Studies Depression Scale (CES-D), to screen for depression (score >16) during hospitalization, and one year after discharge. Depression improvement was defined as the presence of depression at baseline only, persistent or new depression when present both at baseline and at one year after, or after one year only. In a multivariate logistic model we assessed whether one-year: 1) ideal cholesterol management, defined as LDL-cholesterol below 1.8 mmol/l or 50% decrease or use of high-intensity statins (atorvastatin 40 mg or rosuvastatin 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; 6) reporting using drugs or other angiotensin-converting enzyme inhibitors, angiotensin-receptor blockers, or different types of cardiac arrhythmias, including non-sustained ventricular tachycardia, in 19 patients (54%).

**Results:** Between 2009 and 2013, 1,164 patients with ACS were screened for depression both at baseline and at one-year follow-up. Overall, 444 (38.1%) patients had depression; 129 (11.1%) had improved depression at one-year, and 315 (27.1%) had persistent or new depression. Patients with depression were less frequently married (p=0.015), had more diabetes (p=0.03), were more frequently smokers (p<0.001) and anti-depressive drug users (p<0.001) than patients without depression. At one year, factors associated with improvement of depression were intensification of physical activity with multivariate-adjusted odds ratio (OR) 1.96, 95% confidence interval (CI), 1.25–3.06 and smoking cessation for smokers (OR 2.30, 95% CI 1.10–4.78). Rates of ideal cholesterol or blood pressure management, alcohol reduction for at-risk users, and adherence to recommended drugs were similar between improved or persistent/new depression.

**Conclusion:** Intensification of physical activity and smoking cessation were associated with improvement of depression. The results were compared with the ones obtained in a representative age-matched group of adults (NATPOL, 2011).

**Supported by:** The Swiss National Scientific Foundation 2009-2014, (SPUM 33CM30_124112 and SPUM 33CM30_140336)

**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 activation rate (VAR) was used in analysis. Collected data were analyzed by one 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 determined by one way ANOVA F(2,16)=3.12, p=0.047. Dunnett’s T3 test for post hoc revealed that VAR in alcoholic patients during withdrawal was similar to the values obtained in a representative group of adults (NATPOL, 2011). However, the most significant data were revealed in patients in the 3rd group, because they live sedentary lifestyle under persistent examination stress until they pass the entrance examination.

**Conclusions:** How does stress affect cardiovascular risk? 291

**P1693 | BEDSIDE**

Dramatic 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 serious medical, social and economic problem. However, in the socially-deprived segment of the population, which is the focus of this research, data on factors predisposing to CVD are lacking.

**Purpose:** The aim of the study was to assess prevalence and control of cardiovascular risk factors in homeless people and to compare them with general population.

**Methods:** The study included a representative group of 614 homeless people (104 females[F] aged 21–79, mean age 49.0±13.6 years; 501 males[M] aged 18–79, mean age 53.7±11.6 years) at Polish shelters and hostels. The participants’ BMI, blood pressure, fasting serum lipids concentration, C-reactive protein (CRP), glucose, creatinine were determined. The occurrence of smoking and depression was assessed with questionnaire. The results were compared with those obtained in a representative age-matched group of adults (NATPOL, 2011).

**Results:** Hypertension was identified far more often in the homeless than in NATPOL study subjects. (54.9% 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<0.05). Total cholesterol and LDL levels were significantly higher in homeless men (209.4±7.1mg/dl vs 197.1±1.7mg/dl and 133.5±2.2mg/dl vs 123.7±1.4mg/dl respectively). CRP concentration was also higher in homeless subjects, F:5.61±1.5mg/l, M:6.02±0.6mg/l vs F:2.01±0.1mg/l, M:1.81±0.1mg/l, than in general population. Glucose concentration in homeless men was higher compared to general population but the difference was not statistically significant (100.9±2.2mg/dl vs 95.9±0.9mg/dl respectively). There were more smokers in the homeless group than in general population (F:73.3% & M:79.6% vs F:37.8% & M:49.7% respectively; p<0.05). Depressive symptoms according to Beck’s Depression Scale were observed more often in homeless persons (M:28.8% vs 14.9% respectively; p<0.05). Obesity wasn’t dominant in the homeless.

**Conclusions:** CVD risk factors are more increased in the homeless group, especially homeless males, than in general population. The study is congruent with European Platform Against Poverty. The results may be applied in preventive programs, reduction of social inequalities.

**Acknowledgement/Funding:** The grant of Ministry of Science and Higher Education, Poland

**P1694 | BEDSIDE**

Exercise 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 university has detrimental metabolic effects in new university students.

**Methods:** The cross-sectional study in 1777 new university students revealed that the Ronin-samurai group (n=319, 19.9±1.3 years) showed higher BMI (21.6±4.2 vs. 20.8±2.7 kg/m²; p<0.0001), systolic blood pressure (123.5±12.1 vs. 121.2±11.7 mmHg; p<0.001), total cholesterol levels
(180.7±28.6 vs. 178.3±29.3 mg/dL, p=0.035) and alanine aminotransferase (ALT) levels (23.7±28.2 vs. 18.2±17.7 IU/L, p=0.0001) compared to the non-Ronin-samurai group (n=1458, 18.5±0.29 years). Further, the Ronin-samurai period before entering university was a novel and independent factor associated with ALT values (estimated difference = 5.6±1.2 vs. 2.4, p=0.018) in new university students. The 9-weeks follow-up study in students with elevated ALT values (≥40 IU/L, n=94) demonstrated a drastic and spontaneous decrease of ALT values (from 74.9±46.1 to 25.6±18.9 IU/L, p<0.0001) irrespective of the Ronin-samurai period although no lifestyle intervention was performed during the time period.

**Conclusions:** These findings suggest that prolonged entrance examination stress, represented by the Ronin-samurai period, may have detrimental metabolic effects in new university students. Further studies are warranted to clarify whether this “entrance examination-related metabolic abnormalities” could be observed not only in new university students, but also in new high-school students or even in new junior high-school students, if they passed the competitive entrance examination.

**P1695 | BEDSIDE**

**Marker of 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 Electing Cardiac Authority of Thailand study. A total of 1613 participants were enrolled in 2002. Baseline characteristics, outcomes and periodontal parameters [pocket depth (PD), clinical attachment level (CAL), and tooth loss] were recorded. Patients were followed for 11.7±2.4 years for cardiovascular outcomes and all-cause mortality. A multivariable Cox regression was performed to identify associations with events.

**Results:** Total outcome occurred in 190 participants (11.8%), of these 88 (46.3%) were cardiovascular events. There were 60 patients with myocardial infarction (MI) and 28 with stroke (31.6% and 14.7% of total outcome respectively). Mean PD were 2.44±0.68mm. There were 244 subjects (15%) with PD≥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.

**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 MI ≤48 hours of onset in whom the baseline coronary artery disease (CAD) state was verified angiographically is still unclear and was therefore addressed in this study.

**Purpose:** To identify FH from registries of patients with acute MI, the prevalence of FH 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, 29.7% had familial history, 19.9% were under LDL and 9.7% had LDL ≥5 mmol/L. FH prevalence was calculated as unlikely (72.6%), possible (24.6%) and probable/definite (2.8%). In the 2223 patients from FAST-MI 2010, 32.2% had premature CV disease, 24.9% had a family history, 28.1% were on LDLs, and 5.4% had LDL ≥5 mmol/L. FH prevalence was calculated as unlikely (77.9%), possible (19.4%) and probable/definite (2.7%).

**Conclusion:** Our 4-variable algorithm yielded concordant results to determine FH probability in 3 different cohorts of MI patients. In this large population reflecting routine clinical practice in acute MI, a high prevalence of FH was found, suggesting the opportunity for prevention strategies for these high risk patients.

**Acknowledgement/Funding:** PFIZER, Servier, CNAAM-TS

**P1697 | BEDSIDE**

**Remnant cholesterol predicts cardiovascular event risk in patients with type 2 diabetes independently from the baseline coronary artery disease state**

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**Background and introduction:** Remnant cholesterol, which is calculated as total cholesterol minus LDL cholesterol minus HDL cholesterol recently has attracted interest as a marker of cardiovascular risk.

**Purpose:** Whether remnant cholesterol has the power to predict cardiovascular events in patients with type 2 diabetes (T2DM) as well as in non-diabetic patients in whom the baseline coronary artery disease (CAD) state was verified angiographically is still unclear and was therefore addressed in this study.

**Methods:** We enrolled 1774 consecutive patients undergoing coronary angiography for the evaluation of established or suspected stable CAD. Prospectively, cardiovascular events were recorded over a mean follow-up period of 7.5±2.9 years. Diabetes was diagnosed according to ADA criteria.

**Results:** During follow-up, 32.3% of our patients suffered cardiovascular events; the event rate was significantly higher in patients with T2DM (n=513) than in non-diabetic subjects (40.5% vs. 29.3%; p<0.001). Remnant cholesterol significantly predicted cardiovascular events in the total study population, among patients with T2DM as well as among non-diabetic patients, as subjects both univariately and multivariately adjusted (HR 0.90, 95% CI 0.68 to 1.20, HR 0.81, 95% CI 0.56 to 1.17, p<0.001) and after multivariate adjustment including presence as well as extent of baseline CAD (HR 1.15 [1.07–1.24], p<0.001, 1.21 [1.05–1.39], p=0.009 and 1.15 [1.05–1.25], p=0.002, respectively).

**Conclusion:** From our data we conclude that remnant cholesterol predicts cardiovascular event risk in patients with type 2 diabetes as well as non-diabetic patients independently from the baseline CAD state.

**P1698 | BEDSIDE**

**Increased plant sterol deposition in vascular tissue characterizes patients with severe aortic stenosis and concomitant coronary artery disease**

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**Aim:** The aim of the study was to evaluate the relationship between phytosterols, oxysterols, and other markers of cholesterol metabolism and concomitant coronary artery disease (CAD) in patients with severe aortic stenosis who were scheduled for elective aortic valve replacement.

**Methods:** Markers of cholesterol metabolism (plant sterols and cholesterol) as markers of cholesterol absorption and lathosterol as an indicator of cholesterol deposition in tissue were measured in different vascular tissues of patients with severe aortic stenosis.
synthesis) and oxysterols were determined in plasma and aortic valve tissue from 104 consecutive patients with severe aortic stenosis (n=68 statin treatment; n=36 no statin treatment) using gas chromatography-flame ionization and mass spectrometry. The extent of CAD was determined by coronary angiography prior to aortic valve replacement.

Results: Patients treated with statins were characterized by lower plasma cholesterol, cholesterol, and lathosterol concentrations. However, statin treatment did not affect the sterol concentrations in cardiovascular tissue. The ratio of campesterol-to-campesterol was increased by 0.46±0.34 μg/ml (26.0%) in plasma of patients treated with statins. The absolute values for the cholesterol absorption markers sitosterol and campesterol were increased by 18.18±11.59 ng/ml (38.8%) and 11.40±8.69 ng/ml (30.4%) in the tissues from patients with documented CAD compared to those without concomitant CAD. Campesterol oxides were increased by 0.35±0.22 μg/ml (56.2%) in the aortic valve cusps and oxidized sitosterol-to-campesterol ratios were increased by 0.35±0.22 ng/ml (22.7%) in the plasma of patients with CAD. Of note, neither cholesterol nor the ratio of cholesterol-to-campesterol was associated with CAD.

Conclusions: Patients with concomitant CAD were characterized by increased deposition of plant sterols, but not cholesterol in aortic valve tissue. Moreover, patients with concomitant CAD were characterized by increased oxysterol concentrations in plasma and aortic valve cusps.

Acknowledgement/Funding: Netherlands Organisation for Scientific Research (Grant 014-012-010)

P1699 | BEDSIDE Post-prandial remnant-like particles formation in abetalipoproteinemia: prediction of the effectiveness of microsomal triglyceride transfer protein inhibitor on post-prandial remnant-like particles
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Background: Abetalipoproteinemia (ABL) is an extremely rare autosomal recessive disorder, characterized by almost complete absence of apoB-containing lipoproteins. ABL is caused by mutations in microsomal triglyceride transfer protein (MTP) gene, leading to prevention of the formation of chylomicrons.

It has been reported that MTP inhibitor was effective to reduce LDL-C even in homozygous familial hypercholesterolemia (FH) which exhibits 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: OUTF 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 HFLC system in one ABL subject (age 49yr, LDL-C=1mg/dl), four heterozygous FH subjects (mean age=58±3.17 yr, mean LDL-C=240±52.63 mg/dl), and four controls (mean age=61±18.6 yr, mean LDL-C=87.5±15.8mg/dl). Plasma lipoprotein and RLP fraction were determined by HFLC 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/ml×hour, 49mg/ml×hour, 43mg/ml×hour, respectively), whereas, those of FH subjects were significantly higher than those of controls (441±87mg/ml×hour vs 316±133mg/ml×hour, 126±60mg/ml×hour vs 49±11mg/ml×hour, p<0.05, 34±8mg/ml×hour vs 23±12 mg/ml×hour, respectively).

Conclusions: Our results indicate that ABL appeared to have low levels of TG response and diminished remnant lipoprotein formation after fat-load, and that MTP inhibitor should contribute to the reduction of the formation of post-prandial RLP as well as that of LDL-C.

P1700 | BEDSIDE Random blood glucose and incidence of cardiovascular disease among adults without diabetes: findings of the China Kadoorie Biobank
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Background: Previous studies, in predominantly Western populations, have shown the risk of blood glucose levels in adults without diabetes (CVD) among apparently non-diabetic individuals, in both terms of both shape and strength of the relationship. The association is poorly documented in Chinese populations.

Methods: We analysed data from 467 508 men and women aged 35–79 years with no prior history of diabetes or CVD, who were recruited during 2004–2008 into the China Kadoorie Biobank. During ∼7 years of follow-up, 2907 major cardiovascular events (MCE), 18 155 ischaemic stroke (IS), 4254 intra-cerebral haemorrhage (ICH) events and 6156 CVD deaths were recorded. Cox regression models were used to yield adjusted hazard ratios (HR) relating usual levels of random blood glucose (RBG), estimated based on repeat RBG levels measured at a resurvey in 18 000 randomly selected individuals, with disease. All analyses were stratified by age, study area and sex, and adjusted for education, smoking, alcohol, systolic blood pressure and physical activity.

Results: There was a clear positive association between usual RBG levels and risk of CVD, with each 1mmol/L higher RBG associated with 13% (95% CI 10%–15%), 12% (9–15%) and 9% (7–10%) increased risk of CVD mortality, MCE and ICH, respectively. For incident CVD, there was a significant, though moderate, positive association (HR 1.04, 1.01–1.07). The RBG-associated risks varied little by sex, age and other cardiovascular risk factors, and persisted after excluding individuals who developed diabetes during follow-up (n=11 892).

Conclusion: Higher RBG levels within the normoglycaemic range, are independently associated with the risk of major CVDs, especially ischaemic events, in Chinese men and women without known diabetes.

Acknowledgement/Funding: Kadoorie Charitable Foundation; UK Wellcome Trust; Chinese National Natural Science Foundation; BHF; UK MRC; Cancer Research UK; BHF CRE Oxford

P1701 | BEDSIDE Japanese characteristics of the Japanese patients with severe hypertriglyceridemia: Implication of controversy of triglyceride as a causative factor of coronary artery disease
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Background: Few data exists regarding the clinical characteristics of the Japanese patients with extremely high triglyceride level.

Purpose: To investigate clinical characteristics of the Japanese patients with extremely high triglyceride level.

Methods: We investigated clinical characteristics, including the presence of coronary artery disease (CAD), history of pancreatitis, the presence of fatty liver, and the potential causes of elevation of triglyceride for the Japanese subjects with extremely high fasting triglyceride level (∼1000 mg/dl) among 70,368 subjects measured plasma triglyceride for any reasons at Kanazawa University Hospital from April 2004 to March 2014.

Results: We identified 215 (0.31%) subjects (mean age=46yr, male=170, mean BMI=25kgm²) with severe hypertriglyceridemia (∼1000 mg/dl). Among them, 4 (1.9%) subjects were classified to type I, 97 (45.1%) subjects were type IV, and 114 (53.0%) subjects were type V hyperlipidemia, according to the Fredrickson’s classification. As much as 116 (54.0%) intake alcohol, among them, 58 (27.0%) intake heavily (>80g/day), and 91 (41.4%) subjects had diabetes. We have found 59 (27.4%) subjects with transient severe hypertriglyceridemia caused by corticosteroids (N=19), antidepressant (N=18), L-asparaginase and steroids for acute lymphoid leukemia (N=15), hormone replacement therapy for breast cancer (N=6), β-blocker (N=5), hypothyroidism (N=4), pregnancy (N=4), and panhypopituitarism (N=2). As much as 119 (55.3%) subjects exhibited fatty liver. In contrast, only 12 (5.6%), and 17 (7.9%) subjects exhibited any histories of pancreatitis and CAD, respectively.

Conclusion: A variety of situation would cause severe hypertriglyceridemia. Although triglyceride level has been shown as a causal risk factor of coronary artery disease through Mendelian randomization trials, severe hypertriglyceridemia itself does not always contribute to the development of CAD.

P1702 | BEDSIDE Harnessing publicly available genetic data to prioritize therapeutic targets for cardiovascular prevention
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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 dysglycemia.

Methods: We used publicly available data from genome-wide association studies (GWAS) including: Global Lipids Genetics Consortium (GLGC); Meta-Analyses of Glucose and Insulin-related traits Consortium ( MAGIC); DiABetes Genetics Replication And Meta-analysis (DIAGRAM) consortium, and; Coronary ARtery Disease Genome wide Replication And Meta Analysis (CARDIoGRAM) plus The Coronary Artery Disease (CAD) Genetics, collectively known as CARDIoGRAM-plusC4D 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: 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)
and LDL-C/CAD-associated SNPs showed consistent effect directions (binomial P=4.93×10^-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 didn’t 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 causing detrimental drug effects (MAF 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 in patients with dyslipidemia, and in that regard, may have advantages over statins for LDL-C lowering.

Acknowledgement/Funding: Netherlands Heart Foundation, EU-funded Integrated Project CVGenes@Target

P1705 | 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 recorded in the MONICA registry.

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 to 74 years hospitalized for a first or a recurrent ACS, registered in the MONICA registry between 2009 and 2011.

Results: There were 2441 (35.8%) ACS with ST(+), 1548 (22.7%) ACS with ST (-Enz+), and 2823 (41.4%) patients with ST (-Enz-).

The percentage of men was 78% (5339) and 31% of patients had previous history of ischemic heart disease.

The 28-day mortality rate (number of deaths = 760) was 11.2% [8.9–13.4] 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+), 2.4 [2.29–2.38] for (ST-) and 1.5 [1.42–1.67] for Nx (ST-Enz+), and 3.56 [2.8–4.54] for (ST-Enz-).

Conclusions: STEMI patients risk of death was higher at 28 day and lower when middle-term mortality was considered. These patterns were inverse for (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 remained significant; 0.70 [0.5–0.88] for (ST -Enz+) and 3.56 [2.8–4.54] for (ST -Enz-), ACS with no ST elevation and no enzyme elevation.

P1706 | BEDSIDE

Association between epicardial fat and subclinical atherosclerosis in familial hypercholesterolaemia


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Background: Familial hypercholesterolaemia (FH) is a common disorder resulting in severe elevations of blood cholesterol and increased prevalence of subclinical atherosclerosis and high risk of premature coronary heart disease. Pericardial fat, a visceral adipose tissue depot, has been associated with subclinical atherosclerosis in non-FH subjects.

Purpose: Evaluate the association of epicardial fat volume (EFV) in m3, defined as the fat volume inside the pericardial sac, with the presence and extent of subclinical atherosclerosis in patients with heterozygous FH.

Methods: 97 heterozygous FH subjects (35% male, age 45±13 years, LDL-C 281±56 mg/dl) underwent computed tomography angiography and coronary artery calcium (CAC) scoring. EFV was measured in non-contrast images using semi-automated method and indexed by body surface. A multivariate analysis was utilized to assess for an independent association of EFV with coronary atherosclerotic burden.

Results: Age, total cholesterol, LDL-C, HDL-C, apolipoprotein A-I, apolipoprotein B, glomerular 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.

P1707 | 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: Out of 1774 individuals with available information about birth weight, 53.4% were female. Median age was 37 years. Median and interquartile range of birth weight were 3350g (3050g; 3700g). The main results are shown in the table. Across quartiles of birth weight, there was a highly significant decrease in body

Table 1

<table>
<thead>
<tr>
<th>Body parameter</th>
<th>Quartile 1 (n=441)</th>
<th>Quartile 2 (n=446)</th>
<th>Quartile 3 (n=442)</th>
<th>Quartile 4 (n=445)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight</td>
<td>3050g</td>
<td>3350g</td>
<td>3650g</td>
<td>3950g</td>
</tr>
<tr>
<td>BMI</td>
<td>26.8</td>
<td>27.0</td>
<td>27.2</td>
<td>28.0</td>
</tr>
<tr>
<td>Waist</td>
<td>87</td>
<td>89</td>
<td>91</td>
<td>93</td>
</tr>
<tr>
<td>Fat mass</td>
<td>15.4%</td>
<td>15.9%</td>
<td>16.4%</td>
<td>16.9%</td>
</tr>
<tr>
<td>Fat mass&lt;0.5%</td>
<td>0.31</td>
<td>0.33</td>
<td>0.35</td>
<td>0.37</td>
</tr>
</tbody>
</table>

In all quartiles, coefficients were adjusted for age, sex, BMI, eGFR, systolic blood pressure, LDL, HDL triglycerides, HbA1c, education level, alcohol consumption, vegetable/fruit consumption, physical activity, smoking (current or past).
fat mass. In continuous analyses, the beta coefficient (95% confidence interval) per 100 g increase in birth weight was −0.06 to −0.10; −0.03 and p < 0.0001. There was no relationship between birth weight and muscle mass.

**Conclusion:** Among young and healthy adults, there was a highly significant inverse relationship between birth weight and body fat mass. This inverse association may at least in part mediate the adverse cardiovascular outcomes among individuals with low birth weight.

**Acknowledgement/Funding:** Schweizerischer Nationalfonds, Schweizerische Herzstiftung

**PHYSIOLOGY AND CORONARY CIRCULATION**

P1707 | BEDSIDE

**Plasma levels of serotonin as a novel biomarker for coronary microvascular dysfunction in patient with vasospastic angina**

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**Purpose:** Plasma serotonin (5-hydroxytryptamine) is a primary vasoconstrictor released from aggregates of platelets and is involved in the local regulation of coronary microcirculation. We examined the relationship between plasma serotonin levels and vasospastic angina (VSA) with/without concomitant coronary microvascular dysfunction (CMD) in patients with angina.

**Methods and results:** We enrolled 198 consecutive patients (M/F 116/82, 60±12 years old) with coronary artery disease (CAD). Concomitant VSA was diagnosed by vasodilator provocation test. We compared plasma levels of serotonin in VSA patients (16.2±3.7, n=145) and non-VSA (10.3±2.0, n=53) groups (P=0.142). However, the cut-off value was the sole and most powerful predictor (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 mol/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. These results suggest that plasma levels of serotonin are the novel biomarker for the presence of CMD in patients with angina.

P1708 | BEDSIDE

**Pressure-based baseline indices of functionalstenosis severity are affected by changes in systemic hemodynamics**

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**Background:** Indices of functional stenosis severity assessed at resting coronary blood flow have been proposed as an alternative to traditional parameters that require achieving maximal hyperaemia.

**Purpose:** To investigate the influence of changes in heart rate (HR) and arterial pressure (Pa) on coronary microvascular resistance (BMR), stenosis resistance (BSR), and functional indices (CFI) assessed at resting coronary blood flow.

**Methods:** In 18 patients (58±9 years) intracoronary pressure (Pd) and flow velocity (v) distal to a stenosis (54±13% DS) were measured at the following conditions: control (Ctrl); pacing at 40 bpm above sinus HR (Pac); increased venous (iv) adenosine infusion (140 g/kg/min) or after intracoronary (ic) adenosine infusion (360 mcg in the left system and ≥300 mcg in the right coronary artery), were measured following a standard protocol in all the centers.

**Results:** Mean CFI was 0.580±0.185, while mean RPImin was 0.512±0.144. Using linear regression analysis, CFI was significantly related to RPI (Figure 1).

**Conclusion:** Direct quantitative assessment of the peripheral artery collateral circulation by CFI is well reflected in noninvasive measures of tissue oxygenation and should be considered as the reference method for assessment of the peripheral artery collateral circulation.

P1709 | BENCH

**Direct quantitative assessment of the peripheral artery collateral circulation: validation of collateral flow index**

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**Background:** The purpose of this study was to validate collateral flow index (CFI) as a reference method in the assessment of the peripheral artery collateral circulation.

**Methods:** Collateral function of the left superficial femoral artery was determined by CFI and regional perfusion index (RPI) during a 3-minute balloon occlusion. Mean proximal superficial femoral artery pressure (Pa), mean central venous pressure (CVP) and mean superficial femoral artery wedge pressure (Pw) were obtained to calculate CFI: (Pw – CVP)/(Pa – CVP). Transcutaneous oxygen tension was measured at the anteromedial calf (tcpO2calf) and at a reference site at the lower left abdomen (tcpO2ref) to calculate minimal RPI (RPImin) during left superficial femoral artery occlusion: tcpO2calf/tcpO2ref.

**Results:** 86 patients, 66 men (77%), mean age 71±12 years, underwent collateral function determination in the left superficial femoral artery. Mean CFI was 0.580±0.185, while mean RPImin was 0.512±0.144. Using linear regression analysis, CFI was significantly related to RPI (Figure 1).

**Conclusion:** Direct quantitative assessment of the peripheral artery collateral circulation by CFI is well reflected in noninvasive measures of tissue oxygenation and should be considered as the reference method for assessment of the peripheral artery collateral circulation.
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 status of a new technique of optical coherence tomography (OCT) and the relationship between the lesion characteristics and microvascular function.

Methods and results: The index of microcirculatory resistance (IMR) and fractional flow reserve (FFR) was measured at pre-PCI, post-PCI, and follow-up (10 months) in 48 patients treated with elective PCI (male 81.3%, age 66.4±8.5). All patients underwent OCT examination before PCI. The median IMR values at pre-PCI, post-PCI, and follow-up were 24.9 (interquartile range (IQR) 13.1–32.0), 15.7 (IQR 11.6–21.5), and 14.5 (IQR 11.3–19.8), respectively. IMR values significantly decreased immediately after PCI (P < 0.05), and showed no further significant change at follow-up. Greater improvement of FFR values by PCI was significantly associated with greater periprocedural IMR reduction (P < 0.05) 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-pre), 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 post-PCI IMR values in the target vessel were significantly associated with OCT-derived high-risk lesion characteristics, and post-PCI IMR values may help identify patients at high risk for target vessel revascularisation.

P1714 | BEDSIDE
Instantaneous wave-free ratio (iFR) provides the most robust measure of any resting physiological index: the effects of pressure drift and measurement variability on stenosis misclassification


Background: Pressure drift and measurement variability (real-time fluctuations in value during measurement) can result in stenosis misclassification if values cross treatment thresholds.

Purpose: We assessed these variables and investigated their effect on stenosis misclassification with FFR, iFR and whole cycle Pa/Pa indices.

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).

Conclusions: 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.
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 ±3mmHg (from ±3mmHg to ±3mmHg). FFR, iFR and whole cycle Pd/Pa values were recalculated and compared to their respective cutoffs. Measurement variation was analyzed by recalculating values with an offset of ±0.01 units (from -0.03 to +0.03 units). Values were compared to cutoff thresholds as previously described.

Drift and variability were plotted against stenosis misclassification (% of total cohort) across a range of −3mmHg to +3mmHg and −0.03 to +0.03 units respectively. The area under the curve was calculated to compare the diagnostic performance of FFR, iFR and whole cycle Pd/Pa indices. The ROC curves for FFR and iFR and whole cycle Pd/Pa indices were compared to the current gold standard method (FFR). The misclassification rates across the three techniques were compared using the Chi squared test, and p-values for post-hoc comparisons were adjusted using the Bonferroni method.

Results: Mean FFR, iFR and whole cycle Pd/Pa values for the cohort were 0.78 ±0.14, 0.85 ±0.16, and 0.90 ±0.12. Pressure drift across the range of ±3mmHg resulted in 43% (192/447), 55% (246/447) and 72% (329/447) of all stenoses being reclassified with FFR, iFR and whole cycle Pd/Pa respectively (p<0.001). iFR was proportionally more resilient to the effects of drift and measurement variability than whole cycle Pd/Pa by 233% and 254% respectively, when compared to FFR. This results in less stenosis misclassification using iFR than whole cycle Pd/Pa by 233% and 254% respectively, when compared to FFR and whole cycle Pd/Pa. iFR was proportionally more resilient to the effects of drift and measurement variability than whole cycle Pd/Pa by 233% and 254% respectively, when compared to FFR and whole cycle Pd/Pa. iFR is more resistant to drift and measurement variability than whole cycle Pd/Pa. iFR performance is better than conventional PCI when used in treating patients with diffuse disease.

Conclusion: Manual thrombus aspiration reduces microcirculatory resistance indicating better myocardial perfusion compared to conventional PCI in patients with STEMI. However, routine manual thrombus aspiration is not an independent predictor of reduced microcirculatory resistance. Reduction in microcirculatory resistance of 12.3% achieved by thrombus aspiration is not sufficient to allow echocardiographic improvement in STEMI patients at mid-term follow up.

P1717 | BEDSIDE
Investigation of human coronary haemodynamics in normal and stenosed vessels to develop systems to quantify stenosis significance and predict the functional gain of intervention
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Background: Predicting haemodynamic outcome prior to stenting complex and tandem coronary disease could advance interventional decision-making and improve outcomes. We investigated resting coronary haemodynamics in patients undergoing pressure-flow velocity measurements in both normal and diseased vessels before and after intervention, to develop models that predict the improvement in resting pressure index for a given stenting strategy. We sought to combine this with a pressure wire pullback, specifically to quantify the specific haemodynamic contribution of a given stenosis to the observed pressure loss and predict the result of removing the stenosis.

Methods: 301 patients had 567 simultaneous pressure and flow velocity measurements; 75 stenoses had paired data after PCI. Data modeled the change in instantaneous wave-free ratio (IFR) after PCI and develop virtual-PCI algorithms. Intracoronary pressure-wire pullbacks were performed in 32 coronary arteries with tandem and diffuse disease and IFR was calculated beat-to-beat to produce an IFR-pullback which was mapped onto the angiogram. A validated virtual-PCI algorithm was used to produce a post-PCI IFR (iFRpre) which was compared to the observed IFR post real-world PCI (iFRobs).

Results: Wave-free period resting coronary flow velocity was consistent across the spectrum of coronary stenoses (24.5±0.7cm/s across stenoses with FFR 0.29–1.0), with a significant linear rise in stenotic gradient (p<0.001, R² 0.75) and decline in microvascular resistance (p<0.001). Resting pressure indices rose (Δ0.20±0.03, p<0.001) without a significant change in flow velocity (6.8±2cm/s, p=0.67). This was significantly smaller than the equivalent change in hemodynamic index (Δ0.20±0.03, p<0.01), enabling accurate prediction of residual grade of stenosis on the pullback map. In the tandem disease cohort, pre-PCI IFR was 0.78±0.03. Virtual PCI predicted an iFRpre of 0.94±0.01. The observed IFR after real-world PCI was iFRobs 0.93±0.01 with no significant between the predicted and observed delta (ΔiFR- exp: 0.16±0.03 vs iFRobs 0.10±0.03; p=0.48). There is no significant systematic bias (Bland-Altman difference 0.016±0.004).

Conclusions: The behavior of resting physiology in man demonstrates resting flow velocity is maintained by decreasing microvascular resistance despite falling distal pressure. Physiological mapping of tandem coronary stenoses is feasible and virtual-PCI approaches can selectively remove a stenosis and predict the...
change in resting physiology. Virtual-PCI could permit assessment of different stenting strategies in the lab and may advance trials in intervention.

**Acknowledgement/Funding:** Medical Research Council (UK) and British Heart Foundation

### P1718 | BEDSIDE Impact of additional intracoronary nicorandil administration during fractional flow reserve measurement with intravenous ATP infusion


**Background:** Although adenosine triphosphate (ATP) is generally used as a hyperemic agent for fractional flow reserve (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 (180mcg/kg/min) for 3 minutes to measure FFR (ATP-FFR). After additional intracoronary nicorandil administration (2mg/30sec) during intravenous ATP infusion, FFR measured again (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 tend 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.

### P1719 | BEDSIDE Efficacy of pressure-derived indices by contrast medium induced submaximal hyperemia in comparison with fractional flow reserve and hyperemic end-diastolic Pd/Pa ratio

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**Background:** Instantaneous ECG-gated Pd/Pa ratio acquired at end-diastole of hyperemic state has been recently reported to show an improved correlation with Qs/On measured directly with flow-probe, and has been shown to be highly sensitive for detection of inducible myocardial ischemia compared with conventional FFR in animal model.

**Purpose:** We first evaluate if hyperemic ECG-gated end-diastolic Pd/Pa (H-ED-Pd/Pa) shows, as reported, good correlation with conventional FFR in humans. Then, we sought to determine if contrast induced ED-Pd/Pa (C-ED-Pd/Pa) or resting basal IFR can be substituted for conventional FFR with H-ED-Pd/Pa as a standard of reference.

**Methods and results:** Seventy-four intermediate stenosis in 68 patients were prospectively studied. The instantaneous wave-free ratio (IFR) was measured at the basal state. Then, C-ED-Pd/Pa obtained by 6ml/2sec intracoronary contrast medium injection was calculated. Subsequently, conventional adenosine-induced hyperemic FFR and H-ED-Pd/Pa at 60ms before R-wave of the ECG were measured. Obtained measures were 0.896 [0.857–0.938] (IFR), 0.796±0.117 [C-ED-Pd/Pa], 0.83±0.090 (conventional FFR), and 0.76±0.131 [H-ED-Pd/Pa], respectively. Correlation coefficient between hyperemic ED-Pd/Pa and conventional FFR was 0.85 (R2; P < 0.001), and an area under the curve (AUC) was 0.95. Correlation coefficients between hyperemic ED-Pd/Pa were 0.55 (IFR) and 0.85 (C-ED-Pd/Pa), respectively. C-ED-Pd/Pa showed the comparable performance with conventional FFR when H-ED-Pd/Pa was used as a reference standard, and provide a significantly better area under the curve compared with IFR (p = 0.02).

**Conclusion:** Hyperemic end-diastolic Pd/Pa showed a good correlation with conventional FFR in humans as is reported in the animal study. Contrast induced end-diastolic Pd/Pa is a simple and readily usable index for assessing physiological significance of intermediate stenosis, providing the comparable efficacy with conventional FFR.

### P1720 | BEDSIDE The impact of elective percutaneous coronary intervention on coronary microvascular resistance

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**Background:** The influence of elective percutaneous coronary intervention (PCI) on coronary microvascular function has not been fully elucidated. In order to diagnose and treat microvascular dysfunction, it is important to understand the interactions between epicardial lesion and microcirculation.

**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) were measured before, after PCI, and at follow-up (10 months) in 72 patients treated with single vessel uncomplicated elective PCI (male: N=57 (78.2%), age 64±6.3y). The median IMR values before, after PCI, and at follow-up were 21.4 (interquartile range (IQR) 13.1–30.9), 16.2 (IQR 12.4–23.0), and 15.4 (IQR 11.8–20.7), respectively. IMR values significantly decreased after PCI (P=0.003), and showed no further significant change at follow-up. There was a weak but significant relationship between final IMR 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 by PCI was significantly associated with greater reduction of IMR values at follow-up (P=0.007). To investigate the details of serial IMR change, lesions were divided into tertiles based on Pre-PCI IMR value (the lowest Pre-PCI IMR: 11.4 (IQR 9.1–13.4), the intermediate: 21.5 (17.9–24.7) and the highest: 36.8 (30.9–49.4). In the intermediate and the highest tertiles, IMR values were significantly decreased at follow up (P=0.03 and P<0.001, respectively). IMR values of the intermediate tertile were decreased to the same level of those of the lowest tertile at follow up. Whereas follow up IMR values of the highest tertile still remained higher than those of the lowest tertile, the highest tertile showed the greatest decrease of IMR values after PCI than other tertiles (the lowest IMR at follow up: 13.9 (IQR 10.9–15.7), the intermediate: 15.9 (12.4–19.0) and 19.7 (14.2–26.2), P=0.01).

**Conclusions:** Removal of physiologically significant epicardial stenosis leads to a decrease in microvascular resistance in patients with stable angina undergoing electively performed uncomplicated PCI and the effect was maintained up to 10 months. The baseline status of microvascular function is a significant determinant of post-PCI and follow-up microvascular function in these patients.

### P1721 | BEDSIDE Influence of microvascular resistance on anatomical and functional severity of coronary artery disease

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**Background:** Coronary angiography has been standard diagnostic tool for assessing the anatomical severity of coronary artery disease. However, there are mismatches 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 of lesions using 0.014-inch intracoronary dual pressure doppler sensor-tipped guidewire. FFR was calculated as distal pressure (Pa) divided by proximal pressure (Pa). And hMVRI was calculated as distal pressure (Pa) 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 matching lesions, 31 lesions (30%) were included in the mismatch group and 15 lesions (14%) were included in the reverse mismatch group. In all lesions, the mean FFR, diameter stenosis (%) and hMVRI were 0.79±0.11, 56.5±9.9 and 2.23±1.24. hMVRI was 2.03±1.03 in the match group (n=58), 2.96±1.53 in the mismatch group (n=31) and 1.50±0.31 in the reverse mismatch group (n=15). hMVRI was significantly higher in the mismatch group (p = 0.01, by ANOVA). The reverse mismatch group had a tendency of lower hMVRI values. 13 lesions from among 15 reverse mismatch lesions were in left anterior descending artery.

**Conclusions:** There was a considerable mismatching between anatomical and functional severity. And functional physiologic assessment with microvascular function test should be required for percutaneous coronary intervention in myocardial ischemia-related lesions.
P1724 | BENCH
Hyperemic flow velocity falls with worsening stenosis severity: the challenge for non-invasive predictors of coronary physiology
Background: Previous descriptions of coronary physiological behaviour were performed in animal models using external constrictors to mimic stenoses. Human outcome data confirms the value of physiological assessment but there remains limited modern data using high fidelity techniques to describe the phasic physiological response to a stenosis. Simultaneously, computer-simulated physiological testing has gained interest but makes assumptions of a large and uniform increase in flow across all stenoses to simulate a transtentatic pressure drop. Since clinical application requires robust models, we used combined intracoronary pressure and flow velocity measurements in a large clinical cohort to describe the response of the human coronary circulation to a stenosis.
Methods: 467 simultaneous intracoronary pressure and flow velocity assessments from 301 patients were analyzed for coronary flow velocity, transtenotic gradient (TG) and microvascular resistance (MVR). Measurements were made during basal conditions and during hyperemia. The whole cardiac cycle and the resting diastolic wave-free period was assessed. Linear regression, trend analysis and paired analysis was used, according to stenosis severity as determined objectively by fractional flow reserve (FFR).
Results: FFR values ranged from 0.28 to 1.0. With progressive worsening of stenoses, from unobstructed angiographically normal vessels to those with FFR<0.50, hyperemic flow velocity over the whole cycle falls significantly from 45 to 19cm/s, (p<0.01) in a curvilinear pattern. In contrast, resting flow was unaffected by stenosis severity (R² 0.01) and was consistent across all strata of stenoses, with wave-free flow being significantly higher (whole cycle:18±0.5 cm/s wave-free:24.5±0.7 cm/s, p<0.01). Resting resistance showed a decline with stenosis severity (p<0.01), but was unchanged at hyperemia (2.3±1.1, P=0.19). Transtentatic gradient rose with stenosis severity, increasing from 1.7±0.3 to 46±3 mmHg at rest, and from 3.5 to 55 mmHg at hyperemia (P<0.01 for both). Both IFR and FFR were strongly related to transtentatic gradients (R² 0.96 and 0.93 respectively).
Conclusions: With progressive stenosis severity, transtentatic gradient increases alongside a worsening of pressure indices such as IFR and FFR. However, while hyperemic flow falls significantly, resting coronary flow is maintained by compensatory reduction of microvascular resistance, demonstrating coronary auto-regulation. This data will assist in computer flow modeling such as CT-FFFR and virtual-PCI systems potentially provide more credible estimates of human physiology.
**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 Gy² cm, 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 dropped by 37%. Fluoroscopy time was unchanged (table). Coronary multi-vascular disease was the prominent indication for PCI with increasing complexity over the years.

<table>
<thead>
<tr>
<th>Year</th>
<th>DAP (Gy² cm²)</th>
<th>Fluoroscopy time (min)</th>
</tr>
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<tbody>
<tr>
<td>2002</td>
<td>18823</td>
<td>8.42</td>
</tr>
<tr>
<td>2006</td>
<td>23934</td>
<td>7.53</td>
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<tr>
<td>2011</td>
<td>21438</td>
<td>7.52</td>
</tr>
<tr>
<td>2011</td>
<td>21413</td>
<td>7.46</td>
</tr>
<tr>
<td>2010</td>
<td>21407</td>
<td>7.63</td>
</tr>
<tr>
<td>2011</td>
<td>21032</td>
<td>7.76</td>
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</tr>
<tr>
<td>2013</td>
<td>20435</td>
<td>7.92</td>
</tr>
</tbody>
</table>

DAP, dose area product; PCI, percutaneous coronary intervention.

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=177) vs 3.8% (N=44); 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, homogeneous 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 neo-intimal 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 entity of acute coronary syndrome (ACS), however, it is still misdiagnosed and underdiagnosed 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 criteria for SCAD was a separation of the different layers of the artery wall with the creation of a false lumen. Quantitative coronary analysis (QCA) including the minimum lumen diameter, reference vessel diameter, percent diameter stenosis, and lesion length was also measured.

Results: OCT revealed 9 SCADs, 146 PRs, and 109 NRs, respectively. There was no difference in individual coronary risk factors, while the prevalence of patients with more than 3 risk factors was lower in SCAD (11.1% vs. PR: 51.5% vs. NR: 56.6%, p<0.03). The proportion of male and female was different among the groups (Female: SCAD: 66.7% vs. PR: 20.0% vs. NR: 23.6%, P<0.01). In angiographic findings, the distribution of the culprit vessels and the initial TIMI flow were similar among groups (p=0.48, and p=0.95 respectively).

There were no significant differences in reference diameter, % stenosis, and minimum lumen diameter in QCA. The lesion length in SCAD was significantly longer than others in (SCAD: 33.8±28.8 mm vs. PR: 15.6±28.0 mm vs. NR: 14.8±7.5 mm, P<0.01).

Conclusions: We should remind the presence of SCAD when angiography shows long lesion especially in female with less risk factors. In such cases, OCT should be recommended for accurate diagnosis for SCAD.

**P1729 | BEDSIDE**

Framingham risk score 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 coronary artery valve stenosis disease. We aimed to compare 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 >0.80. 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±1.1 vs 1.75±1.1; P<0.01). In patients undergoing CABG, number of surgical grafts per patient was similar between the 2 groups (0.6±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=0.016; p=0.68), revas- culation during follow-up (8.5% vs. 7.5%; Log-Rank=0.096; p=0.76) and non-fatal MI (1.9% vs 2.4%; Log-Rank=0.073; p=0.79) between the 2 groups.

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.
P1730 | BEDSIDE
Features of coronary artery disease in 2776 type 1 diabetes patients undergoing coronary angiography
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Background: In patients 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 (atheromata/stenosis <50%), one-, two-, three- and left main- vessel disease.

Results: Of 2776 type 1 DM (58% male) with complete data on coronary angiogram, mean age was 57 years (SD 11), mean DM duration 35 years (SD 14, range 0–76) 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 higher resolution, however, it reduces total procedure radiation dose. IVUS guided PCI is routinely performed. Optical Coherent Tomography (OCT) is an emerging device to evaluate coronary artery at higher resolution, however, it reduces total procedure radiation dose.

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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.

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 pseudoaneurysm rupture.

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.

Acknowledgement/Funding: The Faculty of Medicine Endowment Fund for Medical Research, Chiang Mai university, Chiang Mai, Thailand

P1733 | BEDSIDE
Rate and predictors of contrast-induced nephropathy after coronary intervention depend on renal function at baseline
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Background: Contrast induced nephropathy (CIN) after coronary angiography or angioplasty (CA) has been shown to be related to mortality. The rate and predictors of CIN when preventive measures are applied are poorly documented.

Methods: All consecutive patients submitted to non-urgent CA in 2014 with low-osmolar contrast medium were stratified for CIN risk: patients with renal dysfunction (defined as eGFR <60 ml/min) had interruption of diuretics and received a 250–500 ml intravenous saline infusion before and after CA. Serum Creatinine (Scr) levels were measured before CA and daily thereafter up to 5 days after CA. CIN was defined as an absolute increase of 44 μmol/L Scr or of 25% over baseline Scr level. Predictors of CIN and of recovery were determined by logistic regression. CIN patients had clinical follow-up for death or end-stage renal dysfunction.

Results: Scr results were available in 958 patients, 72% male, 25% diabetics, median eGFR was 71 ml/min before CA (interquartiles [IQR] =54; 89). Median amount of contrast was 129 ml (IQR= 90; 186). At 2–4 days, CIN was observed in 188 (20%), driven by a 25% increase in Scr (n=185, 19%) whereas 81 (8.5%) had an increase of <44μmol/L Scr or of 25% over baseline Scr level. Predictors of CIN and of recovery were determined by logistic regression. CIN patients had clinical follow-up for death or end-stage renal dysfunction.

Conclusion: Scr results were available in 958 patients, 72% male, 25% diabetics, median eGFR was 71 ml/min before CA (interquartiles [IQR] =54; 89). Median amount of contrast was 129 ml (IQR= 90; 186). At 2–4 days, CIN was observed in 188 (20%), driven by a 25% increase in Scr (n=185, 19%) whereas 81 (8.5%) had an increase of <44μmol/L Scr or of 25% over baseline Scr level. Predictors of CIN and of recovery were determined by logistic regression. CIN patients had clinical follow-up for death or end-stage renal dysfunction.
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 assigned to these categories.

**Results:** The incidence of CN, PE and PR was prior to 11 (23.4%), 9 (19.1%) and 25 (53.2%), respectively. As depicted in table 1 PR was associated with a significantly larger lipid arc and a higher lipid volume index (LVI), whereas frequency of lipid-rich plaques as well as fibrous cap thickness (FCT) remained below statistical significance compared to lesions with CN and PE. In contrast, lesions with CN or PE presented with a higher frequency of calcium and fibrous plaque compared to PR.

**Table 1. OCT findings of underlying plaque features**

<table>
<thead>
<tr>
<th>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>1 (44%)</td>
<td>p=0.001</td>
<td>ns</td>
</tr>
<tr>
<td>Lipid plaque</td>
<td>5 (45.5%)</td>
<td>5 (66.7%)</td>
<td>20 (80%)</td>
<td>p=0.114</td>
<td>ns</td>
</tr>
<tr>
<td>Lipid arc</td>
<td>142±34.3</td>
<td>151±32.1</td>
<td>188±32.6</td>
<td>p=0.007</td>
<td>ns</td>
</tr>
<tr>
<td>LVI</td>
<td>7489±2817</td>
<td>7666±4180</td>
<td>1212±3725</td>
<td>p=0.009</td>
<td>ns</td>
</tr>
<tr>
<td>FCT</td>
<td>0.34±0.1</td>
<td>0.34±0.09</td>
<td>0.31±0.07</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>Macrophages</td>
<td>8 (72.7%)</td>
<td>6 (66.7%)</td>
<td>19 (76%)</td>
<td>ns</td>
<td>ns</td>
</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>

ns, not significant.

**Conclusion:** OCT is a valuable intracoronary imaging device to identify CN, PE and PR in vivo. In patients with diabetes and ACS PR is associated with a higher plaque lipid content but not with the presence of lipid plaques, whereas CN and PE are more frequent in coronary calcium and fibrous plaques. These distinct pathological features may implicate tailored treatment strategies for ACS-patients with diabetes according to the underlying plaque morphology.

### P1735 | BEDSIDE

**Impact of optical coherence tomography findings during percutaneous coronary intervention on 9-month follow-up outcomes**

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**Purpose:** In patients undergoing percutaneous coronary intervention (PCI) for coronary artery disease, the impact of peri-procedural lesion morphologies and stent findings by optical coherence tomography (OCT) on long-term outcomes remains unclear.

We sought to investigate the relationship between peri-PCI OCT findings and the outcomes during follow-up by serial OCT examination.

**Methods:** We evaluated 104 native coronary lesions with stable angina pectoris that underwent elective PCI and follow-up coronary angiography with OCT examination. All lesions were treated with stent implantation (94 lesions with drug-eluting stents [DES]; 10 lesions with bare metal stents [BMS]). Plaque morphologies at the narrowest culprit sites before PCI and the presence of stent findings such as stent edge dissection, tissue prolapse and malapposition just after PCI were investigated. At 9-month follow-up coronary angiography (mean interval: 9.2±1.9 months), the prevalence of in-stent restenosis (ISR) and OCT findings were evaluated.

**Results:** The prevalence of OCT verified CN was 5.3% (n=13). No differences were observed between CN and non-CN groups including patient characteristics and prognosis.

**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 coronary 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.

P1739 | BEDSIDE
Relationship between coronary artery compliance and vasospasm in patients with angiographically normal coronary arteries
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Background: Reduced epicardial coronary arterial extensibility associated with early atherosclerosis may be mediated in part by reduced nitric oxide release.

Methods: Consecutive 15 patients with suspected CS were prospectively enrolled. To diagnose patients as having CS, an acetylcholine provocation test was performed in all 3 coronary arteries. A positive spasm-provocation test was defined as a >75% reduction in arterial diameter. After an intracoronary injection of isosorbide dinitrate, intracoronary ultrasound examination was performed in all 3 coronary arteries and cross-sectional images at the site 3 and 7 cm distal from each epicardial ostium were obtained. In each coronary artery, change of vessel cross-sectional area (VA) and plaque burden (PB) during cardiac cycle was assessed, and coronary artery compliance (CAC) was calculated (Figure). Patients were divided into two groups according to the median value of CAC (0.0287).

Results: CS was induced in 9 arteries of 8 patients. CS positive arteries had diffusely thickened intima than CS negative arteries [average PB, 25.6% (22.1–35.1%) versus 18.1% (14.9–24.6%), p = 0.0001]. CAC value tended to be lower in CS positive arteries than in CS negative arteries (0.0116 [0.0094–0.0309] versus 0.0224 [0.0099–0.0358], p = 0.07). Moreover, the incidence of CS was more frequently in low-CAC group than in high-CAC group significantly (66.7% versus 41.0%, p = 0.04).

Conclusions: This study strongly supports the hypothesis that normal coronary artery extensibility is modulated by the release of endothelium-derived nitric oxide.

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 –8% 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 diagnosis. This technology may reduce time and cost of the coronary diagnosis, enabling a comprehensive decision support system for the physician.

P1741 | BEDSIDE
The role of optical coherence tomography in prediction of coronary ischemia assessed by fractional flow reserve: meta-analysis of diagnostic test accuracy
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Aim: Optical coherence tomography (OCT) has been recently emerged diagnostic imaging tool to assess coronary lesions. However, there is a few data related to OCT in coronary intermediate lesion. Therefore, in this meta-analysis, we aimed to investigate the role of OCT compared to fractional flow reserve (FFR) in intermediate coronary lesion.

Methods: We searched the MEDLINE, EMBASE and Cochrane Library for studies published from January 2000 to January 2014. We included nine trials in which at least one OCT-derived anatomic measurements such as minimal luminal diameter (MLD), minimal lumen area (MLA) and/or area stenosis (AS) compared to significant FFR cut-off value (0.75 or 0.80) into this meta-analysis.

Results: We included nine trials with lesion-level data for 457 coronary lesions in
P1742 | 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 (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 (NCG), presence of yellow plaque (YP) in-stent mural thrombi (ISTM). NCG 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: NCG of BMS 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. NCG of SES was 1.36±0.56 at mid-term and 1.54±1.19 at long-term, indicating that the complete coverage even at long-term. Frequency of YP in SES was 25% at mid-term and 23% at long-term, whereas that in BMS was 11% at mid-term and none at long-term. Frequency of ISTM in SES was 13% at mid-term and 23% at long-term, whereas that in BMS was none at all through a decade.

Conclusion: Vascular healing process after SES implantation remains incomplete through a decade, characterized by low NCG, YP, and ISTM.

P1743 | SPOTLIGHT
Distinct histopathological features of calcified nodule in coronary artery tree

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.

Purpose: The purpose of this study was to clarify development of CN and pathogenesis of CN.

Methods: Thirty eight sections, from 7 CN lesions obtained by autopsy were studied. CN lesions developed to ACS. CN lesion by OCT MLA when compared to FFR may lead to misclassification in up to 20% of the lesions.

Results: Gross morphology of CN showed protruding mass into the lumen with irregular surface. ACS-induced CN developed fibrin thrombi over the nodules with erosion of luminal surface. Although all CNs of non-ACS lesion demonstrated extremely thin fibrous tissue over the nodule, CD31 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 neovascularization was observed beside calcification. Furthermore, we identified distribution of decorin, biglycan, versican and hyaluronan, was examined.

Conclusions: Histological evaluation of CN indicates the distinct histopathological features of CN compared to the conventional atherosclerotic plaque. Abundant fibrin deposition and neovascularization within the nodules suggest the contribution of thrombus formation for the pathogenesis of CN. In addition, proteoglycans may also play an important role for the CN development and progression.

P1744 | 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 membrane cross-sectional area (CSA) every 1 mm axial intervals with OCT in 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 ΔHs-TnT.

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<0.0001). In simple regression analysis, total stent length, lesion area, remodeling index, total plaque volume, lipidic plaque volume and necrotic plaque volume of target lesion were significantly correlated with ΔHs-TnT. The necrotic plaque volume was independently correlated with ΔHs-TnT in multiple regression analysis (p<0.0001).

Conclusion: The volume of necrotic plaque measured by iMAP is associated with ΔHs-TnT in patients with stable angina or silent coronary ischemia.

P1745 | BEDSIDE
Comparison of vascular response to biolimus-eluting stent versus everolimus-eluting stent versus everolimus-eluting stent and two-year serial intravascular ultrasound observation from NEXT
A. Miyazawa1, K. Kozuma2, K. Hibi3, M. Endo4, N. Nakayama5, T. Muramatsu4, T. Akasaka5, Y. Morino2, T. Kimura7 on behalf of NEXT Investigators. 1Iwatsuki Memorial Hospital, Jilin-shi, Japan; 2Iwate University Hospital, Tokyo, Japan; 3Tokyo University Graduate School of Medicine, Kyoto, Japan

Background: The NOBORI™ Biolimus-Eluting versus XIENCE™/PROMUS™ Everolimus-eluting stent Trial Trial (NEXT) was designed for evaluating non-inferiority of biolimus-eluting stent (BES) relative to everolimus-eluting stent (EES). The NOBORI™ Biolimus-Eluting versus XIENCE™/PROMUS™ Everolimus-eluting stent Trial (NEXT) was designed for evaluating non-inferiority of biolimus-eluting stent (BES) relative to everolimus-eluting stent (EES). The NOBORI™ Biolimus-Eluting versus XIENCE™/PROMUS™ Everolimus-eluting stent Trial (NEXT) was designed for evaluating non-inferiority of biolimus-eluting stent (BES) relative to everolimus-eluting stent (EES).

Objective: The aim of this study was to compare the vessel response between BES and EES using serially repeated intravascular ultrasound observation for 2 year after stent implantation.

Methods: Data were obtained from NEXT. Patients with serial (baseline and 12-months follow-up) intravascular ultrasound analysis were available in 110 patients (BES = 56 EES = 54). Twenty-four months follow up IVUS observation was available in 110 patients (BES = 56 EES = 54). Twenty-four months follow up IVUS observation was available in 110 patients (BES = 56 EES = 54). Twenty-four months follow up IVUS observation was available in 110 patients (BES = 56 EES = 54). Twenty-four months follow up IVUS observation was available in 110 patients (BES = 56 EES = 54). Twenty-four months follow up IVUS observation was available in 110 patients (BES = 56 EES = 54). Twenty-four months follow up IVUS observation was available in 110 patients (BES = 56 EES = 54).

Results: Vascular response analysis for ISA, vessel, lumen, plaque, stent and neointima.

Conclusion: The volume of necrotic plaque measured by iMAP is associated with ΔHs-TnT in patients with stable angina or silent coronary ischemia.
tima volume index was minimum in both stents at 12 and 24 months. However, continuous neointima growth was observed through 24 months. (12 month: BES: 0.1±0.2 vs. EES: 0.1±0.1 mm³, p=0.26, 24 month: BES: 0.4±0.6 vs. EES 0.5±0.4, P=0.42).

Conclusion: Two-year IVUS analysis after BES implantation demonstrated comparable vascular response from that after EES implantation.

P1748 | BEDSIDE
Gender independent factor in atherosclerotic plaque characteristics

Background: Gender differences have been reported in the origin and development of coronary artery disease. We studied differences in plaque burden and plaque subtype as assessed by virtual histology intravascular ultrasound (VH-IVUS) and near-infrared spectroscopy (NIRS) between women and men undergoing coronary angiography.

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: Women had a significantly lower median plaque burden than men (36.9 vs. 39.5%, p=0.014). The median LCBI was also significantly lower (p=0.011) in women (30.3) vs. 44.0% than in men (48.1 vs. 91.0%). There were no gender differences in the presence of thin-cap fibroatheroma lesions. Women were older than men (64 vs. 60.7 years), and were more likely to have a history of hypertension (66 vs. 47%). Men were more often classified as smokers (20% vs. 24%) and had longer lesions (median 40.0 mm (inter-quartile range 35.4 to 56.0) vs. 42.1 mm (30.5 to 54.2), p=0.021. After adjustment for these factors, women still had on average 3.4% lower plaque burden (p=0.002) and 0.58 points lower LCBI (p=0.005) than men.

Conclusion: In ATHEROREMO-IVUS, female patients had lower plaque burden and lower LCBI.

P1747 | BEDSIDE
Optical coherence tomography imaging of coronary saphenous vein graft lesions morphology, OCTOPUS registry
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Aim: The accelerated atherosclerosis that occurs in saphenous coronary grafts (SVG) develops much faster as compared to native coronary arteries. The follow-up of SVG lesion’s morphology of SVG was presented by intravascular optical coherence tomography (OCT) in patients post coronary 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 severity and determine a treatment strategy. OCT was able to detect tissue friability, lipid-rich protuberance and thrombus presence was recorded during OCT analysis. There were 24 lesions (18 patients) and 8 ISR analyzed (8 patients) of OCT. De novo lesions of SVG occurred later as compared to ISR in SVG (131±63 vs. 21±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=0.02]. 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±38 vs. 109±55 months post CABG, p=0.307). Heterogeneous tissue was found only in neointima of ISR (18% vs. 0%, p=0.02) at 19 (IQR 12–27) months post stent implantation. The lipid-rich tissue occurred in de novo SVG lesions and in ISR (50% vs. 67%, p=0.39) with no difference in lipid arc [245 (IQR 164–340) vs. 224 (IQR 175–285), p=0.63] and in the thickness of fibrous cap covering lipid core [85 (IQR 60–110) vs. 75 (IQR 55–85), 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.

P1749 | BEDSIDE
Accuracy of IVUS and OCT in identifying functionally significant coronary stenosis according to vessel diameter: a meta-analysis of 2581 patients and 2807 lesions
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Introduction and background: Accuracy of intracoronary imaging to discriminate functionally significant coronary stenosis according to vessel diameter remains to be defined.

Purpose: We performed a meta-analysis to assess the diagnostic accuracy of IVUS and OCT for the prediction of significant coronary lesions determined by FFR.

Methods: Pubmed, Scopus and Google Scholar were searched for studies assessing diagnostic accuracy (AUC, the primary end point), sensitivity and specificity (the secondary end points) of minimal luminal area (MLA) or of minimal luminal diameter (MLD) derived from intravascular ultrasound (IVUS) or optical coherence tomography (OCT) to detect functionally significant stenosis as determined with fractional flow reserve (FFR).

Results: Fifteen studies were included, two with 110 patients analyzing only LM, five with 224 patients and 306 lesions using OCT and nine with 1532 patients and 1881 lesions with IVUS. Median MLA for the OCT studies was 1.96 mm² (1.85–1.98), 2.9 mm² (2.7–3.1) for MLA of all lesions assessed with IVUS, 2.8 mm² (2.7–2.9) for lesions with an angiographic diameter <3 mm, 2.4 mm² (2.4–2.5) for lesions <3 mm, and 5.4 mm² (5.1–5.6) for LM lesions. For OCT-MLA, AUC was 0.80 (0.74–0.86), with a sensitivity of 0.81 (0.74–0.87) and specificity of 0.77 (0.71–0.83) while OCT-MLD had an AUC of 0.85 (0.79–0.91), sensitivity of 0.74 (0.69–0.78) and specificity of 0.70 (0.68–0.73). For IVUS-MLA, AUC was 0.78 (0.75–0.81) for all lesions, 0.78 (0.73–0.84) for vessels with a diameter >3 mm and 0.79 (0.70–0.89) for those with a diameter <3 mm. LM AUC was 0.97 (0.95–0.99).

Conclusion: IVUS and OCT had modest diagnostic accuracy for identification hemodynamically significant lesions, also with specific cut-off for different diameters. Invasive imaging for assessment of LM severity demonstrated excellent correlation with FFR.

P1749 | BEDSIDE
Angiographic assessment of the culprit lesion plaque with intracoronary ultrasound signal attenuation in coronary heart disease
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Background: Intravascular ultrasound (IVUS) studies have described that atherosclerotic plaques with echo attenuation (EA) are correlated with worse outcome after percutaneous coronary intervention, and the recent pathological study had reported that superficial echo attenuation is the reliable IVUS signature for identifying a high risk plaque. Coronary angioscopy (CAS) provides direct visualizations of coronary luminal surface. Few reports that evaluated EA plaques by IVUS and OCT had modest diagnostic accuracy for identification hemodynamically significant lesions, also with specific cut-off for different diameters. Invasive imaging for assessment of LM severity demonstrated excellent correlation with FFR.

Purpose: To assess the morphological characteristics of EA plaques by CAS, and compare the angiographic difference between superficial and deep plaques.

Methods: From the institutional IVUS and CAS database from 2009 to 2014, 30 patients with stable angina and 5 patients with unstable angina pectoris with EA plaques observed at the culprit lesions, who also underwent CAS examination, were included. We first evaluated CAS findings of EA plaques. Then, EA plaques were divided into two groups of the superficial (leading edge of attenuation closer to the lumen than to the adventitia; n=22) EA group and the deep (leading edge of attenuation closer to the adventitia than to the lumen; n=13) EA group. The two groups were compared by the CAS findings.

Results: In total 35 EA lesions, intensive yellow plaque was observed in 11/35 (31%), yellow plaque in 12/35 (34%), light yellow plaque in 8/35 (23%), white plaque in 4/35 (11%), and thrombus was detected in 8/35 (23%), respectively.

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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 = 0.029). 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 (< 5x 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 = 0.02). FFR demonstrated significant stenosis of the LAD in 52%, LAD lesions were considered significant in 29%, compared to 53% of the non-LAD lesions (RCA=39.5%, LM=0%, CX=90%). 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.

Conclusions: Mean age of the total population was 65±10 years. Angiographically, LAD lesions were considered significant in 29%, compared to 53% of the non-LAD lesions (p = 0.02). FFR demonstrated significant stenosis of the LAD in 52%.

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 12 month follow-up after 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 ± 8.6; p < 0.001) as well as strut count normalised to diameter (11.5 ± 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 ± 22.4 mm; p = 0.09 respectively 3.1 ± 2.9 mm; p = 0.267) and incidence of acute stent malapposition (6 vs. 23%; p = 0.299). Further, stent strut density was higher in the ZES group compared to EES and BES (strut count per frame: 11.4 ± 8.6; vs. 7.36; p < 0.001; strut count normalised to diameter: 11.69 vs. 15.12; p = 0.001).

Conclusion: Stent strut density appeared higher in stents with LASM at 12 month. Stent architectures with higher strut density may induce a higher incidence of LASM after 12 month.

P1753 | BEDSIDE
Clinical significance of echo-attenuated plaque on intravascular ultrasound in lesions with stable angiogram in comparison with other types of unstable plaque
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Background: Echo-attenuated plaque (EA) on intravascular ultrasound (IVUS) is related to poor outcomes after percutaneous coronary intervention (PCI) in lesions with acute coronary syndrome (ACS). However, clinical significance of EA in lesions with stable angiogram (SAP) remains unclear.

Purpose: We sought to investigate the relationships among EA and other types of unstable plaque components in lesions with ACS and SAP.

Methods: We investigated 300 lesions (ACS: n=107; SAP: n=193) who under went IVUS and optical coherence tomography (OCT) examination. Differences of plaque morphologies on IVUS and OCT, and post-PCI outcomes were assessed according to clinical status of ACS or SAP, and the presence of EA or not.

Results: EA was more frequently observed in ACS than in SAP lesions (49.1% vs. 28.1%, p < 0.001). SAP lesions with EA showed thicker fibrous cap - thickness (ACS-EA 96±54 μm; ACS-non-EA 173±142 μm; SAP-EA 157±100 μm; SAP-non-EA 230±116 μm; p < 0.001), smaller lipid area (302±67 μm²; 243±111 μm²; p < 0.001), lower frequencies of OCT-plaque rupture on OCT (49.1%; 31.5%; 21.8%; 10.9%; p < 0.001), and lower frequency of transient slow-reflow phenomenon during PCI (62.2%; 18.5%; p < 0.001; strut count normalised to diameter: 11.69 vs. 15.12; p = 0.001).

Conclusion: Stent strut density appeared higher in stents with LASM at 12 month. Stent architectures with higher strut density may induce a higher incidence of LASM after 12 month.
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 hyperfusion in SSc is not known. Therefore, we aimed to determine if patients with SSc have decreased global myocardial perfusion at rest and during adenosine stress.

Methods: Sixteen SSc patients (14 females, 45–74 years) and eleven controls (6 females, 44–66 years) underwent cardiovascular magnetic resonance imaging (CMR). Twelve patients had limited SSc and 4 patients had diffuse cutaneous SSc. One patient had pulmonary arterial hypertension (PAH). Myocardial perfusion (MP) was quantified using coronary sinus flow (CSF) measurements at rest and adenosine stress divided by left ventricular mass (LVM). Myocardial fibrosis was assessed using late gadolinium enhancement (LGE).

Results: There was no difference in MP at rest between patients and controls (1.2±0.2 vs. 1.1±0.1 ml/min/g, P=0.94, Fig.1) whereas SSc patients showed significantly decreased MP during adenosine infusion (2.7±0.2 vs. 4.1±0.4 ml/min/g, P=0.017, Fig. 1). Five out of the thirteen SSc patients investigated with LGE showed fibrosis in the right ventricle 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 hyperfusion 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: After exclusion of patients due to insufficient imaging quality, 45 patients were included in the PMI group and 19 in the control group. Median troponin levels (median ±IQR) in the PMI and control group were 150±190 vs 18±21 ng/L, respectively. Acute Coronary Syndrome was diagnosed in 6 (13%) patients with PMI vs none in the control group. CAD was found in 23 (51%) vs 3 (16%) patients (RR 3.2, 95% CI 1.1–9.5), 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 MRI’s showed cardiac edema. A perfusion defect was observed in 2 patients with PMI vs none without. Medication was optimized in 32 (71%) patients with PMI and 5 (29%) patients in the control group. No major cardiovascular events occurred within 30 days of surgery.

Conclusion: Myocardial injury after noncardiac surgery is associated with CAD. In addition, one third of patients with PMI was diagnosed with pulmonary embolism. Non-invasive cardiac imaging may facilitate an adequate diagnosis and subsequent treatment of patients with postoperative myocardial injury.

Acknowledgement/Funding: none

SAFETY AND EFFICACY OF SECONDARY PREVENTION MEDICATIONS

P1756 | BEDSIDE
Clinical equivalence of evolocumab among patient subgroups in PROFICIO: a pooled analysis of 3146 patients from phase 3 studies
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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 vs eze were similar for both 140 mg Q2W and 420 mg QM doses across age ≤65 years (−65.4%; −64.4% 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%; −65.8% vs pbo, −40.9%; −44.8% vs eze) or neither type 2 diabetes nor metabolic syndrome (−65.3%; −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%; −48.9% vs pbo, −44.2%; −45.5% vs eze), moderate (−66.4%; −65.0% vs pbo, −37.9%; −38.8% vs eze), or low risk (−60.5%; −67.8% vs pbo, −41.5%; −48.5% vs eze).

Conclusion: Patients on evolocumab demonstrated significantly greater reduc-
Optimal medical therapy may be a better initial strategy in patients with chronic total occlusion of a single coronary artery with low ischemic burden.

Methods and results: Between March 2003 and February 2012, we enrolled 2,024 CTO patients in a prospective, observational registry and retrospectively analyzed 435 patients with CTO of a single coronary artery. We divided patients into the OMT group (n=147) and the PCI group (n=288) according to initial treatment strategy. One-to-many (1:N) propensity score matching with non-fixed matching ratio was also performed. The primary outcome measured was the rate of MACE, which included cardiovascular death (OMT vs. PCI: 5.1% vs. 4.8%, HR, 1.14; 95% CI, 0.30–4.42, p=0.85). After propensity-score matching, there were no significant differences between 10.9% of the OMT group versus 41 patients (14.2%) of the PCI group (p=0.38).

Conclusions: As a treatment strategy in patients with single-vessel CTO, PCI did not reduce the risk of MACE or cardiac death. These results suggest that OMT may be a better initial strategy for patients with low ischemic burden, as assessed by low APPROACH and SYNTAX scores.

Dabigatran vs. warfarin in venous thromboembolism: a meta-analysis

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Introduction: Dabigatran has recently been approved for treatment of venous thromboembolism, including pulmonary embolism. The randomized trials testing this drug against warfarin for this indication were non-inferiority trials. However, the non-inferiority margins of these trials were wide (a relative risk of 2.75 or 2.85), which meant accepting a more than 2.5 fold relative risk increase as non-inferior.

Purpose: Because several randomized trials of dabigatran with very similar study designs have now been reported, a meta-analysis of such studies would provide tighter confidence intervals and increase the certainty about the effectiveness of dabigatran vs. warfarin in venous thromboembolism. Our purpose was to perform this analysis.

Methods: The three randomized trials submitted to the US Food and Drug Administration for approval of dabigatran for venous thromboembolism were included. Number of events for the common primary outcome (venous thromboembolism or related death) and number of patients in each group were extracted. Fixed-effect models were used to obtain meta-analytic risk ratios.

Results: Data of a total of 7963 patients were obtained for the primary outcome. In all 3 trials dabigatran was given at a dose of 150 mg twice daily and target INR was 2 to 3 with warfarin. On meta-analysis dabigatran had a risk ratio of 1.20 (95% CI 0.88–1.62) (P=0.3) for venous thromboembolism or related death (Figure).

Conclusions: The confidence intervals of dabigatran for treatment of venous thromboembolism as compared to warfarin are tighter on meta-analysis, ruling out a 65% increase in risk (as compared to the boundary of 175% to 185%) set in the individual trials). Smaller degrees of risk increase compared to warfarin are not ruled out.

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 randomized controlled trials (RCTs) evaluating the impact of prophylactic ascorbic acid on post-CTS AF, intensive care unit (ICU) length of stay (LOS) and total hospital 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 differences (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 included coronary artery bypass grafting (CABG) and/or valve surgery, with the remaining 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 significant 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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**P1762 | BEDSIDE**

Erythropoietin improves long-term neurological outcome in acute ischemic stroke patients: a randomized, prospective, placebo-controlled clinical trial

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Background: Mortality and disability following ischemic stroke (IS) remains unacceptably high in with respect to the conventional therapies. This study tested the effect of erythropoietin (EPO) on long-term neurological outcome in patients after acute ischemic stroke (IS).

Aims of the study: The primary objective was to evaluate the safety and efficacy of two consecutive doses of EPO (5,000 IU/dose, subcutaneously administered at 48 h and 72 h after acute IS) on improving the 90-day combined endpoint of recurrent stroke or death that has been previously reported. A secondary objective was to evaluate the long-term (i.e. five years) outcome of patients who received EPO.

Methods: This was a prospective, randomized, placebo-controlled trial that was conducted between October 2008 and March 2010 in a tertiary referral center. IS stroke patients who were eligible for EPO therapy were enrolled into the study. The safety, tolerability, pharmacokinetics, and pharmacodynamics of subcutaneously administered ALN-PCSSC in subjects with elevated LDL-C on and off of statin therapy.

**Purpose:** We are currently conducting a phase 1, randomized, placebo-controlled, single ascending and multiple dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of subcutaneously administered ALN-PCSSC in subjects with elevated LDL-C on and off of statin therapy.

**Methods:** Subjects ages 18 to 60 years with LDL-C >100mg/dl on and off of statins are being enrolled in the United Kingdom, Clinical Trials.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 measures.

**Acknowledgement Fundings:** Alnylam Pharmaceuticals

**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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Purpose: Although both resting heart rate (HR) and left ventricular ejection fraction (LVEF) are known to be strong predictors for worse clinical outcomes in HF patient population, less is known about the resting HR levels in relation to LVEF. REALITY HF (Resting Heart Rate and Real Life Treatment Modality in Outpatients with Left Ventricular Systolic Dysfunction) data were analyzed for the assessment of any relationship between resting HR and LVEF.

Methods: REALITY HF was a multicenter, prospective, observational, national registry designed to evaluate HF patients’ clinical characteristics and the effects of current treatment modalities on resting heart rate (HR) and enrolled 1251 patients (mean age 61±12 years, 76% male) from 16 centers who were admitted to the outpatient clinic with the diagnosis of chronic HF, LVEF <40% and >18 years of age. 791 patients in sinus rhythm were included in this analysis. Patients with recent acute coronary syndromes, severe hepatic or renal dysfunction, severe chronic obstructive pulmonary disease, severe anemia, hyper-hypothyroidism and pregnant women were excluded from the study. Resting HR was obtained from 12-lead ECG. Patients were classified into 3 groups according to the tertiles of LVEF: lowest ltertile: LVEF <27.6% (n=254), second tertile: LVEF 27.7% to 34.7% (n=305), third tertile: LVEF >34.7% (n=305).

**Results:** At the time of enrollment, 93% of patients were receiving evidence-based HF medication and 82% were on ≥2 drug therapy including ACEI or ARB, beta blocker, aldosterone blocker, diuretic or digoxin. Mean resting HR was 76.8±13.6 bpm and 69.1% of the patients had a resting HR >70 bpm. The resting HR was found to be 78.9±13.6 bpm in those in the lowest tertile, 76.8±13.5 bpm in those in the second tertile and 74.9±14.3 bpm in those in the highest tertile (Kruskal-Wallis, p<0.001). Mean HR was significantly higher in the lowest LVEF tertile compared to the highest LVEF tertile (Mann-Whitney, p<0.003) and significantly higher in the second LVEF tertile as compared to the highest LVEF tertile (Mann-Whitney, p<0.043). Moreover, there was a significant negative correlation between resting HR and LVEF (p<0.001).
Conclusions: The results of this study suggest that resting HR shows a significant inverse correlation with LVEF in patients with chronic HF. Acknowledgement/Funding: This study is supported by Servier.

P1765 | BEDSIDE
Endothelium-enriched microRNAs predict the presence of cardiac allograft vasculopathy
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Aims: Cardiac allograft vasculopathy (CAV) is a limiting factor for the long-term survival of heart transplant recipients. Clinical decisions and care may be improved by the development of prediction models based on circulating biomarkers. The endothelium may play a central pathogenetic role in the development of CAV. We evaluated the hypothesis that endothelium-enriched microRNAs (miRNAs) discriminate between patients with CAV and patients without CAV.

Methods: Fifty-two patients undergoing coronary angiography between 5 and 15 years after heart transplantation were recruited in this cross-sectional study. Circulating levels of endothelium-enriched miRNAs (miR-21-5p, miR-92a-3p, miR-92a-1-5p, miR-126-3p, miR-126-5p) were quantified by real-time RT-PCR. The discriminative ability of logistic regression models was quantified using the concordance statistic (c-statistic).

Results: Median follow-up was 1793 days (9–4079). Median follow-up was 1793 days (9–4079). Twenty-eight patients showed CAV (c-statistic 0.800 (95% CI 0.674–0.926)).

Conclusion: Endothelium-enriched miRNAs have predictive ability for CAV beyond clinical predictors.
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P1766 | BEDSIDE
Improved survival after heart transplantation in patients with cardiac amyloidosis
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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 (ASCST) after HT for AL amyloidosis or simultaneous liver and HT 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 (80%) of the AL patients and 1 patient (14%) of the TTR group were women, mean age 54±8 yrs. 80% of the AL amyloid patients received chemotherapy previous to HT and in 60% of them ASCST was performed after HT. Four patients in the TTR group had a liver-heart transplant (3 simultaneous). Survival of amyloid patients was 91% and 68% after 1 and 5 years HT; there were no significant differences with survival of other HT patients (93% and 74%, respectively). Survival of amyloid patients after 2008 improved significantly compared to patients before this period (100% vs. 75% at 1 year and 100% vs. 25% at 5 years, p=0.016).

Conclusions: Outcomes after HT of patients with cardiac amyloidosis has significantly improved and is similar to survival of other HT recipients. Changes in patient selection and the association of ASCST 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 unique scenario; 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 the detection of chagasic DNA.
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, parasitism 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 calciumin inhibitors, azathioprine (AZA) or mycophenolate mofetil (MMF) and steroids. The p did not received prophylactic benznidazole.

Results: Two out of 29 (7%) ChTx recipients died in the perioperativer 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 strout+. The median time from HTx to clinical Ra was 87 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 cardiac arrest, 1 p in a car collision and 1 acute abdomen. There was no mortality due to Ra.

Conclusions: Ra was observed in 41% of ChTx 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
Background: Left ventricular dysfunction (LV and RV) function after heart transplantation (HT) has not been well described. Our objective was to evaluate 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% in HT vs −20±4±3% in controls, p=0.03), improving progressively until its complete normalization two years after HT (−17±3±8% vs −20±4±3%, p=0.70). TAPSE was impaired in the early post-HT period and increased progressively (12±3±2 mm at baseline vs 18±4±1 mm at 2-years, p<0.001). RV GLS rose during follow-up as well (−17±2±5% at baseline vs 23±2±7% at 2 years, p<0.001), reaching normal values one year after HT (table).

Evolution of left and right ventricle

<table>
<thead>
<tr>
<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>
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<td>LVEF</td>
<td>62±5±4</td>
<td>61±8±1</td>
<td>62±5±7</td>
<td>64±8±4</td>
<td>63±7±3</td>
<td>63±2±6</td>
</tr>
<tr>
<td>LV GLS</td>
<td>−20±4±3</td>
<td>−17±3±9</td>
<td>−17±3±9</td>
<td>−17±3±2</td>
<td>−17±3±3</td>
<td>0.180</td>
</tr>
<tr>
<td>TAPSE</td>
<td>23±4±3</td>
<td>23±4±2</td>
<td>23±3±3</td>
<td>23±5±4</td>
<td>23±6±5</td>
<td>0.011</td>
</tr>
<tr>
<td>RV GLS</td>
<td>−25±8±4</td>
<td>−22±5±4</td>
<td>−22±5±4</td>
<td>−22±5±4</td>
<td>−22±5±4</td>
<td>0.011</td>
</tr>
<tr>
<td>RVLS</td>
<td>−31±6±3</td>
<td>−28±4±5</td>
<td>−28±3±5</td>
<td>−28±3±5</td>
<td>−28±3±5</td>
<td>0.011</td>
</tr>
</tbody>
</table>

Conclusions: The results of this study suggest that resting HR shows a significant inverse correlation with LVEF in patients with chronic HF. Acknowledgement/Funding: This study is supported by Servier.
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 (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=58) or dobutamine (up to 40 mcg/kg, n=4) SE.

Results: We found 54 eligible hearts with normal findings. Of these, 14 were not transplanted due to lack of a matching recipient. The remaining 40 eligible hearts were transplanted in emergency recipients. All showed normal (n=36) or near-normal (minor single-vessel disease, in 4) angiographic and hemodynamic findings at 1 month. 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 myocardia, 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: Heart failure (HF) is a common cardiovascular disease associated with high morbidity, mortality, and healthcare costs. Insulin resistance (IR) is a major contributor to the development of heart failure. Therefore, we aimed to determine the effect of IR on the composite outcome in patients with chronic heart failure.

Methods: We included 107 patients (pts) with chronic heart failure (NYHA class II-IV with left ventricular ejection fraction ≤ 40%) without diabetes who were admitted to our hospital for heart failure. The first 12 months of follow-up were regarded as the baseline period. We measured heart failure-related events (death, transplantation, or hospitalization) and admitted for heart failure. We divided the patients into two groups based on the presence of IR (HOMA index ≥ 1.864). Cox regression analysis was used to searching the predictors of composite outcome during 12 months.

Results: The study involved 107 patients (pts) with CHF (NYHA class II-IV with left ventricular ejection fraction ≤ 40%) without diabetes who were admitted to our hospital for heart failure. We divided the patients into two groups based on the presence of IR (HOMA index ≥ 1.864). Cox regression analysis was used to searching the predictors of composite outcome during 12 months. The model of the predictors of composite outcome during 12 months was HOMA index: OR=1.864 (95% CI: 1.051–3.307), p=0.033, and E/e’ ratio: OR=1.055 (95% CI: 1.027–1.084), p=0.001. The median survival in IR group was 5.5 months, and in non IR group – 11.7 months (p=0.003) – fig. 1.

Conclusion: Insulin resistance is a strong predictor of poor 12-month clinical prognosis in systolic CHF.

P1771 | BEDSIDE

Change in relaxation pattern of the left and right ventricle after freedive training

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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 this 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±7 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-wave 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±10.1 cm/s, p; E-wave deceleration time: 129.8±34.2 vs. 157.8±38.6 ms, p<0.001). Similarly, tissue Doppler imaging-derived early diastolic myocardial velocities measured at the mitral annulus were decreased after the training (e’ septal: 14.5±3.2 vs. 11.2±2.8 cm/s, p<0.01; e’ lateral: 16.8±3.0 vs. 14.5±3.1 cm/s, p<0.05). Systolic parameters of the left ventricle (EF and FS) were not affected. Right ventricle parameters: TAPSE showed significant decrease (26.8±2.8 vs. 21.1±2.7 mm, p<0.001), tissue Doppler imaging-derived early diastolic velocities measured at the tricuspid annulus were decreased after the dive (e’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±4.2 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

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 has not been well defined in different forms of hypertrophic cardiomyopathy (HCM). We aimed to examine parameters of LV deformation in patients with HCM using 3D-MDI and to detect if there were any effects of outflow tract obstruction on deformation patterns.

Figure 1. Kaplan – Meier curves for the composite outcome in patients with chronic heart failure and left ventricular systolic dysfunction depending on presence of IR.
Torsion behaviour, which might have a role in screening subclinical cases. The 3D-MDI hence appears to be able to reflect the changes of untwist and recoil started earlier, quicker with obstruction (66.8±10.1 vs 53.6±3.3 °/s, p=ns) or that in controls (obstructive, 15.7±3.4° vs non-obstructive, 10.7±1.8° , p=0.001). The Tor-R was longer UTT (195.8±20.3 vs 129.1±23.0 ms, p=0.01), the onset of untwist occurred closer to aortic valve closure (90.9±23.0 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 22.5±3.8 %, p=0.01), and both were less than in controls (49.1±6.6 %, p<0.001).

Conclusions: Diastolic dysfunction precedes overt systolic dysfunction in chemotherapy-induced cardiotoxicity

P1774 | BEDSIDE
Dietary sodium restriction decreases blood pressure in patients with heart failure

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Background: Sodium restriction 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 dietary restriction in patients submitted to chemotherapy (Q3) and anthracyclines.

Methods: Consecutive breast cancer patients undergoing Q3 referred for a transhoracic echocardiogram (TTE) between August 2010 and October 2014 were included. Data was collected on baseline characteristics, TTE measurements including tissue Doppler, QT regimen and concomitant therapy. Dietary sodium (SD) was defined as ejection fraction (LVEF) - 55% and diastolic dysfunction as mean E/e' ratio > 13. Patients with baseline SD or DD were excluded. A cut-point defined as dysfunction in > 10% of patients was used to calculate time-related incidence.

Results: 110 patients were submitted to a total of 234 TTE during a mean follow-up of 381 days. Mean age was 56±14.5 yrs, basal heart rate 79±18.8 bpm. Baseline TTE: LVEDD 46.6±7.0 cm, LVESD 28.1±4.6 cm, LVEF 68.3±6.8%, E velocity 76.7±19.8 cm/s, septal e' 8.2±3.1, lateral 10.7±3.8 cm/s. At 1 year, the incidence of DD was 18.0% vs. 8.0% for SD (odds ratio 2.25, p=0.0028, chi sq). The threshold for > 10% of patients with DD was reached after 203 days, while for SD only after 378 days. DD preceded significant LVEF decline by 175 days for this quartile. The Kaplan-Meier survival function for DD and SD after Q3 is plotted on graph 1.

Conclusions: HFPEF is associated with lower SA compared to HFREF. However, high NE levels play a role in terms of prognosis. According to this observation, further investigation on the potential role of beta-blocker use in HFPEF should be studied.

Figure 1 shows survival in HFPEF patients according NE.
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 biopsy samples (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) indicating that not only in the LV but also in the RA the postprandial inci-
dence 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 proteins in the human heart with diastolic dysfunction is chamber spe-
cific, 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 post-
operative atrial fibrillation in diabetic patients with coronary artery disease.

Our study addresses important aspects of the underlying mechanisms of diabetes-
associated diastolic dysfunction, which will be crucial in developing new treat-
ments.

Acknowledgement/Funding: National Heart Foundation Tianzhu 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 endothe-

lial 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 semi automatic vessel wall tracking system. Although increased carotid IMT is reported to be associated with LVDD, there is limited data regarding brachial IMT. The aim of this study was to investigate the relationship between brachial IMT and LVDD.

Methods: A total of 211 patients (mean age 63±15 years, 50% men) with sus-
ppected coronary artery disease (CAD) underwent FMD by ultrasound using 10-
MHz linear array transducer. Brachial IMT was automatically measured on A-

real-time mode images of the far wall of the same right brachial artery. Left ventricular structure (left ventricular mass index [LVM], left atrial volume index [LAVI]) and function (Early diastolic annular velocity [e']) were assessed using echocardiogra-
phy. LVDD was defined using E/e’, LVM, and LAVI according to ASE guideline.

Results: Semi-automatic measurement of brachial IMT was feasible in all sub-
jects. Of all, brachial IMT and FMD were 0.33±0.07mm and 5.6±2.7%. Brachial IMT was thicker in patients with hypertension (0.34±0.07mm vs. 0.31±0.07mm, p<0.001) and male (0.34±0.07mm vs. 0.31±0.07mm, p=0.002) compared to no-
hypertension and female, respectively. Brachial IMT was related to FMD (r=-0.152, P=0.027), age (r=0.184, P=0.007), LVM (r=-0.19, P=0.019) and septal e’ (r=-0.171, P=0.014). FMD was related to age (r=-0.269, P<0.001), septal e’ (r=-0.261, P<0.001), s’ (r=0.170, P=0.021) and lateral s’ (r=0.181, P=0.014).

Next, patients were classified into four groups according to the median value of
brachial index and FMD. The prevalence of LVDD in the larger IMT and the lower FMD group (47%) was significantly higher than others (31%) (p<0.024). Multiple logistic analysis revealed that LVDD was associated with the larger IMT and the lower FMD (OR: 2.077, 95% CI: 1.068 to 4.038, p<0.031) along with hypertension (OR: 1.962, 95% CI: 1.022 to 3.769, p=0.043) and diabetes mellitus (OR: 0.043, 95% CI: 0.203 to 0.797, p<0.009).

Conclusion: The simultaneous measurements of the brachial IMT and FMD may be informative for assessment of LVDD.

P1777 | BEDSIDE
Association of arterial stiffness and elevated left atrial pressure in patients with and without diastolic dysfunction - a subgroup analysis from Diast-CHF
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Background: The interaction between arterial stiffness and left atrial pressure (LAP) as a diagnostic and prognostic marker of diastolic dysfunction and heart failure with preserved left ventricular ejection fraction (LVEF) has not been sys-
tematically investigated so far.

Material and methods: Ninety-seven patients (mean age 66 years, 53% female, mean LVEF 61%) with at least one cardiovascular risk factor (e.g. hypertension, diabetes) for the development of heart failure or with a previous diagnosis of heart failure, elevated LAP was determined based on the recommendations of the American Society of Echocardiography E/MVe’ ≥13, left atrial volume index ≥34 ml/m2. LAP has been correlated with data from annotation topology and pulse wave analysis (Augmentation-Index-Ax normalized by 75 b/min- Aix@75, pulse wave velocity-

PWV).

Results: Ninety-seven patients (38%) demonstrated an elevated LAP. These pa-
tients were significantly older (68±5.7 vs 63±5.7 years, p<0.001), demonstra-
ted a higher body mass-index (29.8±4.6 vs 28.0±5.0; p<0.01), hypertension (89.7% vs 73.1%, p<0.01), hypercholesterolemia (32.0% vs 21.3%, p<0.05), dyspnea on exertion (28.4% vs 16.6%, p<0.05) and peripheral edema (25.3% vs 10.2%, p<0.01). Aix@75 and PWV were significantly elevated in patients with elevated LAP (29.2±6.7% vs 27.4±6.7%, p<0.05 and 12.2±2.7 m/s vs. 10.5±2.6 m/s, p<0.001, respectively) and correlated with posterior wall thick-
ness (r=0.167, p<0.01; r=0.292, p<0.01), left ventricular mass index (r=0.192, p<0.05; r=0.195, p<0.01), LVEF (r=0.200, p<0.01) and its endogenous inhibitor PLB was re-
served by grants from the Ger-
man Federal Ministry of Education and Research (#01GI0205; #01EO1004)

P1778 | BEDSIDE
Association of cystatin C with heart failure with preserved ejection fraction. Potential role of altered collagen metabolism
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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 hy-
pothesized 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 hyper-
tensive origin. Cardiac morphology and function was assessed by echocardiogra-
phy. Circulating levels of cystatin C, the pro-fibrillar matrix protein collagen type oxy-
pontin, and biomarkers of collagen type I synthesis (carboxy-terminal propedep of procollagen type I, PICT) and degradation (matrix metalloproteinase-1, MMP-1, and its inhibitor TIMP-1) were analyzed by ELISA. 20 elderly subjects with no known cardiac disease and normal age-adjusted renal function were used as a control group. In vitro studies were performed in cardiac human fibroblasts.

Results: Compared to controls, cystatin C was increased (P<0.001) in HFPEF patients, even in those with normal age-adjusted estimated glomerular filtration rate (eGFR) 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 the ePCWP (P<0.01), TIMP-
1 (P<0.001) and osteopontin (P<0.001) and inversely correlated with MMP-1:
TIMP-1 (P<0.01), but no association was found with PICT or MMP-1. All these
associations were independent of the eGFR and a number of potential confound-

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<0.03) and higher E/e'(19.9±7.1 vs. 13.9±4.3, P<0.0001). HFpEF with low a’ had significantly lower cardiac event-free survival than HFpEF with high a’ (Log rank, P=0.02).

**Conclusion:** Impaired LA function may be associated with worse prognosis in HFpEF.

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**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 determine risk for new-onset HFpEF versus normal diastole and preexisting HFpEF.

**Methods:** We studied 96 patients. We obtained peripheral blood samples to analyze aSxL and Lp-PLA2 levels at the time of the coronary angiography for the diagnosis of CAV. Cardiac allograft vasculopathy (CAV) remained one of the major limitations in long-term survival in Heart Transplantation patients (TC). Its diagnosis relies on invasive methods and often is 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 aSxL (protein involved in vascular remodeling) and Lp-PLA2 (marker of atherosclerosis).

**Methods:** We studied 96 TC. We obtained peripheral blood samples to analyze aSxL and Lp-PLA2 levels at the time of the coronary angiography for the diagnosis of CAV. Cardiac allograft vasculopathy was diagnosed 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, aSxL levels were significantly higher (46.7 vs 73.9, P=0.03) in patients with CAV (CAV 1.2.3) compared to patients without CAV (CAV0). In the logistic regression analysis aSxL levels >74 were associated with increased risk of CAV (Odds Ratio= 2.367; 95% 1015–5520; p=0.04)

**Conclusion:** Monitoring the levels of aSxL 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.
HEART FAILURE: FROM BENCH TO BEDSIDE IV

P1783 | 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 (HFpEF) are similar to those with HF with reduced EF. Resting heart rate (RHR) is recognized as a predictor of cardiovascular (CV) mortality.

Purpose: To investigate if RHR has diagnostic and/or predictive value in HFpEF.

Methods: 217 patients (pts) with clinical HF, with EF greater than 50% and diastolic dysfunction were included. Pts with atrial fibrillation or flutter were excluded. The parameters evaluated: NYHA class, RQS, quality of life (QoL), score, indexed left atrial volume (ILAV), E/E’ ratio and NT-proBNP value.

Results: Initially, pts with E/E’ ratio between 15–25 were divided into pts with serum NT-proBNP higher than 220 pg/mL considered as having HFpEF (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 HFpEF (AUC 0.713, CI 0.637–0.789). Subsequently, 114 pts (age 56.9±24 years, 56 males) with confirmed HFpEF (74% in NYHA class II, 18% in class I and 20% in class III) were followed up for 1 year. The end-point - adverse outcome (AO)- comprised: death, myocardial infarction, stroke, hospitalization for acute HF, increased NYHA class (p=0.004). The KCCQ overall and clinical summary scores were significantly different between patients with and without diastolic dysfunction. Univariate logistic regression analysis revealed 6-months walk test was significantly shorter in systolic dysfunction group (228.5±79.8 m vs. 317.2±92.2 m, p<0.001). The KCCQ overall and clinical summary scores were significantly lower in the group with systolic dysfunction (36±11.2 vs 46±5±11.8, p=0.002, respectively).

Conclusion: Occasional or regular alcohol intake is associated with better diastolic function in general population amongst ethnic minority groups.

P1784 | BEDSIDE
Echocardiography was used to establish presence of diastolic dysynchrony in patients with DCM and its association with quality of life (QoL).

Methods: Sixty patients with DCM were subjected 6-minutes walk test and full echocardiographic examination. All patients filled 2 quality of life (QoL) questionnaires: the Minnesota Living with Heart Failure Questionnaire (MLWHF) and the Kansas City Cardiomyopathy Questionnaire (KCC). Tissue Doppler echocardiography was performed using a 6- basal, segmental model to assess time to peak 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 = time in peak to systolic velocity (SD-S) and early diastolic velocity (SD-E). Sixty and nine matched heart care. However, the centers that perform autopsies are an important tool to confirm hypothesis clinically. Faculty of Medicine Clinics Hospital (HC-FMUSP), Sao Paulo, Brazil

HEART FAILURE: FROM BENCH TO BEDSIDE IV

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, the diastolic dysfunction has been extensively studied, little is known about diastolic dyssynchrony. The aim of this study was to estimate the prevalence of systolic and diastolic dyssynchrony in patients with DCM and its association with quality of life (QoL).

Methods: Sixty patients with DCM were subjected 6-minutes walk test and full echocardiographic examination. All patients filled 2 quality of life (QoL) questionnaires: the Minnesota Living with Heart Failure Questionnaire (MLWHF) and the Kansas City Cardiomyopathy Questionnaire (KCC). Tissue Doppler echocardiography was performed using a 6- basal, segmental model to assess time to peak 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 = time in peak to systolic velocity (SD-S) and early diastolic velocity (SD-E). Sixty and nine matched heart care. However, the centers that perform autopsies are an important tool to confirm hypothesis clinically. Faculty of Medicine Clinics Hospital (HC-FMUSP), Sao Paulo, Brazil

Conclusion: Occasional or regular alcohol intake is associated with better diastolic function in general population amongst ethnic minority groups.

P1786 | BEDSIDE
Riociguat treatment for patients with pulmonary hypertension due to heart failure with preserved ejection fraction

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Background: Riociguat, a stimulator of soluble guanylate cyclase, is a novel pulmonary and systemic vasodilator that has been approved for pre-capillary forms of pulmonary hypertension (PH). In a proof of concept study, single-dose administration of riociguat has shown favourable effects in patients suffering from PH due to heart failure with preserved ejection fraction (PH-HEF).

Purpose: The aim of the present study was to evaluate safety and efficacy of riociguat administration in consecutive patients diagnosed with PH-HEF.

Methods: This was a prospective, open-label, non-randomized single-centre study. Eligible patients (enough) received riociguat in addition to standard heart failure treatment. Riociguat was started at a dose of 0.5mg per day and was up-titrated within 8 weeks to a maximum of 2.5mg per day. Baseline work-up of patients and re-evaluation after 6 months of therapy included the assessment of blood pressure, NYHA functional class, exercise capacity as measured by the 6-minute walk test (6MWT) as well as serum NT-proBNP.

Results: 115 patients (114 males and 1 female) were included in the study. No adverse events occurred during the observation period. No systemic blood pressure drops were encountered (144/77mmHg at baseline and 142/71mmHg at follow-up; p=0.351). NYHA functional class significantly improved from NYHA: 2.75±0.46 at baseline (p<0.001). NT-proBNP levels decreased slightly from 1695 pg/mL ± 2377 to 1426 pg/mL ± 1611 (p=0.476). The baseline 6MWT improved from 306±129 m to 324 ± 119 m; (p=0.208).

Conclusion: Although preliminary, our data indicate that long-term treatment with riociguat is safe in patients with PH-HEF. The trend towards beneficial effects clinical effects of long-term treatment remains to be confirmed.
diomyopathy, age (younger than 18 years-old), pericardial diseases and post-operative shock. Discrepancies between clinical and necropsy 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:** We reviewed 1226 cases and included 500. On the necropsy data, the most common causes at high risk of poor outcomes were ischemic 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: 118 (64%) 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 cardiacogenic 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 (19.8%) 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 misdiagnoses in patients with heart failure can be related to the severity of this syndrome, what supports the importance 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 approaches.

**P1788 | BENCH**

NGAL/MMP9 complex: from kidney injury to worsening of heart remodelling in cardiorenal syndrome type II

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**Methods:** We studied the role of congestion in the development of kidney injury assessed by the signs of congestion, hypertrophy and dilatation of the right ventricle. BNP, sCreatinine, both kidney and heart NGAL, MMP-9, sCytokines, Kidney and heart cell death, assessed by TUNEL, were also studied.

**Results:** Rats with HF showed higher BNP (CHF 4.8±0.5, C 1.5±0.2 ng/mL and sCreatinine (CHF 70680±4337 vs C 32120±4961 AU, p=0.001) rose significantly and inflammatory cytokines were significantly increased. sCreatinine was also increased in CHF rats. A higher number of kidney cell death, assessed by TUNEL, were also studied.

**Conclusion:** In this model of CHF with prevalent congestion, kidney injury is characterized by tubular damage and systemic inflammation. The enhanced enzumatic activity of the upregulated NGAL complexed with MMP9 produces extra-cellular matrix degradation. This may worsen heart remodelling and perpetuate the vicious circle of kidney/ heart damage.

**P1789 | 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 disease at high risk of poor outcomes. The phenylephrine method – “gold standard” for BRS evaluation – is difficult to be widely applied into clinical examination. 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 y, LVEF: 34±7%, all receiving ACE-I/ARB and beta-blocker) in addition to standard clinical assessment, echocardiography and cardiology exercise testing, underwent BRS evaluation with 3 methods: the phenylephrine (BRS-phe), the sequence (BRS-seq), and the controlled-breathing (BRS-cb).

**Results:** There were only modest correlations between BRS calculated using each method: BRS-phe and BRS-seq: r=0.31, BRS-cb and BRS-seq: r=0.43 (all p>0.05). Phenylephrine-derived groups differed in age (60±11 vs. 56±11 y, p=0.03), The occurrence of HF was demonstrated by signs of congestion, hypertrophy and dilatation of the right ventricle. Eleven anilmals were taken as control. The occurrence of HF was demonstrated by signs of congestion, hypertrophy and dilatation of the right ventricle. The internation was due to heart failure in 26 (21.8%) and to cardiacogenic shock in 23 cases (19.3%).

**Conclusion:** Only 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 related to congestion. Persistent congestion at hospital discharge is associated with increased risk for mortality and rehospitalizations. Recently, hemoconcentration (HC) has been suggested as a surrogate for successful decongesion during fluid removal in AHF.

**Methods:** We treated 704 patients with AHF and volume overload. Congestion was assessed at admission and discharge using a 9-point scale (0 to 8) as follows: JVP ≥8 cm water (1 point), hepatomegaly (1 point), peripheral edema (Absent/trace, 0 points; slight 1 point; moderate, 2 points; marked, 3 points; and anasarca, 4 points), pulmonary rales (1 point), and third heart sound (1 point). A composite score 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 <0.55% (Simpson’s biplane) or fractional shortening <27%. Subclinical systolic dysfunction was identified by peak systolic mitral anular velocity in septal and lateral position (< 0.6 and 6.7 cm/s respectively) using pulsed wave tissue Doppler (TDI) and by global longitudinal strain <18% using 2 dimensional speckle tracking echocardiography (2D STE). Diastolic dysfunction (DD) was defined by early diastolic velocity (e’) of the septal <8 cm/s or the lateral mitral annulus <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’d, E/A ratio) and pulmonary venous flow (S/D ratio, Ar-A duration), left atrial volume and E/e’ ratio.

Results: Mean age was 62.0±7.8 years with mean follow-up time since diagnosis of 12.0±1.4 years. 112 (52%) was treated for left sided BC. 129 (60%) received anthracyclines with the cumulative dose of 360 mg/m² eprubicin. None were treated with 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 though TDI peak systolic velocities or 2D STE. However DD occurred in 142 (66%) compared to 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 (1.5–6.5), p=0.03 respectively) while anthracyclines were not. Multivariate analysis showed some association of borderline significance (OR 2.4 (1.1–5.8), p=0.06) in multivariable modelling.

Conclusion: LV DD is markedly more frequent in long term BC survivors than in controls particularly after manually planned radiotherapy and anthracycline containing chemotherapy. Parameters of systolic function did not discriminate between patients and controls.

P1792 | 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. Study patients were stratified with EMB methods into J-sheath group (n=40) and old-method group (n=4). Routine surveillance EMB were performed weekly 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) as compared to that in old-method group (log-rank p <0.0001, Figure).

Conclusion: Comparison of conventional measures to estimate right ventricular function in patients after heart transplantation using 3D and speckle-tracking echocardiography


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.
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: 45±7 vs 51±4% [−12%], FAC: 43±7 vs 48±6% [−10%]). TAPSE: 15±4 vs 22±3 mm [−32%], all p < 0.05). There was no correlation between TAPSE and EF in HTx patients, whereas free wall longitudinal strain correlated with it (r=0.39, p < 0.05). Notably, FAC reflected reliably (r=−0.74, p < 0.001). Patients over one year after HTx had better TAPSE (17±4 vs 14±5 mm in patients within one year, p < 0.05), whilst EF did not differ between the two groups (43±6 vs. 46±7%, p=NS). TAPSE correlated with the time elapsed after HTx (r=0.60, p < 0.001). FAC is not a reliable measure of RV systolic function in patients underwnt transplant. Wall strain describing longitudinal shortening provides a better estimate. If 3D echocardiography is not available, FAC is the method of choice to assess RV performance. Our data also suggest a dominant radial component in RV function. In time, longitudinal function can recover.

**P1790 | BEDSIDE**

Evaluation of left ventricular myocardial mechanics and synchrony in heart transplant patients using three-dimensional echocardiography


Speckle-tracking echocardiography gained particular interest as it allows to quantify sensitive and predictive parameters of myocardial function in numerous cardiac conditions. Accurate 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. Patients with history of allotraft rejection were excluded. Beyond standard echocardiographic protocol, we acquired 3D datasets from apical view using multi-beat reconstruction from 4 or 6 cardiac cycles. Using a dedicated software for LV quantification (4D LV-Function 3), LV end-diastolic (EDV), end-systolic (EDV) volumes, ejection fraction (EF) were measured. Furthermore, global longitudinal (GLS) and circumferential strain were quantified by 3D speckle tracking analysis. Systolic dysynchrony index (SDI) derived from 16 subvolumes of the LV was also assessed. EDV of healthy subjects was higher, however, EF was similar in the two groups (HTx vs. control: EDV: 123±34 vs 94±24 mL, p = 0.01; EF: 62±8 vs 64±4%). TAPSE did not differ either (GCS: −30±7 vs −31±5%). Interestingly, GLS was significantly decreased in HTx patients compared to controls (−18±4 vs −21±1%, p < 0.01). SDI referring to intraventricular dysynchrony was higher in HTx patients (93±3 vs 42±2%, p < 0.01).

Despite the lack of known pathology and maintained ejection fraction, 3D longitudinal strain may indicate subclinical LV dysfunction in HTx patients. Mild degree of intraventricular dysynchrony is also suggested to be present. Further enrolment and follow-up may verify the importance of our results.

**P1791 | BEDSIDE**

Time (not) to RELAX?

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Introduction: Little has changed in the years in the way we treat acute heart failure. Recently, the results of the RELAX-AHF trial suggested that recombiant human serelexin could have impact on both clinical improvement and outcome of hospitalized patients.

Purpose: To verify which patients admitted to an acute heart failure treatment unit could have been enrolled in RELAX-AHF trial, according to its inclusion and exclusion criteria.

Methods: Retrospective analysis of patients admitted to an acute heart failure unit between 2003 and 2012. Patients were considered “RELAX-AHF-eligible” if they met the following criteria: BNP < 350 pg/L, systolic blood pressure < 125 mmHg, serum creatinine > 1.3 mg/dL. Data regarding the main modifiable cardiovascular risk factors, BNP value, creatinine, hemoglobin and sodium at the time of admission were evaluated. Mortality among those who fulfilled eligibility criteria and those who did not was also compared.

Results: Of a total of 983 patients, only 53 (5.3%) could have been enrolled the RELAX-AHF study. The majority (82.7%) were male and the average age was 62±9 years. Idiopathic (44.7%) and ischemic (19%) myopathies were the most prevalent etiologies. There were no statistically significant differences regarding age, systolic BP, heart rate, hemoglobin, creatinine, sodium or BNP between RELAX-AHF-eligible and non-RELAX-AHF eligible patients (p > 0.05). No statistically significant difference was found in mortality between RELAX-AHF eligible and non-RELAX-AHF eligible patients (44.2% vs 39.8%, p = 0.444).

Conclusion: Potentially eligible RELAX-AHF patients are a minority of acute heart failure patients if an advanced heart failure unit population is to be considered. Therefore, the external validity of the RELAX-AHF finding should be made with caution in regard to the type of population.
± 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 patients with HF and advanced CKD.

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 advanced CKD (eGFR <30 mL/min/1.73m2) with HF and stage 3b-5 CKD and analysed for s-K+. Change from baseline (Δ) endpoint by s-K+ strata: >5.0–5.5 (mild) and >5.5–6.0 mEq/L (mod/severe) in A-DN; 5.1–5.5 (mild) and 5.5–6.5 mEq/L (mod/severe) in OP.

Results: Of HF pts with advanced CKD, 66 had mild and 66 had mod/severe HK. Over the entire study period.

Conclusions: Patiromer significantly reduced s-K+ in HK patients with HF and advanced CKD. HF pts with CKD ≤40% were more sensitive to change in serum K+ levels. 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, with wk 4. AEs were predominately mild-to-moderate GI complaints; AEs led to patiromer discontinuation in 6 pts in each study over the entire study period.

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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±8.0 years; M47%) with LBBB revealed during annual check-up were enrolled into the study. History of CAD had 34(51.5%) patients, hypertension - 64 (94.1%), 4 patients had no overt heart diseases after thorough examination. There were no patients with EF below 45%, and NYHA class >II. Fifty two (76.5%) of 68 patients had taken the recommended medication, mainly ACE-inhibitors and beta-blockers; however, 16 patients refused the recommendations. Follow-up period duration was 32±13 months (6–58 months). 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=24; 95% CI: 1.00–1.52).

In the beginning of the study only 19 (21,1%) patients had signs of atrioventricular (AV) dysynchrony. During the FU period 10 (14.7%) new cases of AV-dysynchrony have occurred. Multivariate analysis showed the influence of chronic heart failure (CHF; OR 6.91; 95% CI: 1.95–24.5; p=0.003), and heart rate (HR; OR=1.84; 95% CI: 1.19–2.87; p=0.02).

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, BNP 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 (68.29±15.63 ms vs. 61.95±8.55 ms; p=0.005). However, it worsened in patients who refused them (55.62±18.96 ms vs. 64.38±15.04 ms; p=0.032).

Conclusions: heart failure with preserved ejection fraction (HFpEF). The aim of the study was to evaluate prognostic significance of visit-to-visit BPV in patients with stable HF and reduced ejection fraction (EF).

Methods: Retrospective analyses included 100 pts (80 men, age 64±9.3yrs, BP 127.6±15.1/77.9±8.3mmHg, HR 72.3±10.4 bpm) with stable II-III NYHA class and 100 pts (80 men, age 64±9.3yrs, BP 127.6±15.1/77.9±8.3mmHg, HR 72.3±10.4 bpm) with stable II-III NYHA class. The endpoints included death, myocardial infarction (MI), stroke, hospitalisation for HF.

Results: we investigated 1160 patients (mean age 72.8±13.7 years old, male 40.1%), with 484 (41.7%) patients with HFpEF. We observed progressive hyponatremia in 116 patients (10.0%). During median 520 days follow-up, 199 (17.2%) patients died (16.9% in HFpEF, and 14.7% in HFpEF). In all patients, progressive hyponatremia was independently associated with all-cause mortality (Hazard ratio [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 HFpEF (p<0.001, log rank test) but not in the group with HFpEF (p=0.162, log rank test). In the patients with HFpEF, progressive hyponatremia remained as independent predictor for all-cause (HR 2.04, 95% CI 1.20–3.49, 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 HFpEF. The impact of progressive hyponatremia on long adverse outcome was different between HFpEF and HFpEF.

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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 a strong significant predictor of adverse outcomes in patients with stable HF. 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 14.8±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.

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**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 heart failure.

**Methods:** Patients with a diagnosis of HF at a health maintenance organization in Israel, 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 Arab subjects of younger age compared to Jewish subjects (OR 1.97, 95% CI 1.1–3.5, p=0.02 for age 40-59 years). Arab subjects had significantly higher prevalence of 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.
Conclusions: Fluid overload was identified as a predictor of an adverse prognosis in patients with HFP EF. 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 systolic function

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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 aortic stiffness and left ventricular (LV) diastolic function. However, there have been few studies regarding the relationship between arterial stiffness and left ventricular end-diastolic pressure (LVEDP) in exercise or ambulation. Thus, this study was designed to investigate the relationship between arterial stiffness and the degree of change in exercise induced LVEDP in patients with HFpEF.

Methods: This study population was composed of 156 patients who underwent left cardiac catheterization, coronary angiography, transesophageal echocardiography and brachial-ankle pulse wave velocity (baPWV) during same admission period. In patients with non-significant coronary stenosis and normal left ventricular ejection fraction, the passive leg-raise exercise with bolus injection of levosimendan was performed during LV catheterization under polygraphy monitoring. The LVEDP was measured by automatically mechanical measurement.

Results: The mean age was 59.83±13.15 years, average RbPWV 1533.30±392.85 mmHg and LbPWV 1524.13±419.23 cm/s. As the average LVEDP was 20.66±7.33 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±2.55 mmHg. The LVEDP measured at rest and at leg-raise were significantly correlated with the degree of LVEDP variation during active leg-raise was well correlated with baPWV (R=0.273, p<0.02 for RbaPWV, R=0.272, p<0.02 for LbPWV). The subjects with increased LVEDP by active leg raise had significantly higher value of baPWV than those with decreased LVEDP (1393.35±287.62 mmHg vs. 1530.20±376.91 mmHg for RbaPWV, p<0.01, 1380.69±281.70 mmHg vs. 1522.63±392.10 mmHg for LbPWV, p<0.01, respectively).

Conclusion: BaPWV, non-invasive marker of central arterial stiffness, was closely associated with the degree of LVEDP variation during active leg-raise exercise, whereas it was not correlated with absolute LVEDP values at rest and during passive leg raise. It indicates that the coupling of ventricular-arterial stiffness is dynamic rather than static process.

P1810 | TRANSCEND

Benign transgenic model overexpressing endothelial beta3-adrenoceptor: a new model for heart failure with preserved ejection fraction

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Background: Heart failure (HF) with preserved ejection fraction (pEF) is a growing health burden affecting the elderly. Patients express impaired cardiac relaxation and filling with various comorbidities (hypertension, diabetes, or renal failure). Due to the lack of patient biopieces and accurate animal models, its physiopathology is not completely understood and no specific treatment is available to improve patients quality of life.

Purpose: In this context, our team developed a novel rat model of HFP EF. Its characterization could allow to better understand disease physiopathology and to determine new therapeutic targets.

Materials and methods: A new transgenic rat model is a transgenic rat (Tg3) which overexpressed in endothelium human β3-adrenoceptor gene upon ICAM2 promoter. Cardiac function of 15, 30 and 45 weeks-old males was investigated by echography (VIVID7). At 45 weeks, arterial and left ventricular pressure were measured using a pressure probe (Millar Instruments Inc.). Rats were then sacrificed to measure myocardial fibrosis by picrosirius red staining analyzed upon polarized light, which allowed to distinguish type I and III collagen. Pulmonary and renal vasculature was also investigated by histological studies.

Results: At 45 weeks of age, Tg3 rats presented an increased in left ventricle end diastolic pressure (LVEDP), WT: 5.6±1.2 mmHg; Tg3: 11.74±1.1 mmHg. This is a characteristic of an increase in LV stiffness, without any arterial hypertension. Cardiac echography showed an altered filling pattern with an increase in early-to-late filling (E/A) ratio (WT: 1.14±0.01; Tg3: 1.32±0.04; p<0.01), with a pre- and post-load dependent pattern. An adverse outcome despite no difference in arterial blood pressure. This effect was similar between WT and Tg3 rats at 15 weeks-old, showing that diastolic dysfunction appeared with ageing among Tg3 rats. Cardiovacular alterations were correlated with a significant increase in collagen I (WT: 2.07±0.16%; Tg3: 2.67±0.19%)
Heart failure: from bench to bedside II

P1812 | BEDSIDE
Retained cardiac implantable electronic devices post orthotopic heart transplantation: prevalence and complications
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Introduction: Increasing numbers of patients referred for consideration of heart transplantation have Cardiac Implantable Electronic Devices (CIEDs). Despite efforts to remove the implanted device with direct traction intra-operatively, complete lead removal is not possible due to adherence to the vessel wall with associated complications.

Methods: A single centre review of Orthotopic Heart Transplants (OHT) from August 2007 to September 2013 was conducted, assessing frequency and complications of the retained hardware.

Results: Of 113 patients undergoing OHT during this period, 94 patients (83%) had CIEDs at the time of transplant surgery. 17 patients (18%) with CIEDs pre-transplant were noted to have retained hardware on post-operative chest radiographs. Isolated retained hardware was noted in 5 patients (5%), including 2 right atrial leads, 2 pacemaker leads and 1 defibrillator lead. In 12 patients (13%), dual-chamber CIEDs were noted to have retained hardware, including 4 patients (4%) with retained right atrial leads, 2 patients (2%) with retained right ventricular leads, and 6 patients (6%) with retained left ventricular leads.

Conclusion: The high retention rate of CIEDs post OHT is emerging as an area of concern. This study also reports retained hardware associated with pulmonary and renal alterations. In contrast, this was contraindicated in patients with retained hardware.

P1813 | BEDSIDE
Predictive value of PAPP-A, sCD40L, and anti-HLA antibodies in cardiac transplant recipients
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Introduction: Pretransplant levels over median of PAPP-A (11 mIU/L) and sCD40L (6.7±1.5 pg/ml) were higher in patients with high mPAP as compared to those with “lower” mPAP (p < 0.01, 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).

Methods: A total of 217 patients underwent heart transplantation (HTx) during the period from 2008 to 2014 (mean follow-up 53.1±26.89 month); 25 (17.9%) women and 115 (82.1%) men. Initial diagnostic evaluation was performed on admission for renal transplantation. Patients were divided into two groups: low mPAP (≤15 mmHg) n=88 and high mPAP (>15 mmHg) n=129.

Results: The median mPAP was 15 mmHg (IQR 12–19 mmHg) and the median mPCWP was 8 mmHg (IQR 6–11 mmHg). Kaplan Mayer curves of “high” versus “low” mPAP (median split) showed significantly better survival in those with “lower” mPAP (p = 0.001). Other factors independently associated with mortality were age at transplant (risk ratio 1.03, CI 1.01–1.04, p = 0.002) and serum creatinine 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.

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 adapted and optimized. Retained hardware also limits the use of CMR for non-invasive assessment of rejection with future diagnostic implications. Complete removal of CIEDs is recommended during OHT and when this is not possible, leads should be left in a state to allow for extraction at a later date if required.
6.5±1.3 vs 15.0±1.5. In the in vivo human hearts, there was an increase of the end-diastolic pressure (EDP) from 12±3 to 18±3 mmHg after the increase of the end-diastolic volume (EDV) from 182±32 to 205±32 mL, and a subsequent drop of the EDP, after 15 minutes of adaptation, to 12±4 mmHg, whereas the EDV did not decrease significantly (187±30 mL). 

**Conclusion:** Our results showcase a new mechanism of diastolic adaptation, which consists of an acute decrease in LV stiffness after stretch. This mechanism was also observed in the in vivo human heart and is preserved at the myocardial level. This original description identifies a new element central to the cardiac response to haemodynamic overload.

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**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 (HFPEF) lack desirable diagnostic sensitivity and specificity.

**Purpose:** We hypothesized that in HFPEF, increased LAP leads to an increase in LA to left ventricle (LV) size ratio due to relative dilatation of LA and reduction of hypertrophic LV cavity size. Our aim was to determine if the left atrial to left ventricular diameter ratio (LA/LV) on 2D echocardiography (2D Echo) is a diagnostic marker of elevated LAP.

**Methods:** We retrospectively identified 81 consecutive HFPEF subjects with elevated left atrial pressure (intravenous inotropes, 60; ventilated, 10; mean: CI 1.9 L/min/m2; CVP 19 mmHg; TERMACS 1 Level while 15 of them had survived after a successful resuscitation 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 infection (n=15), 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 stratagically in severe congestive heart failure. With the introduction of meticulous wound care, mortality has been significantly reduced, and management as an outpatient is achievable, however, readmissions are still frequent.

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**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 (HFpEF and HFrEF) after staged palliations in patients with univentricular heart disease remain unknown as is the question whether cardiосphere-derived cell (CDC) transfer may have impact on either type of cardiac dysfunction.

**Purpose:** We sought to characterize the heart failure patients, include HFpEF and HFrEF, with single ventricular physiology and investigate the clinical responsiveness after CDC therapy.

**Methods:** Forty-three patients, aged 2±1.4 years, undergoing staged shunt procedures were divided into two groups by cardiac function based on cMRI (HFrEF: EF<40%, n=30; HFrEF: EF≥40%, n=13). Baseline characteristics and cardiac function measurement by cMRI and echocardiogram during the staged palliation with or without additional intraventricular CDC infusion were assessed.

**Results:** Compared with HFrEF patients, HFpEF patients showed increased cardiac volume (P<0.02) and mass index (P=0.04), those were associated with reduced global circumferential strain in HFrEF compared with HFpEF (P=0.0004). Although there was no difference in the incidence of late gadolinium enhancement detected by cMRI in both groups (20% in HFpEF and 15% in HFrEF), ventricular diastolic dysfunction identified by early diastolic strain rate (e’sr) was higher in HFrEF patients compared with HFpEF group (46% vs. 27%). When patients underwent staged shunt procedures, HFpEF group had significant reduction in EF and atrial strain (P<0.02), resulting in increase in Tei 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 HFrEF group, HFpEF patients demonstrated a marked improvement in EF (P<0.001), right ventricular elastance (P=0.0001), right atrial fractional area change (P=0.01) and reduced E-wave/e’sr (P=0.049). However, patients with HFrEF had no significant change. Similarly, diastolic function improvements were found in the CDC-treated HFrEF group but not HFrEF patients as shown by increased atrial fractional area change (P=0.01) and reduced E-wave/e’sr (P=0.049). However, patients with HFrEF had no significant change. A marked improvement in EF (P=0.0001) 3 months after CDC infusion. Similarly, diastolic function improvements were found in CDC-treated HFrEF group but not HFrEF patients as shown by increased atrial fractional area change (P=0.01) and reduced E-wave/e’sr (P=0.049). However, patients with HFrEF had no significant change. A marked improvement in EF (P=0.0001) 3 months after CDC infusion. Similarly, diastolic function improvements were found in CDC-treated HFrEF group but not HFrEF patients as shown by increased atrial fractional area change (P=0.01) and reduced E-wave/e’sr (P=0.049). However, patients with HFrEF had no significant change.

**Conclusions:** HFpEF 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

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**TREATMENTS OF HYPERTENSION**

**P1818 | BEDSIDE**

**Impact of fixed-dose combination of perindopril/amlopidine 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/amlopidine 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/amlopidine was effective and well tolerated. Target blood pressure level was achieved in 70% of the patients. The LV mass index, as calculated from 137 (104–163) g/m² to 123 (105–149) g/m² with the LV ejection fraction raised from 68.7±7.3% to 70.9±7.1% (p=0.012). The basal LV circular strain and strain rate improved significantly after 6 months of treatment (Table). There were no significant changes in longitudinal and radial deformation throughout the study period.

**Dynamics of myocardial deformation**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>6 month</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global longitudinal LV strain, %</td>
<td>-16.1±2.8</td>
<td>-16.2±2.2</td>
</tr>
<tr>
<td>Global longitudinal LV strain rate, 1/s</td>
<td>0.96±0.15</td>
<td>0.96±0.2</td>
</tr>
<tr>
<td>Basal circular LV strain, %</td>
<td>-19.5±4.3</td>
<td>-19.7±4.6</td>
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<tr>
<td>Basal circular LV strain rate, 1/s</td>
<td>1.3±0.3</td>
<td>1.41±0.37</td>
</tr>
<tr>
<td>Basal radial LV strain, %</td>
<td>25.6±11.2</td>
<td>25.8±11.2</td>
</tr>
<tr>
<td>Basal radial LV strain rate, 1/s</td>
<td>2.03±0.54</td>
<td>2.03±0.46</td>
</tr>
<tr>
<td>Apical circular LV strain, %</td>
<td>-29.2±7.4</td>
<td>-29.8±7.7</td>
</tr>
<tr>
<td>Apical circular LV strain rate, 1/s</td>
<td>1.84±0.55</td>
<td>1.86±0.57</td>
</tr>
<tr>
<td>Apical radial LV strain, %</td>
<td>26.2±11.9</td>
<td>27.1±10.4</td>
</tr>
<tr>
<td>Apical radial LV strain rate, 1/s</td>
<td>1.56±0.57</td>
<td>1.63±0.46</td>
</tr>
</tbody>
</table>

Values are given as mean ± standard deviation.

**Conclusions:** The treatment with fixed-dose combination of perindopril/amlopidine is associated with improved basal LV strain and strain rate without significant dynamics of longitudinal and radial deformation.

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**P1819 | BEDSIDE**

**Combination with low-dose dextromethorphan improves the effect of amlopidine monotherapy in clinical hypertension**

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**Background:** Amlodipine (AM) is one of the most widely used antihypertensive drugs. Dextromethorphan (DXM), a non-opioid cough suppressant, was reported with potential neuro-protection by inhibiting NADPH oxidase. We previously demonstrated that combination of low rather than high dose of DXM with AM could improve blood pressure (BP) reduction in hypertensive animals. 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 were enrolled and baPWV were measured every year (mean follow up periods 4.5 years). All subjects were divided into two groups: optimal medical therapy group and sub-optimal therapy group.

**Results:** The blood pressure control predictors in 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 treatment failure rates. 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 rate 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.

**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.

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**P1820 | BEDSIDE**

**The blood pressure control predictors in hypertensive patients with and without ischemic heart disease**

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Blood pressure (BP) decreasing till target level prevents complications. Ischemic heart disease (IHD) is factor that could influence on antihypertensive effectiveness. There was not compared the predictors of target BP achievement in population of AH patients without and with IHD. That is the aim of our study.

There were included 9821 hypertensives (mean age 58.9±0.24 yrs) in 350 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.

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 (> 100 mmHg) levels: risk of not target BP achievement increased in 3.83/2.81 times for 1st group and in 3.92/2.5 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 decrease (≥ 0.52, p=0.001). Only 28.3% of 1st group and 19.5% of 2nd (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.
P1822 | BEDSIDE
Hypotensive effect of dinitrosoiron complex with glutathione (DNIC): clinical trials on healthy volunteers and patients with stable hypertension and in case of hypertensive crisis
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Aim: To examine the safety of dinitrosoiron complex (DNIC) administration in healthy volunteers and the hypotensive effect of DNIC in patients with essential hypertension and uncomplicated hypertensive crisis.

Materials and methods: The first part of the study included single intravenous infusion of the drug (5 mg/kg or 0.2 Imoles/kg of DNIC, respectively) in 14 healthy male volunteers. The next part of the study included 30 patients aged 35 to 73 years (mean age 55.5±10.8). All patients had essential or symptomatic arterial hypertension. 13 patients (43.3%) had hypertensive crisis at the point of inclusion, 17 patients (56.7%) had persistent elevation of blood pressure. DNIC was injected at a dose of 1.5 or 3 mg per kg of body weight. The administration of DNIC stopped at the point of 20% blood pressure reduction from initial. Patients’ blood pressure was monitored during intravenous injection of DNIC and 24 hours after.

Results: The response of healthy men on DNIC administration manifested as a 3–4 min drop by 24–27 mm Hg of both diastolic and systolic AP with its subsequent stabilization within the next 8–10 h. The heart rate quickly normalized after an initial increase. Cardiac output was unchanged despite reduced cardiac filling. A comprehensive analysis of clinical and biochemical data failed to establish any significant pathological changes in these parameters.

All hypertensive patients (11/100%) had a reduction of blood pressure by at least 20% from baseline. Dynamic of blood pressure reduction was similar in case of both doses (1.5 mg/kg or 3 mg/kg). The maximum decrease of blood pressure was fixed at 6–8 min after the injection. During the next 8 hours a gradual individual increase in blood pressure with stabilization at a level of 2–3 mm Hg higher than a baseline level was observed in all patients. We also marked significant difference in the level of blood pressure reduction in case of different doses (1.5 mg/kg and 3 mg/kg).

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.

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: The first part of the study was an assessment 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, and thus improved blood pressure control under a fixed dose combination tablet.

Discussion: The results clearly demonstrate the strong adherence under the FDC of bisoprolol and amlodipine. As a consequence, the blood pressure control is improved and thus, the risk of cardiovascular events decreased.

Acknowledgement/Funding: This study was supported by Merck KGaA, Darmstadt, Germany

P1824 | BENCH
Persistence of initial antihypertensive therapy in patients of outpatient specialized cardiac clinic
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Aim: To analyze the persistence of initial antihypertensive therapy (AHT) of outpatient specialized cardiac clinic of Moscow for 6 months.

Study design: Study includes two stages. The first stage included studying of medical records of all patients with arterial hypertension (AH) (1766 persons), who came for the first time to specialized cardiac clinic, and extraction of medical data for every patient coming to the clinic in 2010 year. The second stage included telephone survey of 1419 patients at 6 months after the first visit to the clinic in order to get data about degree of adherence.

Results: On the first visit hypertension treatment was recommended to all patients, with 6 months antihypertensive medications received 91.1% of them, p<0.001. During 6 months 74.9% of patients changed treatment scheme, and 52.4% of the patients made the decision to change the treatment regimen of cardiovascular diseases by themselves, without any physicians’ recommendations. A significantly higher chance of non-persistence with recommended treatment scheme was find in patients who had medications reimbursement (OR 2.4, 95% CI 1.8 to 3.0, p<0.001). And, tunnel biomedical are still required as a first line drug in old women. This study aimed to investigate clinic and home BP lowering effect of fimasartan in postmenopausal women with hypertension.

Methods: K-Mets Study recruited 10,375 hypertensive patients treated with fimasartan in Korea. Among them, 382 premenopausal women (preMPW) and 990 postmenopausal women (postMPW) with 3 months follow-up data and fimasartan as a first antihypertensive drug were selected.

Results: Baseline clinic systolic BP (SBP) (preMPW 152.9±15.2 vs. postMPW 152.8±13.5 mmHg) was not different, but diastolic BP (DBP) was lower in preMPW (95.7±9.4 vs. postMPW 91.9±9.4 mmHg; p<0.001). After 3 months, clinic SBP and DBP declined effectively in both groups (Table). Home morning and night SBP were not different in both groups, but DBP of postMPW was lower both in the morning and night. After 3 months, home SBP showed a similar decline in the morning (preMPW –21.3±17.9 vs. postMPW –20.4±17.3 mmHg) and at night (preMPW –23.1±15.8 vs. postMPW –22.2±19.2 mmHg). Home DBP after 3 months was not different in both groups, but it was more decreased in preMPW in the morning (preMPW –13.3±12.0 vs. postMPW –10.0±10.6 mmHg; p<0.005) and at night (preMPW –13.8±10.3 vs. postMPW –9.7±10.9 mmHg; p=0.001).

Conclusions: Fimasartan lowered both clinic and home BP effectively in postmenopausal women as well as in premenopausal women with hypertension.

P1825 | BEDSIDE
Clinic and home blood pressure lowering effect of fimasartan in postmenopausal women with hypertension
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Background and purpose: Although the activation of renin-angiotensin system is suggested as one possible mechanism of postmenopausal hypertension, calcium channel blockers are still recommended as a first line drug in old women. This study aimed to investigate clinic and home BP lowering effect of fimasartan in postmenopausal women with hypertension.

Methods: K-Mets Study recruited 10,375 hypertensive patients treated with fimasartan in Korea. Among them, 382 premenopausal women (preMPW) and 990 postmenopausal women (postMPW) with 3 months follow-up data and fimasartan as a first antihypertensive drug were selected.

Results: Baseline clinic systolic BP (SBP) (preMPW 152.9±15.2 vs. postMPW 152.8±13.5 mmHg) was not different, but diastolic BP (DBP) was lower in preMPW (95.7±9.4 vs. postMPW 91.9±9.4 mmHg; p<0.001). After 3 months, clinic SBP and DBP declined effectively in both groups (Table). Home morning and night SBP were not different in both groups, but DBP of postMPW was lower both in the morning and night. After 3 months, home SBP showed a similar decline in the morning (preMPW –21.3±17.9 vs. postMPW –20.4±17.3 mmHg) and at night (preMPW –23.1±15.8 vs. postMPW –22.2±19.2 mmHg). Home DBP after 3 months was not different in both groups, but it was more decreased in preMPW in the morning (preMPW –13.3±12.0 vs. postMPW –10.0±10.6 mmHg; p<0.005) and at night (preMPW –13.8±10.3 vs. postMPW –9.7±10.9 mmHg; p=0.001).

Conclusions: Fimasartan lowered both clinic and home BP effectively in postmenopausal women as well as in premenopausal women with hypertension.
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 Berlin’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 RHHTN was found in 46 patients (12,9%). Baseline NT-proBNP values in patients with RHTN (n=46) were higher than in general group (250±60 pg/ml vs 86±30 pg/ml, p<0.05). 1 patient with RHTN had fatal hemorrhagic stroke, 1 patient ischemic stroke, 2 – transient ischemic attacks, 2 developed permanent atrial fibrillation, 1 patients had successful coronary revascularization, 1 acute coronary syndrome. Baseline NT-proBNP level in patients with RHTN and poor prognosis was higher compare patients with uncomplicated RHTN (372±30 pg/ml and 170±100 pg/ml, p<0.05). Discrepancies were confirmed after adjustment for BP level, size of heart chambers by 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
Dietetics, having a tendency of more antihypertensive effect at a low temperature, reduce the seasonal variability of blood pressure
K. Nomoto1, T. Mitsui1, M. Miyagi1, M. Kokubo1, A. Shimizu1, T. Murohara2. 1National Center for Geriatrics and Gerontology, Department of Cardiology, Obu, Japan; 2Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan

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 via 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 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. The difference of the average monthly systolic blood pressure was also observed in the 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
Cirulating miR-21 and eNOS in subclinical atherosclerosis in patients with hypertension
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Background: Primary hypertension (HT) is a highly prevalent pathological condition that is considered one amongst the traditional risk factors for cardiovascular disease (CVD) and is an important cause of adult morbidity and mortality worldwide.

Purpose: The aim of this study was to evaluate the relationship of miR-21, nitric oxide (NOx) and endothelial nitric oxide synthase (eNOS) with subclinical atherosclerosis in carotid arteries by measuring CIMT in patients with hypertension compared to healthy controls.

Methods: A total of 28 hypertensive and 28 healthy controls were enrolled. CIMT was evaluated by ultrasonosgraphy and CIMT=0.8 accepted as increased CIMT (CIMT).

Results: CRP, miR-21 expression levels and CIMT measurements were significantly higher in the hypertension group than in the control group (p<0.009, p<0.002 and p correc., respectively). NOx and eNOS levels were significantly higher in the lower hypertension group than in the control group (p<0.001 and p<0.001). Microalbuminuria levels in both groups were within normal limits. MR-21 was positively correlated with the clinical systolic blood pressure, clinical diastolic blood pressure, CRP and CIMT. miR-21 was negatively correlated with NOx and eNOS.

Eighteen patients with hypertension had CIMT. MR-21 expression and CRP levels were significantly higher (p<0.001 and p<0.001), whereas NOx and eNOS levels were significantly lower in patients with CIMT (p<0.001 and p<0.001).

The characteristics of the groups

<table>
<thead>
<tr>
<th>Controls (n=28)</th>
<th>Hypertensive subjects (n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>p</td>
<td>Gender (female/male)</td>
</tr>
<tr>
<td>Age, years</td>
<td>45±5.3</td>
</tr>
<tr>
<td>CIMT (mm)</td>
<td>0.55±0.12</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>1.3±1.2</td>
</tr>
<tr>
<td>NOx (μmol/L)</td>
<td>14.8±7.2</td>
</tr>
<tr>
<td>eNOS (pg/ml)</td>
<td>913.3±136.2</td>
</tr>
<tr>
<td>miR-21 expression level</td>
<td>24±5.5</td>
</tr>
</tbody>
</table>

Conclusions: The decreased levels of NOx and eNOS found in this study indicate the co-existence of endothelial dysfunction and hypertension once more. In the absence of microalbuminuria, the increased miR-21 expression in patients with hypertension made us to consider that miR-21 might be involved in the early stages of atherosclerotic process in hypertensive patients.

Acknowledgement/Funding: This work was supported by grants from the Research Fund of Istanbul University (Project Number: 40447).

P1829 | BEDSIDE
Persistence of fixed and free combination of ramipril and amloidipine in hypertension
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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 prolonged effective pharmacologic treatment. Non-adherence might be involved in the early stages of atherosclerotic process in hypertensive patients.

Purpose: Our aim was to evaluate the persistence on one-year treatment with the free or fixed combination of ramipril and amloidipine in hypertension.

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 or fixed combinations of ramipril and amloidipine, 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 amloidipine 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 amloidipine 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 January 2013 to December 2014.
Results: The study revealed a 3-fold increased risk of hemorrhagic stroke in patients receiving NOA in addition to antithrombate 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, the 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 treatment with PAR1 antagonists or direct thrombin inhibitors.

Conclusion: In patients with ACS, the addition of a NOA to antithrombate 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 antithrombate 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 NOA 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).
**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). Based on in vitro assays we selected several polysaccharide polymers for further in vivo studies.

**Purpose:** The aim of the present study was to find the most efficient in vivo UFH antidote.

**Methods:** We administered UFH (300 U/kg) alone or followed by γ-cycloexodrin (GCD-GTMAC, 10.8 mg/kg), low (Dex6-GTMAC, 9.6 mg/kg) or high (Dex40-GTMAC) molecular weight dextrans substituted with GTMAC groups at a ratio of 0.5 (Dex40-GTMAC2, 12.5 mg/kg) or 0.65 (Dex40-GTMAC3, 7.5 mg/kg) per a glucose unit, and protamine (3 mg/kg) to 84 male Wistar rats developing electrically induced arterial thrombosis. The efficacy endpoints were: arterial thrombus weight, tail bleeding time, activated partial thromboplastin time (aPTT) and anti-factor Xa activity. We measured blood count and blood pressure directly in the carotid artery of rat to exclude the worst tolerated polymers. We also compared the immune response to Dex40-GTMAC3 and protamine administered once a week to female mice for 36 days.

**Results:** Dex-GTMAC was the most potent and, similarly to protamine, reversed all the measured endpoints when administered in a non-hypotensive dose (Table 1). Unlike Dex6-GTMAC3, Dex6-GTMAC was hypotensive and decreased, whereas GCD-GTMAC increased red blood cell count, hematocrit and hemoglobin values. In contrast to protamine, Dex40-GTMAC3 did not induce immune response.

**Conclusions:** Dex40-GTMAC3 was found to be the most efficient UFH antidote in vivo.

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**Table 1. Reversing of UFH effects**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Vehicle</th>
<th>UFH</th>
<th>UFH+Dex40-GTMAC3</th>
<th>UFH+Protamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombosis weight (mg)</td>
<td>0.9±0.17</td>
<td>0.57±0.03</td>
<td>0.86±0.25</td>
<td>0.82±0.28</td>
</tr>
<tr>
<td>Bleeding time (seconds)</td>
<td>104.3±6.4</td>
<td>167.2±14.2</td>
<td>106.3±15.5</td>
<td>102.2±6.5</td>
</tr>
<tr>
<td>aPTT (seconds)</td>
<td>20.3±1.1</td>
<td>28.6±2.8</td>
<td>29.8±5.2</td>
<td>26.2±4.3</td>
</tr>
<tr>
<td>Anti-factor Xa activity (U/mg)</td>
<td>0.13±0.02</td>
<td>0.03±0.02</td>
<td>0.45±0.11</td>
<td>0.18±0.08</td>
</tr>
</tbody>
</table>

***P<0.001 vs. vehicle; **P<0.05; *P<0.01; #P<0.001 vs. UFH, Mann-Whitney test. Results are shown as mean ± SD, n=8-10.

**Conclusions:** Documented efficacy, immunogenic and hemodynamic neutrality of Dex40-GTMAC3 makes this novel UFH antidote advantageous over other polysaccharide polymers and protamine.

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**YOUNG INVESTIGATORS AWARDS SESSION: AGING AND SENESCENCE**

**1834 | BENCH**

Telomere length predicts clinical outcomes post-revascularization procedures: its role as a novel biomarker of systemic oxidative stress and cardiovascular aging

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1University of Oxford, RDM, Cardiovascular Medicine Division, Oxford, United Kingdom; 2Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

**Background:** Short telomere length (TL) characterizes biological senescence. Increased oxidative stress could induce telomere shortening, contributing to cardiovascular disease (CVD). We explored the value of TL as a biomarker of cardiovascular redox state and evaluated its predictive value post-revascularization procedures.

**Methods:** Two cohorts (500 patients undergoing percutaneous coronary intervention (PCI) following ST-elevated myocardial infarction (STEMI) and 648 pts undergoing CABG surgery) were followed up prospectively. TL was measured in all patients by LCMPCR. Systemic oxidative stress was evaluated by plasma malondialdehyde (MDA). Vascular NADPH-oxidase-derived superoxide was measured by chemiluminescence in saphenous vein segments (SV) from the CABG patients. In 35 CABG patients, TL was also measured in DNA from SVs. Patients were genotyped for two functional SNPs (rs4673 & rs10492525) in the CYBA gene (NADPH-oxidase subunit p22phox).

**Results:** TL predicted all-cause (A)/ CVD mortality (B) and non-fatal ACS (C) post PCI, all independently of chronological age. In CABG pts, short TL predicted poor clinical outcome. High plasma MDA was linked to shorter baseline TL. High NADPH-oxidase activity was associated with short TL in SVs (F). Using Mendelian randomization, the additive effect of rs4673G & rs10492525C, linked to increased NADPH-oxidase activity in SVs (G), also led to shortened TL in both cohorts (H), suggesting a causal relationship between oxidative stress and TL.

**Conclusions:** We present 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 aging.

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**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 contributor 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. NRG-1 is an endothelial growth factor, which has powerful cardioprotective and anti-atherosclerotic effects but its role in ageing remains unexplored.

**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 vitro and in the aorta of diabetic mice in vivo.

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**1836 | BENCH**

Matricellular protein CCN1-mediated premature senescence is a negative regulator of cardiac fibrosis

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**Introduction:** Premature senescence is a tumour suppressive mechanism leading to p16INK4a and/or p53-p21CIP1/WAF1 mediated cell cycle arrest upon telomere shortening or oncogenic signaling. Recent studies have demonstrated a novel role for premature senescence in liver and skin fibrosis and identified Cystein-rich 61 protein (CCN1) as a key regulator.

**Purpose:** To investigate the pathophysiological role of CCN1-mediated prema-

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**Methods:** Two established murine models of cardiac fibrosis, transaortic constriction (TAC) and cardiacmyocyte-specific beta1 adrenergic receptor transgenic mice (beta1-TG), were employed to study the role of premature senescence in the heart. Fibrosis was detected by Sirius Red staining and Realtime PCR (Col1a2, Col3a1). Cellular senescence was quantified by immunohistochemistry, histochemistry and Realtime PCR of p16INK4a, p21CIP1/WAF1 and senescence-associated beta-galactosidase (SA-β-GAL).

**Results:** Senescence marker p16INK4a and/or p53-p21CIP1/WAF1 mediated cell cycle arrest upon telomere shortening or oncogenic signaling. Recent studies have demonstrated a novel role for premature senescence in liver and skin fibrosis and identified Cystein-rich 61 protein (CCN1) as a key regulator.

**Objective:** To investigate the pathophysiological role of CCN1-mediated prema-

**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 aging.
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 vasculopathy 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. The telomere length (TL) and telomerase activity (TA) are considered as biomarkers of cellular aging. It is crucial to determine the role of telomere biology in different vascular 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 (9.75): “short” telomeres and “long” telomeres. Vessels changes were more pronounced in patients with “short” TL: PWV 14.1±3.22 m/s vs. 11.78±3.26 m/s (p<0.016), IMT 1.00±0.15 mm vs. 0.84±0.16 mm (p<0.001), PP 2.63±0.31 mm vs. 1.36±0.26 mm (p<0.003), FVM 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=−0.50, p=0.0003), IMT (r=−0.39, p=0.0006), FVM (r=−0.49, p=0.0003), NDV (r=−0.41, p=0.0004), FPG (r=−0.42, p=0.003), CRP (r=−0.40, p=0.004), TA (r=−0.32, p=0.035).

Then patients were divided into 2 groups by the median of TA (0.33): “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.

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 TLR-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.

Figure 1
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±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 novel potential prophylactic and therapeutic target in ACS.

1840 | BEDSIDE
Impact of aortic valve stenosis on coronary hemodynamics and the instantaneous effect of transcatheter aortic valve implantation

Background: Aortic valve stenosis (AS) induces compensatory alterations in the left ventricle, leading to alterations in coronary hemodynamics. Relief of AS by transcatheter aortic valve implantation (TAVI) decreases ventricular afterload and is expected improve microvascular function immediately.

Purpose: We evaluated the effect of AS on coronary hemodynamics and the immediate effect of TAVI.

Methods: Intracoronary pressure and flow velocity were simultaneously assessed at rest and maximal hyperemia in an unobstructed coronary artery in 27 AS-patients before and immediately after TAVI, and in 28 patients without AS.

Results: Baseline flow velocity was higher and baseline microvascular resistance was lower in AS-patients as compared to controls, which remained unaltered post-TAVI. In AS-patients hyperemic flow velocity was significantly lower as compared to controls (4.5±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) in AS-patients was lower, 1.9±0.5 vs 2.7±0.7 in controls (p<0.001). Improvement in coronary hemodynamics after TAVI was most pronounced in patients with post-TAVI aortic regurgitation. In these patients (n=20), hyperemic flow velocity increased significantly from 46.2±15.47 to 56.5±17.44 cm/s post-TAVI (p=0.003). HMR decreased from 2.03±0.71 to 1.66±0.45 (p=0.003). CFR increased significantly from 1.9±0.4 to 2.2±0.6 (p=0.009) (Figure 1).

Conclusion: The vasodilatory reserve capacity of the coronary circulation is reduced in AS. TAVI induces an immediate decrease in hyperemic microvascular resistance and a concomitant increase in hyperemic flow velocity, resulting in immediate improvement in coronary vasodilatory reserve.

1841 | BENCH
Incremental diagnostic value of combined non-invasive assessment of endothelial shear stress and molecular imaging of inflammation for the early identification of high-risk plaque
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Introduction: Low endothelial shear stress (ESS) and inflammation are key pathobiologic components for the development of high-risk atherosclerotic plaques.

Purpose: To test the hypothesis that the combination of non-invasively assessed ESS with molecular imaging of inflammation can predict the formation of high-risk plaque.

Methods: 12 hereditary hyperlipidemic rabbits underwent imaging of the thoracic aorta with a 256-slice CT- and a 1.5T MRI at 6 months (baseline, BL) and 12 months (follow-up, FU). We calculated the ESS at BL using CT-based 3D reconstruction of thoracic aortas and computational fluid dynamics. We selected 5-mm-long aortic subsegments (n=76), and classified ESS into low, intermediate and high (A). In each subsegment, we quantified plaque composition by CT (B) and wall thickness by MRI at BL and FU. Molecular MRI at BL and FU assessed the severity of inflammation using ultraslam superparamagnetic nanoparticles (C). Plaque size and inflammation were evaluated by histopathology at FU (D).

Results: Subsegments with low BL ESS exhibited a significantly higher non-calcified plaque volume at FU by CT (E) and significant increase in wall thickness and plaque inflammation by molecular MRI (FG) compared to intermediate/high ESS subsegments. These subsegments with low BL ESS developed high-risk plaque features by histopathology at FU (D). The composite of low ESS and severe inflammation by molecular MRI at BL was the strongest predictor of plaque progression and high-risk plaque formation (composite ESS/Inflamm.: AUC=0.89, 95% CI 0.8–1.0; ESS only: AUC=0.84, 95% CI 0.7–0.9; inflammation only: AUC=0.74, 95% CI 0.8–0.8).

Conclusion: This study provides novel evidence that low ESS and severe inflammation have incremental diagnostic value for the early identification of high-risk plaque.

YOUNG INVESTIGATORS AWARDS SESSION: POPULATION SCIENCES

1842 | BEDSIDE
30-year survival among patients with myocardial infarction before 50 years of age compared with the general population: a nationwide cohort study
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Background: Long-term mortality after myocardial infarction (MI) in young age remains unclear.

Purpose: To examine 30-year mortality among young MI patients compared with the general population.

Methods: Using medical registries, we identified all patients with MI before 50 years of age in Denmark during 1980–2009 (n=21,693), established a sex- and age-matched general population cohort (n=216,930), and ascertained all-cause and cause-specific mortality risks and rate ratios (MRRs). We adjusted for age, sex, and cardiovascular and non-cardiovascular comorbidity.

Results: The 30-day mortality risk after MI was 12.5% in 1980–1989, 8.4% in 1990–1999, and 3.2% in 2000–2009. While the 1–10-year mortality risk remained around 4% in the general population across calendar periods, it decreased in MI patients from 24.2% in 1980–1989 to 12.7% in 1990–1999 and 8.9% in 2000–2009. Compared with the general population, MI patients had an adjusted MRR of 3.36 (95% CI: 3.20–3.52) within 1–10 years, and 2.69 (95% CI: 2.59–2.79) within 11–30 years. However, throughout the study period, the MRR decreased by 4.5-fold within 30 days (from 468 to 97), 3-fold within 31–365 days (from 11.32 to 3.7), and 1.5-fold within 1–10 years (from 2.80 to 1.89). Examining cause-specific mortality risks, the highest risk was from CVD deaths (95% CI: 2.42–2.80), followed by non-CVD deaths (95% CI: 2.04–2.32). In addition, we observed a significant increase in mortality from CVD (95% CI: 1.19–1.38) and all-cause (95% CI: 1.13–1.25) death in young MI patients compared with the general population in 2000–2009.

Conclusion: The risk of death among young MI patients remains relatively high despite significant improvements in survival. Further research is needed to identify specific strategies to improve outcomes among young MI patients.
A healthy lifestyle was strongly associated with greater HRV in this population. The relationship was attenuated but remained significant after additional adjustment for age, educational status, alcohol consumption and family history of cardiovascular disease. All ECG studies were systematically post-processed, and the standard deviation of normal RR Intervals (SDNN) was used as the main parameter of HRV. Healthy lifestyle habits were summed to a lifestyle score with a scale from 0 to 5 (from the lowest to the most healthy). One point was given for never smoking cigarettes in the past, having a BMI <25 kg/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 ≤80 mmHg 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 across lifestyle score categories.

Methods: 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 (–5.85–8.42), 6.99 (0.20–13.79), 14.99 (8.19–21.79), 20.39 (13.28–27.50) and 24.60 (15.9–33.3), respectively (p for trend <0.0001). Using SDNN as a continuous variable, we found a β-estimate (95% CI) of 5.56 (4.31–6.81). p<0.0001. This relationship was attenuated but remained significant after additional adjustment for conventional HR (β-estimate (95% CI) 3.48 (2.30–4.65); 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 large sample of young and healthy adults, underscoring the importance of a healthy lifestyle for optimal cardiovascular protection. Our study also suggests that a substantial part of this beneficial effect is explained by 24-hour HR, and that the additional information provided by HRV seems to be small.

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 season, current and previous smoking status, alcohol consumption and family history of cardiovascular disease. The median PM2.5 level was 2.8 μg/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 (HR=1.32 [1.21, 1.44]), with a one-day lagging period. In multivariable analyses, PM2.5 remained independently predictive of HF incidences (HR=1.14 [1.03, 1.27]). 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 4 μg/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 4 μg/m³, which is far below the daily Australian national standard of 25 μg/m³.

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 the 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 31810 men and 33504 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 22.0–22.6). Mean number of cigarettes smoked per day was in women 10.8 (95% CI 10.6–11.1) and in men 15.7 (95% CI 15.4–15.9). Smoking more than a pack of cigarettes per day (21–30) increased the risk of SAH in women more than in men with a HR of 8.2 (95% CI 3.8–17.8) and 3.6 (95% CI 2.0–6.3). There was a difference in HRs by sex which was significant in all cigarette-per-day categories (LRT p<0.007). Among smokers mean pack years was in women 11.8 (95% CI 11.4–12.1) and in men 19.8 (95% CI 19.4–20.3). When high number of pack years (≥31) was compared to low (0–5), 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 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.

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 ACEI or ARB treatment at baseline.

Conclusion: 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.
ing treatment. Risk of all-cause mortality, cardiovascular mortality or AVR were assessed by Cox regression analyses.

Results: A total of 11,560 patients with AS receiving ACEI or ARB treatment (mean age 76.0 years [SD 10.1], 49.5% male) were matched and analyzed. baseline treatment and quality 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 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).

Conclusions: In this nationwide cohort of AS patients, treatment with ACEIs and ARBs was associated with a significantly lower risk of all-cause mortality, cardiovascular mortality and AVR. RAS inhibition may be beneficial in reducing cardiovascular adverse events and mortality in AS patients.

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 11,560 patients with AS receiving ACEI or ARB treatment 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, 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 life, defined as >3h/week of organized physical training (70% competitive athletes). Information about the background were available from the referring coroners and all the patients underwent a complete macroscopic and microscopic evaluation.

Results: The most common aetiology implicated was SD with normal heart (sudden cardiac 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 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% IC 1.15 to 3.88, p = 0.01 and HR 0.96 95% IC 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 exercise. 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 years) underwent echocardiography and cognitive function assessment using the Community Screening Instrument for Dementia score (CSID). Hippocampal volume was measured by MRI. Fasting bloods including NT-proBNP levels were measured.
See output in appendix.
The increasing survival of children with congenital heart disease (CHD) provides a challenge to health care systems about how to deal with the increasing cardiovascular disease in adults in Chile seems to attenuate this adaptive diastolic response. Titin phosphorylation, which is known to increase myocardial distensibility, is probably involved in this new myocardial response to stretch in both animals and humans.

NURSING AND ALLIED HEALTH PROFESSIONS INVESTIGATOR AWARD

1854 | BEDSIDE

Influence of childhood socioeconomic disadvantage in the incidence of cardiovascular disease in adults in Chile

C. Nazzal1, F. Frenz1, F. Cerecera1, G. Cavada1, J. Kaufmann2.

Background: The theory posits that socioeconomic disadvantage in childhood is associated with development of adult cardiovascular disease (CVD) through different mediating pathways, including health behaviors associated with risk factors and adult socioeconomic position (SEP). The aim of the study is to determine the effect of low socioeconomic position (low PSE) in childhood on the incidence of CVD in a Chilean cohort, before and after adjustment for risk factors and other covariates.

Methods: The longitudinal analysis of a representative sample of Chilean adult population 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 index), 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 estimating equations (GEE). Logistic regression 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. 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. The 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)

1855 | BEDSIDE

Antihypertensive treatment based on risk of cardiovascular disease or levels of risk factors? Findings from the Irish Longitudinal Study on Ageing (TILDA)

C.M. Murphy1, E. Shelley2, R. Clarke3, K. Bennett4, T. Fahey5, R.A. Kenny1.

Background: Guidelines on prevention in clinical practice advise treatment on the basis of estimated risk of cardiovascular disease (CVD). We examine the relationship between antihypertensive treatment and blood pressure classification, cumulative risk factor status and absolute cardiovascular disease risk based on Systematic COronary Risk Evaluation (SCORE).

Design and methods: This analysis uses data from the first wave (2009–2011) of TILDA for those aged 50–64 without reported CVD or diabetes (n=3077). Self-reported risk factors include smoking and physical activity. Objective measures include systolic blood pressure (SBP) (+10 mmHg to adjust for antihypertensive medication), low-density lipoprotein cholesterol (+1 mmol/L to adjust for statin therapy), obesity (body mass index >30). Logistic regression was used to identify antihypertensive users and establish blood pressure class, cumulative risk factor status and SCORE risk category.

Results: Over a third of this cohort had a SBP >140 mmHg (36.0%, 95% CI 34.3%-37.7%), 65.9% (95% CI 64.2%-67.6%) had an LDL-Cholesterol >3 mmol/L, 19.1% (95% CI 18.0%-19.9%) were overweight and 43.6% (95% CI 29.6%-32.9%) were obese and 25.9% (95% CI 24.2%-27.5%) reported low levels of physical activity. Almost a quarter had 3 or more CVD risk factors. One fifth were on antihypertensive treatment (n=617). Logistic regression analysis revealed an increasing positive trend in antihypertensive treatment by blood pressure grade, cumulative risk factor status and SCORE risk category. However, the adjusted odds ratio for treatment in the SCORE high risk (<5%) group is lower than in the other two groups.

Conclusions: Despite guidelines which recommend the use of models to estimate total CVD risk in order to adjust antihypertensive therapy, these findings suggest that antihypertensive treatment in this cohort is more focused on single risk factors as opposed to absolute risk. This calls for a policy response to support public health guidelines in practice.

Acknowledgement/Funding: HRB Interdisciplinary Capacity Enhancement (ICE) grant 2012/07, Department of Health, Irish Life PLC, Atlantic Philanthropies

1856 | SHOTLIGHT

Can ambulance nurses adequately risk stratify patients with chest pain? A comparison between prehospital (ambulance) and hospital (ER) chest pain triage, using the HEART score


Background: A Delphi methodology was used. Twenty-nine patients with CHD aged 50–64 (19.5% females) and 29 parents of children with CHD aged 15 to 24 years, and 16 healthcare providers who had involved the management of adolescents and adults with CHD completed the two-round Delphi study between February–June 2014. Sixty-four issues based on eight dimensions of health (23), family (3), individual (5), interpersonal interaction (6), employment (1), economics (1), spirituality (2) and policy (18) were identified following our previously qualitative findings and a review of the literature. Central tendency and level of dispersion were computed to establish consensus.

Methods: Consensus of health care needs was reached on 25 issues, including health (8), family (2), individual (5), interpersonal interaction (2), and policy (8), which were classified as the importance and moderate to high agreement for all of the three groups. Opinions between three groups differed significantly on 12 issues related to health (9), family (2), and policy (1). Of all issues “to encourage self-managing of health condition” and “to cultivate positive attitude toward illness” were very important and the three groups had a strong agreement in this matter.

Conclusions and implications: The results of this study will be used as the basis for establishing the validity and reliability of the transitional health passport for adolescents into adulthood. 

Acknowledgement/Funding: NSC 101-2314-B-030-006-MY2
tual emergency room (ER) by physicians. The HEART score provides a validated, quick and simple risk stratification tool. However, most chest pain patients are assessed by ambulance nurses pre-hospital. Earlier ambulance triage gives the opportunity to bring the “right patient to the right place”.

**Purpose:** Our study investigates the comparison between pre-hospital chest pain triage by ambulance nurses with hospital physicians triage at the ER using the modified-HEART score, where “T” is a single high sensitive Troponin T (hs-cTnT) measurement.

**Methods:** Patients with acute onset chest pain (STEMI excluded) who called the EMS, from June 2013 to December 2014 were assessed at FMC by ambulance nurses. The hs-cTnT blood sample being taken and the HEART score assessed, as to establish an ambulance modified-HEART score. All patients were transported to the ER and managed by emergency physicians according to standard care without knowledge of the pre-hospital hs-cTnT result. The hospital modified-HEART score was established using medical records. Both the ambulance- and the hospital modified-HEART score agreement were assessed using Cohen’s Kappa statistics.

**Results:** A total of 548 patients were included. Results are depicted in Table 1. Overall, there was a moderate agreement between the two disciplines (Kappa value of 0.490). 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**

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</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**

F. Jansen, T. Stumpf, G. Nickenig, N. Werner. University Hospital of Bonn, Medical Clinic II, Bonn, Germany

**Background:** We explored the effect of Endothelial microparticles on neointima formation in a model of acute vascular injury in vivo and on VSMC proliferation and migration in vitro.

**Methods and results:** Mice treated with EMP showed a significantly reduced neointima formation. Furthermore, EMPs treated with EMP displayed significantly reduced proliferation and migration capacities in vitro, both at cholesterollowered 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 neointimaformation 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 the data for miR-126 for the regulation of neointimaformation reduction.

**Conclusions:** EMP reduce neointima formation and decrease proliferation and migration of vascular smooth muscle cells in a microRNA-126-LRP6-dependent mechanism.

**1953 | BENCH**

**MiR-223-3p post-transcriptionally regulates the expression of F3, the human tissue factor gene, and TF expression in acute coronary syndrome**

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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 F3, the human TF gene, is complex and needs to be explored further.

**Purpose:** To investigate if microRNAs (miRNAs) post-transcriptional regulate the TF expression as its 3’UTR contains predicted binding-sites for several miRNAs.

**Methods:** TaqMan Array Human MicroRNA A+B Cards were used to screen for differentially expressed miRNAs in a cell based system where TF can be down-regulated. The Dual-Luciferase Reporter (DLR) Assay system (Promega) was used to investigate if miR-223–3p and the 3’UTR of F3 functionally interact. 105 patients with ACS defined as NSTEMI or STEMI included in the REBUS (Relevance of Biomarkers for future risk of thromboembolic events in Un Selected post-myocardial infarction patients) study were included in a biomarker sub-study. Using flow cytometry TF surface expression was analysed on platelets and CD62P+ platelet-derived microparticles (PMPs) at inclusion and after 1 year (n=99). 32 patients from the REBUS sub-study were included for miRNA analysis at inclusion and after 1 year (n=26).

**Results:** 211 differentially expressed miRNAs were identified in the screen during TF down-regulation. One of these, miR-223–3p, has a predicted binding site in the 3’UTR of F3. In U937–1 cells undergoing differentiation with vitamin D3 miR-223–3p increased over time while F3 expression decreased. Transfecting a synthetic miR-223–3p mimic into the high level TF expressing human breast cancer cell-line MDA-MB-231 led to a significant reduction in TF expression. The Dual Luciferase assay confirmed binding of miR-223–3p directly to the 3’UTR of F3. In ACS patients we found that miR-223–3p expression was significantly reduced in patients from the acute event (p<0.001) and this reduction the levels of circulating TF are elevated months after the first cardiac event, proving that the molecular regulation of F3, the human TF gene, is complex and needs to be explored further.

**Conclusion:** MiR-223-3p regulates the expression of TF post-transcriptionally via binding to the 3’UTR of the TF mRNA. One year post ACS miR-223–3p expression is reduced in platelets and MPs is increased. MiR-223–3p regulation of TF expression constitutes a novel molecular mechanism in the control of the coagulation process.

**1954 | BENCH**

**Differential effects of microparticles from patients with coronary artery disease as compared to healthy subjects on endothelial cell functions: critical role of miR-222**


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**Background:** Shed microvesicles (SMV) within the circulation might originate from various cell types. We hypothesized that SMV release from leukocytes is enhanced in coronary artery disease (CAD), an inflammatory condition, and might affect the cellular responses of adherent endothelial cells (e.g. microRNA content) of SMV and their effect on the vascular endothelium.

**Methods:** SMVs were isolated from plasma of healthy subjects or patients with CAD. Flow cytometry was used to quantify platelet, endothelial cell and leukocyte-derived SMVs. The capacity of SMV to support human aortic endothelial cell survival, inflammatory activation and re-endothelialisation was assessed following ex vivo exposure. Content of pro-apoptotic, pro-angiogenic and pro-inflammatory miR species was quantified by RT-qPCR. SMVs of H or CAD donors were transfected by electroporation with mirco or PowerInhibitor of miR-222 or with scrambled control oligonucleotide (con). Prior to washing and exposure to endothelial cells.

**Results:** While SMV of healthy donors (H) supported in vitro re-endothelialisation (27.7±11.3% increase vs. PBS), SMVs from CAD patients had lost this capacity (0.8%±8.5% decrease vs. PBS, p<0.05). Leukocyte-derived and endothelial cell-derived SMVs, but not overall SMVs or platelet-derived SMVs were increased in patients with CAD. The number of leukocyte-derived SMVs...
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 AST1R.

**Conclusions:** Our data demonstrate a divergent role of miR-155 in regulation of the different forms of vascular growth via the suppression of different target genes. Its expression in both endothelial and bone marrow derived cells is essential for arteriogenesis in response to hindlimb ischemia in mice.

**1957 | BENCH**

**EMMPRIN is a major pro-angiogenic component of cardiac progenitor cell derived exosomes**

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Background: Exosomes are small nano-sized vesicles carrying cell-specific contents including miRNAs, miRNAs and proteins. Exosomes secreted by human cardiomyocyte progenitor cells (CMPCs) are able to induce endothelial cell migration and sprout formation in vitro, and can therefore be considered an important mediator in the angiogenic process during tissue repair. Several pro-angiogenic factors are present in CMPC-derived exosomes, of which one is the extracellular matrix metalloproteinase inducer (EMMPRIN). EMMPRIN plays an important role in angiogenesis by inducing the production of for example MMPs and VEGF, thereby promoting extracellular matrix modulation and activation of endothelial cells. Here, we investigated the role of exosome-derived EMMPRIN in angiogenesis.

**Purpose:** To elucidate the role of EMMPRIN in the pro-angiogenic effect of exosomes from CMPCs.

Methods: Exosomes were isolated from CMPC-conditioned medium by differential centrifugation. The presence of EMMPRIN was assessed by nanospray, sucrose-gradient separation and Western Blotting. The angiogenic potential of CMPC exosomes was assessed by accepted assays for endothelial cell migration in vitro and in vivo. The functional involvement of EMMPRIN was assessed by using an EMMPRIN neutralizing antibody and by knockdown of EMMPRIN in the donor CMPCs and their secreted exosomes.

Results: CMPCs release exosomes that are characterized by traditional sizes (30–100nm) and marker expressions (CD9, CD63, CD81). Moreover, they are enriched for EMMPRIN and able to induce endothelial cell migration, tubule formation and sprouting and are therefore pro-angiogenic. Incubation of endothelial cells with CMPC exosomes resulted in an abrogation 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 vitro. In vivo matrigel plug assays, migration of endothelial cells with EMMPRIN knockdown exosomes was markedly reduced compared to migration with normal CMPC exosomes.

**Conclusion:** EMMPRIN is enriched in CMPC derived exosomes, and is a major component of their pro-angiogenic activity. Reduction of EMMPRIN levels on exosomes inhibits their pro-angiogenic effects in vitro and in vivo angiogenesis assays.

**1955 | BENCH**

**MicroRNA of exosomes affects vascular function and neovascularization**

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Background: Adaptive neovascularization after arterial occlusion is an important compensatory mechanism in cardiovascular disease and includes both the remodeling of pre-existing vessels to collateral arteries (arteriogenesis) as well as angiogenic capillary growth. We now aimed to identify regulatory microRNAs involved in the modulation of neovascularization after femoral artery occlusion in mice.

**Methods and results:** Using miRNA-transcriptome analysis, we identified miR-155 as a downregulated miRNA during hindlimb ischemia. Correspondingly, inhibition of miR-155 in umbilical vein endothelial cells (HUVECs) had a stimulatory effect on proliferation and angiogenic tube formation via de-repression of its direct target gene 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) and increased number of infiltrating circulating cells as well as an attenuated expression of the pro-angiogenic cytokine TNF-α/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 (BMDM) 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 wide type mice transplanted with miR-155−/− bone marrow cells displayed a comparable phenotype to global miR-155 knockout mice.
monocytes were primed with 1 μg/ml LPS for 4h and subsequently stimulated with either 5 mM ATP or 20 μM N- Glicerol. Two established inflammasome activators, MP release was quantified by flow cytometry using TruCount. Stimulation of HCAEC and monocytes with both N- Glicerol 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: 1468±2477 MMP/μl) and N- Glicerol for 8h (Mean: 37107±6727 MMP/μl). Highest EMP-release by HCAEC was detected after stimulation with ATP for 8h (Mean: 791±1074 EMP/μl) and N- Glicerol for 48h (Mean: 4658±6594 EMP/μl). Inflammasome activation in THP-1 cells using ATP and N- Glicerol was confirmed by the release of IL-1β into the cell supernatant (ATP: Mean: 432±2 pg/ml; N- Glicerol: Mean: 80±2.6 pg/ml). While there was much less release of IL-1β detectable in supernatant of HCAEC treated with 100 ng/ml TNF-α for 24h, subsequent treatment with 1 μg/ml LPS for 4h followed by treatment with 20 μM N- Glicerol (Mean: 2.16±0.32 pg/ml). Inflammasome activation in HCAEC treated for 24h with 100 ng/ml TNF-α and subsequently for 24h with 5 mM ATP could be shown by Caspase-1 Assay (Activity: 2.02 fold by control), while treatment of these cells with N- Glicerol, TNF-α or LPS alone did not lead to an activation of Caspase-1. Incubation of HCAEC for 2h with EMP derived from HCAEC treated with 100 ng/ml TNF-α for 24h, subsequent treatment with 1 μg/ml LPS for 4h followed by incubation with 20 μM N- Glicerol for 48h lead to significant cell death shown by Viability Assay (Mean: 72% ± 6.86% Cell Viability). Furthermore, treatment of HCAEC with EMP derived from HCAEC treated with 1 μg/ml LPS for 4h and subsequent treatment with 20 μM N- Glicerol for 48h lead to reduced cell migration and proliferation shown by Scratch Assay (73% cell free area after 24h).

Conclusions: We show for the first time that N- Glicerol and ATP two established inflammasome activators, lead to inflammasome activation and release of microRNAs by vascular cells. Furthermore, we could demonstrate that these microRNAs, when given to other vascular cells, cause cell death accompanied with reduced cell migration and proliferation.

1961 | BENCH

Mir33 antagonism increase cholesterol efflux and atheroma regression by increasing caveolin1 expression in hypercholesterolemia rabbits

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Introduction: Mir-33 embedded within introns of the Srebp gene, inhibits the expression of ABCA1, thereby attenuating cellular cholesterol efflux to nascent HDL. Antagonism of mir-33 promotes reverse cholesterol efflux (RCE) and regression of atherosclerosis in both mice and non-human primates. Caveolin-1 also regulates cellular cholesterol homeostasis and promotes RCT. However, the relation between mir-33 and caveolin-1 remain unknown.

Purpose: We aimed to clarify the interaction between mir-33 and caveolin-1 on HDL-mediated cholesterol efflux in J774 macrophage and hypercholesterolemia rabbits.

Methods: Rabbits (N=5 per group) were fed with 2% hypercholesterolemic diet. At the end of 5 weeks, rabbits were injected subcutaneously with 5 mg/kg antisense miR-33 or mismatch anti-miR-33 or saline twice weekly for 2 weeks and then weekly for another 3 weeks, than sacrificed at end of 8 weeks. In vitro study, J774 cells were loaded with 100 μg/ml cholesterol in DMEM, incubating the cells for 24–48 h at 37°C, than transfected with 60nM miR33 antagonon.

Results: Hypercholesterolemia rabbits treated with anti-miR-33 showed increased 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 was increased after caveolin-1 siRNA treatment.

Conclusion: These findings demonstrate that caveolin-1 play an important role in mir33 regulated lipid metabolism, and may identify a new target for enhance cholesterol efflux and atherosclerosis treatment.

1960 | BENCH

Inflammasome-induced intercellular signalling mechanisms via microparticles

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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

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 there was no effect on VCAM-1 expression. Reduced ICAM-1 expression after EMP treatment resulted in diminished monocyte adhesion in vitro. In vivo, systemic treatment of ApoE−/− mice with EMP significantly reduced murine endothelial ICAM-1 expression and infiltration of macrophages into atherosclerotic plaques. In order to explore the underlying mechanisms, Taqman microRNA-array was performed and microRNA (miR)-222 was identified as the strongest regulated miR between EMP and endothelial cells. Follow ing experiments demonstrated that miR-222 was transported into recipient endothelial cells by EMP and functionally regulated expression of its target protein ICAM-1. Interestingly, after simulating diabetic conditions, EMP derived from glucose-treated ECs contained significantly lower amounts of miR-222 and showed reduced anti-inflammatory capacity in vitro and in vivo.

Conclusions: Endothelial microparticles promote anti-inflammatory effects in vitro and in vivo by reducing endothelial ICAM-1 expression via the transfer of functional microRNA-222 into recipient cells. In pathological hyperglycaemic conditions, EMP-mediated miR-222-dependent anti-inflammatory effects are reduced.

1959 | BENCH

Endothelial microparticles reduce ICAM-1 expression in a microRNA-222-dependent mechanism

F. Jansen, K. Baumann, G. Nickenig, N. Werner. University Hospital of Bonn, Medical Clinic II, Bonn, Germany

Objective: Endothelial microparticles (EMP) are released from activated or apoptotic cells and can be taken up by adjacent endothelial cells, but their effect on vascular inflammation after engulfment is largely unknown. We sought to determine the role of EMP in endothelial cell inflammation.

Methods and results: In vitro, EMP treatment significantly reduced TNF-α-induced endothelial ICAM-1 expression on mRNA and protein level, whereas there was no effect on VCAM-1 expression. Reduced ICAM-1 expression after EMP treatment resulted in diminished monocyte adhesion in vitro. In vivo, systemic treatment of ApoE−/− mice with EMP significantly reduced murine endothelial ICAM-1 expression and infiltration of macrophages into atherosclerotic plaques. In order to explore the underlying mechanisms, Taqman microRNA-array was performed and microRNA (miR)-222 was identified as the strongest regulated miR between EMP and endothelial cells. Following experiments demonstrated that miR-222 was transported into recipient endothelial cells by EMP and functionally regulated expression of its target protein ICAM-1. Interestingly, after simulating diabetic conditions, EMP derived from glucose-treated ECs contained significantly lower amounts of miR-222 and showed reduced anti-inflammatory capacity in vitro and in vivo.

Conclusions: These results suggest that exosomal miRNA especially angiogenic 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)
IMPACT OF THE ENVIRONMENT ON ANTICOAGULATION IN NON-VALVULAR ATRIAL FIBRILLATION

1970 | BEDSIDE

Predicting Intracranial bleeding in patients with atrial fibrillation using several bleeding risk scores

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Several clinical risk factors have been incorporated into clinical risk stratification schemes to estimate the risk of bleeding in patients with atrial fibrillation (AF). However, intracranial hemorrhage (ICH) is a life-threatening complication of anti-coagulation and clinicians need to weigh the risk of ICH far more than the risk of all major hemorrhages. The purpose of this study was to evaluate the predictive value of current bleeding risk stratification schemas for ICH and gastrointestinal (GI) bleeding in a cohort of unselected patients with AF.

Methods: Patients with AF were identified in a database and followed up between 2000–2010 for mortality, stroke and bleeding events. We evaluated the predictive value of several risk stratification schemas in this cohort whether patients were treated with anticoagulation or not. Among 8962 patients with AF, 789 severe bleeding events, 126 ICH and 141 GI bleeding events were recorded during a follow-up of 8771052 days. We compared the predictive value of the HAS-BLED score with 2 other bleeding risk schemas (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) 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 GI bleeding with 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 variables.

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.

1971 | BEDSIDE

Major bleeding, hospitalisation rates and healthcare costs among non-valvular atrial fibrillation patients naive 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.

Methods: Adult patients diagnosed with AF (ICD-9-CM 427.31 & 427.32) and newly treated with novel oral anticoagulants (NOAC) in the United States between January 1, 2010 and December 31, 2010 were included in this analysis. NOAC bleeding was defined as any bleeding event that occurred in the NOAC treatment period. The primary outcome was overall bleeding event incidence, including major bleeding (bleeding requiring hospitalisation or resulting in death), as well as major bleeding and major non-major bleeding. The cumulative incidences of stroke, bleeding or death were 0.8% and 1.7% at 30 days, in dabigatran and warfarin groups respectively with a hazard ratio of 2.5 (95% CI 0.5–12.5; p = 0.257). 

Conclusion: Anticoagulation treatment with dabigatran allows shorter time to cardioversion than warfarin, and appears to be an effective and safe alternative treatment strategy.

Acknowledgement/Funding: The study was supported by an unrestricted research grant from Boehringer-Ingelheim.

1972 | BEDSIDE

Time to cardioversion and risk 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

Purpose: Evaluate the time to cardioversion and risk of subsequent cardiovascular complications in patients treated with dabigatran or warfarin.

Methods and results: 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 in dabigatran and warfarin groups respectively.

Conclusion: Major bleeding, hospitalisation rates and healthcare costs among non-valvular atrial fibrillation patients naive to oral anticoagulation and newly treated with novel oral anticoagulants

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Background: Minimizing the risk of major bleeding is an important objective in using antithrombotic therapy, but less is known about non-major (NM) bleeding.

Purpose: We describe the cumulative incidence and location of NM bleeding, as well as how it was managed, in ARISTOTLE.

Methods: In ARISTOTLE, 18,201 patients with AF were randomized to apixaban vs. warfarin; median follow-up was 22 months. 18,140 patients who received at least 1 dose of study drug were included in this analysis. NM bleeding was defined according to ISTH criteria and included the first bleeding event of both clinically relevant non-major and minor bleeding, not preceded by a major bleeding event.

Results: NM bleeding was 3 times more common than major bleeding (12% [n=2204] vs 3.9% [n=692]). Like major bleeding, NM bleeding was less frequent with apixaban (10.1% [918/9088]) than warfarin (14.2% [n=1286/9052]) (HR [apixaban vs. warfarin] 0.68 [95% CI 0.62–0.74] (Figure). The most frequent sites of NM bleeding were: hematuria (16.4%), epistaxis (14.8%), hemotoma (11.5%), and bruising/ecchymosis (10.1%). Clinically relevant NM bleeding was associated with an increased risk of overall death (HR 1.70 [1.32–2.18]). Medical
or surgical consultation was more common among patients with NM bleeding. Risk of GI related CRNM bleeding compared to apixaban for NVAF patients was estimated.

**Results:** We studied 8,785 NAVF 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).

**Hazard ratio (95% confidence Interval)**

<table>
<thead>
<tr>
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<th>Daiabatan vs. apixaban</th>
<th>Rivaroxaban vs. apixaban</th>
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<tbody>
<tr>
<td>Major bleeding</td>
<td>0.99 (0.88, 1.10)</td>
<td>1.36 (1.23, 1.52)</td>
</tr>
<tr>
<td>Intracranial</td>
<td>1.17 (0.83, 1.63)</td>
<td>1.47 (1.07, 2.01)</td>
</tr>
<tr>
<td>GI</td>
<td>1.06 (0.85, 1.30)</td>
<td>1.54 (1.26, 1.89)</td>
</tr>
<tr>
<td>Other</td>
<td>0.95 (0.82, 1.09)</td>
<td>1.35 (1.19, 1.54)</td>
</tr>
<tr>
<td>CRNM</td>
<td>1.07 (0.98, 1.15)</td>
<td>1.43 (1.34, 1.54)</td>
</tr>
<tr>
<td>GI</td>
<td>1.24 (1.08, 1.42)</td>
<td>1.49 (1.31, 1.69)</td>
</tr>
<tr>
<td>Other</td>
<td>1.00 (0.91, 1.10)</td>
<td>1.45 (1.32, 1.58)</td>
</tr>
<tr>
<td>Any bleeding</td>
<td>1.06 (0.99, 1.13)</td>
<td>1.41 (1.32, 1.50)</td>
</tr>
</tbody>
</table>

Adjusted for age, sex, one-year baseline comorbidities and medication use.

**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 NAVF patients for the first 6-month after treatment initiation.

**Acknowledgement/Funding:** Research grant was received by Dr. Tepper from Pfizer, Inc

### 1976 | BEDSIDE

**Association between atrial fibrillation and risk of seizure disorder:**

**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 patients with AF.

**Background:** Renal impairment confers an increased risk of stroke, death, and bleeding in anticoagulated patients with AF. The CHADS2 score is a useful scheme for risk stratification of thromboembolic events in patients with AF.

**Methods:** The ARISTOTLE trial was supported by Bristol-Myers Squibb and Pfizer

**Conclusion:** 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.
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 bleeding risk. Great care is required to optimize anticoagulation. Just as NOACs may be more convenient to use than warfarin, so too must health systems adapt their systems of care, so that NOACs can be provided in a telemedicine-based coagulation service substantially to improve outcome and should be evaluated for a translation to new drugs for oral anticoagulation.

Acknowledgement/Funding: Ministries of Health and Economics, Rheineland-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

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Introduction: Patients with atrial fibrillation have a five-fold increased risk of stroke, which can be effectively reduced with oral anticoagulant therapy. How- ever, elderly patients with atrial fibrillation and a 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 registers 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 person-ally acquired data.

Methods: Our study includes elderly patients from 2 medical institutions: one 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 medication reports. The Clopper-Pearson method was used for the 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 tor-sion of 94 falls. In both cohorts of patients with and without falls, the average CHA2DS2VAsc score was 5 and HASBLED score was 3. Incidence of bleeding in the cohort with falls was significantly higher by 86.6% (95% confidence interval [CI] = 78.7% to 91.1%, p<0.0001), than in the cohort without falls. Incidence of minor bleeding (WHO grade 1) was also significantly higher in the cohort with falls (16.9% [CI] = 1.20% to 38.5%, p=0.0419), than in the cohort without falls. However, the incidence of severe bleeding (WHO grade 4) was significantly higher by 17.3% [CI] = 6.17% to 37.8%, p=0.0023) in the cohort without falls, than in the cohort with falls. Incidence of severe bleeding (WHO grade 4) after a fall was 1.06% [CI] = 0.03% to 5.79%.

Conclusions: Our study showed that the incidence of minor bleeding in patients on warfarin and documented falls is higher, but surprisingly incidence of severe bleeding is lower, than in patients without falls. This suggests that spontaneous bleeding is more dangerous than bleeding after a fall, indicating that HASBLED
should be preferred over “the risk of falling”. Furthermore, the incidence of bleeding after a fall is quite low and according to our study we can recommend warfarin to patients with CHA2DS2VASc ≥ 3, despite the high risk of falls.

**WHAT IS NEW IN AORTIC VALVE DISEASE**

**1980 | 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 primary analysis focuses on patients with MR: grade II. Patients with any other mitral valve pathology (e.g. mitral stenosis, prosthetic mitral valve) were excluded. MR was graded on a 0–3 scale (0 = none, 1 = mild, 2 = moderate, 3 = severe). Severity of MR, TR and PA-pressure were defined as primary endpoints and assessed at baseline and consecutively at 1, 3 and 6 months after TAVI. Secondary endpoints included in-hospital mortality as well as TAVI-complications according to VARC-criteria.

Results: 106 (20.5%) patients with MR: II (age 80.9±6.6y, female 66 (62.3%), Euroscore 32.9±18.1) were included in this analysis. In this subgroup, mean mitral valve gradient was decreased during TAVI from 40.7±16.8mmHg to 10.2±7.4mmHg (p<0.001). The reduction in left ventricular (LV) afterload was associated with a significant decrease of MR from 2.21±0.34 at baseline to 1.79±0.65 at hospital discharge (p<0.001) and remained significantly below baseline after 1 (n=52; 1.61±0.58), 3 (n=37; 1.75±0.59) and 6 months (n=35; 1.61±0.58) month. This was associated with a significant reduction of PA-pressure from 47.6±13.8mmHg to 37.9±11.8mmHg (p<0.05) and a decrease of TR-severity from 1.88±0.79 to 1.53±0.8 (p<0.05) after 1 month. Post-operative NYHA-class (3±0.5 vs. 2.5±0.55; p<0.001) as well as 6-minute walking distance (94.1±94.1m vs. 162.4±114.4m at 1 month vs 249.0±132.94m at 3 month; p<0.001) improved, demonstrating a functional benefit in patients with MR: II at 30 days after TAVI. In-hospital mortality was 3.7% (n=4). At 1, 3, 6 and 12 month after TAVI, mortality was 6.6% (n=7), 15.0% (n=16), 17.1% (n=18) and 22.6% (n=24), respectively.

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.

**1983 | BEDSIDE**

Impact of diabetes mellitus on short- and midterm mortality after transcatheter aortic valve implantation

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Background: Diabetes mellitus (DM) is an established risk factor for cardiovascular disease. The role of DM as a predictor of complications and outcomes after transcatheter aortic valve implantation (TAVI) remains to be further clarified. Therefore, it was the aim of the study to evaluate the impact of DM on short- and midterm mortality after TAVI.

Methods and results: Consecutive TAVI patients treated between 01/2006 and 10/2013 were prospectively stratified according to the presence of DM and DM treatment. All-cause mortality at 30 days and one-year mortality were defined the primary end points and periprocedural stroke, bleeding and access-site-related complications as secondary end points. All end point definitions were subject to the Valve Academic Research Consortium-II (VARC-II) definitions.

Overall, 1450 patients were included: 614 patients (42.3%) had DM at admission (dietary treatment (DM) n=142 (23.1%); oral medication (oDM) n=220 (35.8%); insulin treatment (iDM) n=248 (34.9%)). The day mortality did not differ between patients with DM compared with patients without DM (noDM: 8.0%; DM: 7.5%; p=ns) and according to diabetes treatment status (noDM: 8.0%; DM: 8.0%; oDM: 5.1%; iDM: 4.9%; p=ns). One-year mortality after TAVI was not significantly different in patients with DM compared with patients without DM (noDM: 24.0%; DM: 26.3%; p=ns). Diabetes treatment had no significant influence on one-year survival after TAVI (noDM: 24.0%; DM: 28.8%; oDM: 23.7%; iDM: 27.3%; p=ns). Periprocedural stroke (major/minor/TIA), periprocedural bleeding (life-threaten- ing/major/minor), access-site-related complications (major/minor) were not significantly different between diabetics and non-diabetics. A higher rate of VARC-2 acute kidney injury was observed in the subgroup of diabetics.

Conclusion: The presence of DM did not significantly affect periprocedural rates
of stroke, bleeding, access-site related complications as defined by VARC-II cri-
teria. 30-day and one-year mortality after TAVI were unaffected by the presence of DM at baseline, questioning its use in contemporary risk prediction models.

1984 | BEDSIDE

Determinants and prognostic value of B-type natriuretic peptide in patients with aortic valve stenosis


Background: Usefulness and prognostic value of natriuretic peptides in aortic stenosis are still under discussion.

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 (< 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-

cary artery disease (p = 0.03), rhythm (p = 0.007) and diastolic function (p < 0.0001). Consequently, in asymptomatic patients with moderate/severe AS with normal left ventricular ejection fraction and in sinus rhythm, NT-proBNP was associated to AS-related events in univariate (p = 0.009) but not after adjustment for AS severity (p = 0.12). Finally, repeated NT-proBNP measurements at 1 year did not improve its predictive value (p = 0.43).

Conclusion: The present study clearly shows the limits of NT-proBNP in AS and raises caution regarding its use, at least as a single factor, in the decision-making process of asymptomatic patients with AS.

1985 | BEDSIDE

Pre-existing and new-onset atrial fibrillation: a meta-analysis of mortality outcomes and cerebrovascular events in 13,795 patients undergoing transcatheter aortic valve implantation


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-
tients with baseline AF, 30-day all-cause mortality was similar to patients in sin-
us rhythm. Conversely, long-term all-cause mortality was significantly greater in AF patients than in patients with baseline sinus rhythm (HR: 1.66, 95% [CI]: 1.43 to 1.92, p < 0.0001). Surprisingly, baseline AF was not predictor of CVE at long-term follow-up (HR: 1.68, 95% [CI]: 0.86 to 3.30, p = 0.13). NOAF patients showed a similar short- and long-term all-cause mortality, when compared to patients in sin-
us rhythm, whereas experienced significantly higher incidence of CVE at short-
term follow-up (HR: 2.54, 95% [CI]: 1.51 to 4.25, p < 0.001). Only a trend towards a higher incidence of CVE was observed at long-term follow-up (HR: 1.44; 95% [CI]: 0.50 to 4.10, p = 0.497).

Conclusions: Pre-existing AF, but not NOAF, is predictor of all-cause mortality in patients undergoing TAVI. Moreover, NOAF is related to the occurrence of CVE at short-term follow-up. Similar to SAVR, the optimal management and risk strat-
ification of these patients need to be further investigated in ad-hoc trials.

1986 | BEDSIDE

Predictors of mortality in patients with aortic stenosis: the role of myocardial fibrosis

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Purpose: Myocardial tissue characterization with cardiovascular magnetic reso-
nance (CMR) late gadolinium enhancement (LGE) is associated with worse short term prognosis in patients with aortic stenosis (AS). We investigated the long term effect of myocardial fibrosis in AS patient survival.

Methods: Consecutive patients with moderate or severe AS underwent CMR between 2003 and 2008. They were characterized by blinded observers into 3 groups based on the CMR LGE findings: those with midwall fibrosis, those with infarction fibrosis and those with no fibrosis. Each patient was followed for 5 years.

The end-point was all-cause mortality.

Results: Overall 143 patients (68±14 years; 97 male) were followed prospec-
tively. 81 patients had significant coronary disease and 80 underwent aortic valve replacement during this time. 44 died during the follow up period: 21/54 (39%) in the midwall fibrosis group, 16/40 (40%) in the infarction group and 7/49 (14%) in the no fibrosis group. Patients with either midwall fibrosis [HR 2.6 (95% CI 1.3–5.2, p = 0.005)] or infarction [HR 2.7 (95% CI 1.3–5.6, p = 0.004)] showed increased all-
cause mortality when compared to patients with no fibrosis (log 1, no LGE/fibrosis in black, midwall fibrosis in red, infarction in green). On multivariable analysis, only age, ejection fraction (EF), wall thickness and midwall fibrosis were significantly associated with prognosis.

Conclusion: Patients with moderate or severe AS with midwall fibrosis on CMR have a worse 5 year survival when compared to patients with no fibrosis. Mid-
wall fibrosis remained an independent adverse predictor of survival at 5 years providing incremental predictive value to EF.

Acknowledgement/Funding: NIHR Cardiovascular Biomedical Research Unit of Royal Brompton & Harefield NHS Foundation Trust and Imperial College London

1987 | BEDSIDE

Overestimation of bicuspid aortic stenosis severity by echocardiography

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Objectives: Current guidelines for classifying aortic stenosis (AS) severity are established without differentiating between bicuspid and tricuspid AS. We inves-
tigated the relationship between mean pressure gradient (MPG) and aortic valve area (AVA) between bicuspid and tricuspid AS, and assessed the impact of stroke volume (SV) estimation on classification.

Methods: Patients with mild to severe AS (100 tricuspid and 48 bicuspid) under-
went comprehensive echocardiography and cardiovascular magnetic resonance imaging (MRI). The relationship between AVA and MPG was modeled using non-
linear regression, and thresholds were compared between tricuspid and bicuspid AS. We further compared the effects of Doppler- and MRI-derived stroke volume (SV) on severity classification of tricuspid and bicuspid AS.

Results: Thresholds for severe AS (AVA < 1.0 cm²) in tricuspid and bicuspid were similar with Doppler-derived SV (MPG of 26 versus 27 mmHg respectively), but there was >10 mmHg difference with CMR-derived SV (MPG of 30 versus 42 mmHg respectively; see Figure). Compared to MRI, echocardiography underesti-
mated the left ventricular outflow tract area (LVOTarea) and consequently the SV, to a greater extent in bicuspid compared to tricuspid AS (LVOTarea: −0.98±0.84 versus −0.20±0.73 cm³ respectively; SV: −6.8±12.5 versus −2.9±11.4 mL/m² re-
spectively). Indeed, planimetrized LVOTarea on MRI was larger in bicuspid com-
pared to tricuspid AS (4.82±1.6 versus 3.60±0.69 cm² P < 0.001).

Conclusion: Patients with moderate or severe AS with midwall fibrosis on CMR have a worse 5 year survival when compared to patients with no fibrosis. Mid-
wall fibrosis remained an independent adverse predictor of survival at 5 years providing incremental predictive value to EF.

Acknowledgement/Funding: NIHR Cardiovascular Biomedical Research Unit of Royal Brompton & Harefield NHS Foundation Trust and Imperial College London
Background: Transcutaneous aortic valve implantation (TAVI) is a standard procedure for high-risk patients. The peri-procedural myocardial infarction (MI) has been linked to worse prognosis. According to the VARC-2, MI is defined by a rise in cardiac troponin (cTn) and creatine kinase MB (CK-MB); however, many patients have elevated cTn levels without clinical evidence of MI.

Purpose: The aims of this study were to establish reference values of cTn levels, measured with a high-sensitivity assay, in TAVI patients and to assess its peri-procedural diagnostic and prognostic value.

Methods: High-sensitivity troponin I (hs-cTnI) and CK-MB levels were assessed prior to, and up to 3 days after transfostral (TF) or transapical (TA) TAVI in 505 patients. Patients were followed up for 12 months.

Results: In total, 47.9% of patients had elevated hs-cTnI concentrations at baseline. According to VARC-2 nearly all TA-AVI patients (99.5%) showed a MI based on hs-cTnI compared with 4.2% based on CK-MB. In TF-AVI patients, 81.1% had a type 1 MI. The TAVI cohort 99th percentile for hs-cTnI was 855.4 ng/L rise in CK-MB

Conclusion: Echocardiography overestimates aortic stenosis severity in patients with bicuspid aortic stenosis due to inaccuracies in the measurement of LVO/area and stroke volume consequently, the AYA.

Acknowledgement/Funding: British Heart Foundation

PREMATURE CARDIOVASCULAR AGING

2013 | BEDSIDE

Glycemic excursions trigger senescence-associated pathways and vascular ageing features in patients with type 2 diabetes

F. Paneni1, S. Costantini1, R. Battista1, G. Capretti1, S. Chiandotto1, M. Volpe3, F. Costentino1, K. Ibrahim.

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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: To test the present standard of care and 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 blood 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 (AUPIp). 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 mononocytes, and expressed as fold change (FC).

Results: Patients with and without GE did not differ for age (62±8 vs. 61±14 years, p=NS), gender (60% vs. 67% female, p=NS), BMI (27.3±3.9 vs. 29.5±5.6 kg/m², p=NS), diabetes duration (13±11 vs. 15±10 years, p=NS), CV risk factors and glucose-lowering medications. PP was significantly higher in GE than in non-GE patients (85±35 vs. 45±35 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<0.01). Subjects with glucose fluctuations also showed upregulation of miR-146a and DNA damage gene Ataxia Telangiectasia Mutated (ATM, FC=10.4, p<0.05). In GE patients, ATM and p53 were significantly induced (FC=7.6, p<0.05) and p21/WAF1/G1P1 (FC~5.2, p<0.05).

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.

2014 | BEDSIDE

Assisted reproductive technologies-induced premature vascular ageing persists and evolves into arterial hypertension in adolescents

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Background: Assisted reproductive technologies (ART) induce vascular dysfunction and premature vascular ageing in young apparently healthy children and mice. In adult ART mice, premature vascular ageing translates into arterial hypertension. Given the young age of the human ART population, the evolution and long-term consequences of ART induced vascular alterations are unknown.

Purpose: We speculated that vascular alterations persist in ART adolescents and young adults.

Methods: We, therefore, 5 years after the initial assessment, reassessed vascular function (flow mediated dilation, FMD, pulse wave velocity, PWV, and carotid

were treated with vitamin K antagonists (VKA), 94% of them received one platelet inhibitor in addition (20 patients ASS, 10 patients clopidogrel). In 69 patients anti-coagulation was directed with direct oral anticoagulants (DOAC), 24 of them received a single therapy with DOAC (34.8%), 43 of them received DOAC in combination with one platelet inhibitor (62.3%) and only two patients received a triple therapy. Overall 2 patients died within the first 30 days after TAVI. There were no differences in stroke and bleeding frequency between the VKA and DOAC group within the first 30 days after implantation. But, 3 months after TAVI, patients who were treated with DOAC showed less bleeding, thrombosis and mortality in comparison to VKA-patients. Furthermore, no differences were seen between DOAC single therapy or DOAC with one platelet inhibitor.

Summary: Until now, no universal standard for anticoagulation strategies for patients with atrial fibrillation undergoing TAVI exists. In this registry study patients who were DOAC had a lower risk for bleeding than patients treated with VKA. 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

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F. Paneni1, S. Costantini1, R. Battista1, G. Capretti1, S. Chiandotto1, M. Volpe3, F. Costentino1, 1 Karolinska Institute, Cardiology Unit, Stockholm, Sweden; 2 University Hospital Centre Vaudois (CHUV), Lausanne, Switzerland

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Results: Patients with and without GE did not differ for age (62±8 vs. 61±14 years, p=NS), gender (60% vs. 67% female, p=NS), BMI (27.3±3.9 vs. 29.5±5.6 kg/m², p=NS), diabetes duration (13±11 vs. 15±10 years, p=NS), CV risk factors and glucose-lowering medications. PP was significantly higher in GE than in non-GE patients (85±35 vs. 45±35 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<0.01). Subjects with glucose fluctuations also showed upregulation of miR-146a and DNA damage gene Ataxia Telangiectasia Mutated (ATM, FC=10.4, p<0.05). In GE patients, ATM and p53 were significantly induced (FC=7.6, p<0.05) and p21/WAF1/G1P1 (FC~5.2, p<0.05).

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.

2014 | BEDSIDE

Assisted reproductive technologies-induced premature vascular ageing persists and evolves into arterial hypertension in adolescents

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Background: Assisted reproductive technologies (ART) induce vascular dysfunction and premature vascular ageing in young apparently healthy children and mice. In adult ART mice, premature vascular ageing translates into arterial hypertension. Given the young age of the human ART population, the evolution and long-term consequences of ART induced vascular alterations are unknown.

Purpose: We speculated that vascular alterations persist in ART adolescents and young adults.

Methods: We, therefore, 5 years after the initial assessment, reassessed vascular function (flow mediated dilation, FMD, pulse wave velocity, PWV, and carotid...
intima media thickness. IMT in 54 ART young adults (16.4 ± y) and 43 controls (17.6 ± y) together with 24 h ambulatory blood pressure measurements.

**Results:** The main new findings were 2-fold: First, premature vascular ageing persisted in ART adolescents, as evidenced by decreased FMD (P < 0.01), and increased IVIM (P < 0.009) and IMT (P < 0.01), compared to controls. Endothelial dysfunction and arterial stiffness were comparable to the one observed 5 years ago, whereas IMT had increased in ART subjects (P < 0.01). Second and most importantly, 24 h blood pressure was markedly higher in ART than in control subjects (119.6 ± 13 vs. 115.7 ± 11 mmHg, P = 0.02, vs. ctrl).

**Conclusion:** These findings provide the first evidence that ART-induced premature vascular ageing persists in adolescents and translates into arterial hypertension. These data further underscore the potential of ART to increase cardiovascular risk in this exponentially growing population.

**2015 | BEDSIDE**

Premature cardiac senescence in patients with lamin A/C mutations: at least 5 years gap from electrical to mechanical dysfunction

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**Background:** The LMNA gene encodes nuclear proteins lamin A/C. Its mutations have been associated with a number of pathological conditions like progeria syndromes and heart disease. Cardiac manifestations include dilated cardiomyopathy (DCM) and arrhythmias.

**Purpose:** We proposed to evaluate if cardiac manifestations follow a determinate temporal order in people bearing LMNA gene mutations, thus reflecting different stages of the ageing of the heart.

**Methods:** We prospectively examined 17 patients (age 41±16; 59% males) with LMNA gene mutations for ≤2 y follow-up (FU). Complete cardiac evaluation including baseline ECG, trans-thoracic echocardiogram (TTE) and cardiac magnetic resonance (CMR) was performed at the time of genetic diagnosis. Regular FU with 2-yearly clinical evaluation, ECG, echocardiogram and 24-h Hotter monitoring was obtained.

**Results:** At presentation, only 4 patients were symptomatic (palpitations or dyspnoea on effort) and they were already known to suffer from DCM and atrial fibrillation (AF). In all the remaining patients (n=13), baseline TTE was at worst normal, with no moderate or severe left ventricle (LV) dilatation and LVEF 55±5%. In this group, however, CMR was normal or they were found in 8 patients (62%); the remaining 5 (38%) showed late gadolinium enhancement (LGE) with midwall involvement of apical basal segments of interventricular septum (IVS) and posterior-inferior LV wall. Baseline ECG showed 1st degree atrioventricular (AV) block and/or QRS duration > 120 ms in 4/5 patients with LGE vs. 1/8 patients without LGE (p < 0.01). During FU, the occurrence of events in patients with and without LGE was, respectively: 2nd degree AV block (2/5 vs. 0.8 at 2±0.5 y; p < 0.01); AF (2/5 vs. 1/8 at 3±1.5 y; p = n.s.); non-supported ventricular tachycardia (NSVT) (3/5 vs. 1/8 at 4±1 y; p = n.s.); ICD shocks in patients implanted in primary prevention (3/5 vs. 1/8 at 4±1 y; p = n.s.); and non-sustained ventricular tachycardia (NSVT) (2/5 vs. 0/8 at 2±0.5 y; p = 0.035). These findings provide the first evidence that ART-induced premature vascular ageing persists in adolescents and translates into arterial hypertension. These data further underscore the potential of ART to increase cardiovascular risk in this exponentially growing population.

**2023 | SPOTLIGHT**

Could occupational determinants impact on changes in blood pressure over a five-year follow-up? Results from the VISAT study

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**Background:** Among many factors involved in increased Blood Pressure (BP), occupational environment is often suspected, but its responsibility remains uncertain.

**Purpose:** To assess the impact of a large panel of occupational factors exposures on changes of BP over a 5-year follow-up period.

**Methods:** A sub-study from VISAT (ValeASsemeNt Sarde 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 used to determine which occupational factors interact 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.

**Receiver Operating Characteristic (ROC) curves were used to determine whether occupational factors could improve the prediction of BP changes.**

**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 against changes in BP. Among psychosocial factors, only taking on several tasks at the same time, occupational factors and taking into consideration opinion of workers tended to be associated with a protective effect (OR < 0.70, p < 0.10). Comparing areas under the ROC curves revealed that occupational factors significantly improved the prediction of SBP changes, compared to taking into account only the classic cardiovascular risk factors (p < 0.041).

**Conclusion:** Psychosocial factors appear as the major determinants of changes of BP over time with a dual effect, whereas biomechanical occupational factors play a minor role. Because occupational factors are potentially modifiable, a targeted preventive strategy could be implemented.

**2024 | BEDSIDE**

Hypertension prevalence, awareness, treatment and control in four states of India: the DISHA study baseline results

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**Background:** Hypertension prevention and control, a national public health priority as it affects more than 110 million adults in India. Awareness, treatment and control are reported to be very low in Indian setting.

**Purpose:** To describe prevalence, awareness, treatment and control of hypertension in four states in India using baseline risk factor survey of DISHA study.

**Methods:** DISHA study, a cluster randomized control trial of hypertension prevention and control in India. There were 12 villages randomly identified each from
five different districts of states of Puducherry, Gujarat, Madhya Pradesh, and Himachal Pradesh. Villages were randomly assigned into intervention and control, if distance between them was less than 10Km one was replaced with another randomly selected village. A detailed baseline survey of risk factors of CVD was completed. Approximately 300 participants were selected from each village.

**Results:** Baseline survey results of 24 intervention (n=6663) and 24 control (n=7150) clusters in four sites are presented here. Mean age of study population was 39.0 years (SD=14.8 years). Nearly half (46%) of studied population was males. Prevalence of hypertension was 23.1% (95% CI: 22.4–23.8). One in four of hypertensive individuals were aware about hypertension and one in seven of them achieved blood pressure control status (Figure 1)

**Conclusion:** Hypertension affects one in four individuals in India and awareness, treatment and control rates are very low in Indian settings. This calls for innovative methods for prevention and control. DISHA study tests effectiveness of task-shifting of front-line health workers for imparting lifestyle education for prevention and control of hypertension in both rural and urban settings in India.

**ANTICOAGULATION IN NON-VALVULAR ATRIAL FIBRILLATION**

2031 | BEDSIDE

**Rivaroxaban vs. warfarin with concomitant aspirin use in patients with atrial fibrillation: findings from the ROCKET AF trial**


**Abstract 2031 – Figure 1**

**Background:** The safety and efficacy of concomitant aspirin (ASA) use in patients with atrial fibrillation (AF) treated with rivaroxaban, compared with warfarin, for stroke and systemic embolism prevention are not known.

**Methods:** In the double-blind ROCKET AF study, 14,264 patients with non-valvular AF were randomized to rivaroxaban 20 mg (15 mg for CrCl<60 mL/min) once daily or dose-adjusted warfarin. Concomitant ASA use was left to investigator discretion and assessed at baseline. Outcomes including stroke and systemic embolism, myocardial infarction (MI), vascular death, and major and non-major clinically relevant (NMCR) bleeding were compared between groups. Multi-variable modeling was done to adjust for baseline risk factors.

**Results:** A total of 2025 (36.5%) patients had ASA use at baseline (mean dose 92 mg), 30.6% of whom had known coronary artery disease. Patients receiving concomitant ASA were more likely to have prior MI (22% vs. 14%, p < 0.001) and heart failure (68% vs. 59%, p < 0.001). Relative efficacy of rivaroxaban versus warfarin was similar with and without ASA use for stroke prevention/systemic embolism (p = 0.95 for interaction), and major or NMCR bleeding (p = 0.76 for interaction) (Figure). Irrespective of ASA use, fatal bleeding was less frequent with rivaroxaban (0.4% vs. 0.8%, p = 0.003) compared with warfarin.

**Conclusion:** Rivaroxaban was non-inferior to warfarin for the prevention of stroke or systemic embolism, and was associated with less fatal bleeding, irrespective of concomitant ASA use.

**Acknowledgement/Funding:** ROCKET AF was funded by Janssen Pharmaceuticals and Bayer.

**2032 | BEDSIDE**

**Stroke and bleeding outcomes with apixaban versus warfarin in patients with high creatinine, low body weight or high age receiving standard dose apixaban for stroke prevention in atrial fibrillation**

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**Background:** In the ARISTOTELE trial comparing apixaban with warfarin in pts with AF, apixaban 2.5 mg was used in pts with 2 or more dose reduction (DR) criteria: age ≥ 80 years, creatinine ≥ 1.5 mg/dL, weight ≤ 60 kg. Pts assigned 2.5 mg of apixaban vs. warfarin (n=831) had similar reductions in stroke/SE and major bleeding to pts assigned 5.0 mg of apixaban vs. warfarin (n=17,370).

**Methods:** We compared pts assigned to apixaban 5.0 mg or warfarin with 1 of 3 DR criteria with pts with 0 of 3 criteria. Stroke/SE and major bleeding rates, hazard ratios and 95% CIs were evaluated, and interactions between treatment and the presence of 1 vs. 0 DR criteria were determined.

**Results:** Among pts assigned 5.0 mg of apixaban or warfarin, 4046 (23%) had one DR criteria. These pts were older (77 vs. 69 years), lighter weight (86 vs. 70 kg), and had worse renal function (creatinine 1.00 vs. 1.07 mL/min) than pts with no DR criteria. Pts with one DR criteria had more stroke/SE and major bleeding but had similar benefits of apixaban vs. warfarin on stroke/SE (p=0.41) and major bleeding (p=0.65). 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.
Methods: By cross-linkage of individuals in multiple Danish nationwide registries, we identified all patients discharged with non-valvular AF from 1997 to 2011. Patients with serum creatinine measurements available from Danish medical laboratories within 12 months before baseline were classified according to estimated glomerular filtration rate (eGFR). The risk of stroke/systemic thrombembolism (TE) and major bleeding associated with the level of kidney dysfunction was determined using cox regression analyses adjusted for factors in the CHA2DS2-VASC and the HAS-BLED scores. Patients with eGFR >90 ml/min/1.73m² were used as reference.

Results: From a total of 124,455 non-anticoagulated patients with AF, we identified 27,356 patients with available serum creatinine measurements. After adjustment for factors in the CHADS2-VASc score, kidney dysfunction was associated with an increased risk of stroke/TE; hazard ratios 1.82 (95% CI 1.35–2.44), 1.17 (95% CI 0.96–1.42), 1.18 (95% CI 1.03–1.34), 1.03 (95% CI 0.91–1.18), in patients with eGFR <15 (n=412), 15–29 (n=1333), 30–59 (n=10,017), and 60–90 (n=11,593) ml/min/1.73m², respectively. After adjustment for factors in the HAS-BLED score, kidney dysfunction was associated with an increased risk of major bleeding; hazard ratios 2.41 (95% CI 1.76–3.31), 1.74 (95% CI 1.40–2.16), 1.32 (95% CI 1.14–1.52), 1.04 (95% CI 0.90–1.20), in patients with eGFR <15, 15–29, 30–59, and 60–90 ml/min/1.73m², respectively.

Conclusions: CI of stroke/TE, time-varying eGFR

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 diabetes using combined FDG-PET/PMRI imaging


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 the morphological and biological aspects of these plaques with MRI and FDG-PET imaging.

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 MR 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 the ischemic stroke compared to the contralateral side (39% vs. 16%; p=0.001). For all other AHA lesion types, no significant differences were found between ipsilateral and contralateral sides. Plaques containing a lipid-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; 3.14±1.14 vs. 2.63±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). plaques containing high-resolution MRI and FDG-PET in non-stenotic atherosclerotic plaques ipsilateral to the stroke, supporting a causal role for these plaques in stroke. Combined PET/MRI system provides unique diagnostic means to non-invasively co-register morphological and molecular signals for the more specific identification of high-risk plaques.

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. Combined PET/MRI system provides unique diagnostic means to non-invasively co-register morphological and molecular signals for the more specific identification of high-risk plaques.
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 Intentional Multicenter) registry is an international multicentre registry including patients with suspected coronary artery disease undergoing CCTA. Our analysis is based upon 15219 patients. The primary endpoint was all-cause mortality. The Framingham risk-score, the Morise score and the NCEP ATP III score were calculated and correlated to the primary endpoint. The CONFIRM score implemented the number of proximal segments containing calcified or mixed plaque tissue and the number of obstructed coronary segments to the NCEP ATP III score.
Results: During follow-up, 982 patients died. Figure 1 shows receiver-operating curves for all 4 scores. Prediction of the primary endpoint was significantly higher for the combined CONFIRM score (c-index 0.7, green curve) compared to the Framingham risk score (c-index 0.67, p<0.0001, red curve), the Morise score (c-index 0.61, p<0.0001, red curve) and the NCEP ATP III score (c-index 0.68, p<0.0001, dark blue curve).
Conclusion: The CONFIRM score, based on CCTA parameters and clinical risk factors, demonstrates a significantly improved prediction of all-cause mortality risk than traditional risk scores over a 5 year follow-up period.

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 compared to that of the current standard of care based on functional testing.
Methods: We conducted a prospective randomised controlled trial in 350 patients with stable chest pain who had been referred for evaluation of possible coronary artery disease to the outpatient clinic of four hospitals in the Netherlands between August 2012 and July 2013. Patients were randomly allocated to the 2:1 and respectively 7:1, CONFIRM (CCTA) and current standard of care based on functional testing or a diagnostic strategy with cardiac CT (1:2 ratio) using a computer-generated block randomisation sequence stratified by centre.
Main outcome measures: The study’s three main endpoints were reduction of chest pain and improved quality of life (effectiveness); major adverse events (safety); and costs (efficiency) after one year of follow up.
Results: We included 350 patients with a mean age of 55±8 years (55% women). The angiographic driven strategy was significantly more effective for patients randomized to cardiac CT as compared with functional testing, the final diagnosis was sooner established (7 vs 26 days; p<0.0001), there was less downstream testing (25% vs. 53%, p<0.0001) and the total diagnostic costs were lower ($369 vs $440; p<0.0001). The cumulative radiation exposure was higher in the cardiac CT group (6.6±8.7 mSv versus 6.1±9.3 mSv; p<0.0001). At an average of 446 days (1.2 years) of follow up, MACE-free survival was 96.7% for patients randomized to cardiac CT and 87.7% for patients randomized to functional testing (P=0.011).
Conclusion: A cardiac CT approach provides at least equally and perhaps more effective and safe care. Despite the modest size in our setting, the cardiac CT approach is associated with fewer tests, diagnosis faster and lower costs.

2102 | BESIDE
Coronary atherosclerosis features for the prediction of ischaemic events (CAFE-PIE study): a CT scan integrated score from a bi-center registry
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Objective: 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. We evaluated plaque type (soft, mixed and calcified), minimum CT density (HU), contour, length as well as presence of spotty calcium, ring-like sign and positive remodeling in all culprit lesions and in non-culprit segments, if stenosis was >50% (Figure1). We included in the analysis 214 coronary segments (70 culprit and 144 non-culprit).
Results: In culprit lesions (n=70) compared to non-culprit lesions (n=144) frequency of soft plaques (60% vs. 43%, p<0.001), positive remodeling (70.2% vs. 54.3%, p<0.03) and uneven contour (91.7% vs. 68.7%, p<0.0002) 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<0.002 and 16.8±13.4 mm vs 13.2±6.9 mm, p<0.01, respectively). Uneven contour was the most sensitive sign of plaque’s vulnerability (91.7%), and ring-like sign, such as spotty calcium – the most specific (78.3% and 72.9% respectively). Receiver-operator characteristic curve analysis identified the optimal cutoff value of minimum plaque density and length for discrimination between culprit and non-culprit lesion as 40 Hounsfield units (HU) and 13.5 mm respectively. The combination of soft plaque with a minimum density <40 HU and uneven contour occurred in a third of cases in culprit lesions and almost two times less in non-culprit (31.67% vs. 17.91%, p<0.004) and could be characterized by a high specificity (82.1%) and negative predictive value (72.7%).
Conclusions: Thus, the most specific features of culprit lesions in patients with ACS include positive vascular remodeling, length < 13.5 mm, minimum CT-density < 40 HU, soft plaque’s type and presence of uneven contour, as well as a combination of the last three features.
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. Specifically a consideration regards those patients with obstructive CAD and in which both the extent and the features of non-obstructive CAD could lead to a reclassification to a higher risk profile and thereby to a different cardiovascular treatment.

Acknowledgement/Funding: no funding

2103 | BEDSIDE
Cardiac spectral CT scan to diagnose acute myocarditis

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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: 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 scans 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 dyspnea (12%), and 71% of patients had a recent history of viral infection. Mean CRP was 69±73 mg/l and troponin levels were 6.5±6.0 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, this technique may be used as a non-invasive alternative to ICA during the follow-up exams for CAV.

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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Objective: Aim of this study was to assess the prevalence and distribution of extracardiac findings (ECF) on cardiac CT in the general population and to investigate their predictive value on all-cause mortality (ACM).

Methods: Participants aged 45–75yrs from the prospective population-based Heinz Nixdorf Recall Study were studied by non-contrast enhanced cardiac CT for quantification of coronary artery calcification (CAC). Experienced radiologists, blinded to risk factors, evaluated ECF among 556 consecutive CTA cases concerning the presence of clinical relevant (=requiring further diagnostic investigations or treatment) ECF. Prevalence and distribution of ECF were examined for different age classes, Framingham Risk Score (FRS: low, intermediate, high risk) and predefined CAC-score categories (0.1–99.100–399; ≥400). Association of ECF with ACM during a mean follow-up period of 10.2±2.1yrs was assessed by Cox proportional hazards regression analysis. Adjustment was performed for established cardiovascular risk factors (CVRF: age, sex, hypertension, diabetes, smoking an cholesterol levels) and CAC. ROC-analysis with c-statistics were used to examine the predictive value of ECF on ACM in addition to CACRVF and CAC-score.

Results: Within 4610 participants (mean age 59.7±7.8yrs, 49.5% male), 208 (4.5%) subjects had at least one clinical significant ECF. A total of 371 ECF was found, whereas tumor-suspected lesions (95 [2.0%]), enlargement of the thoracic aorta (65 [1.4%]) and structural pulmonary diseases (45 [1.0%]) were the most frequent findings. Prevalence of ECF increased with age (45–54 yrs: 39/1417 [2.8%]; 55–64 yrs: 75/1815 [4.1%]; ≥65 yrs: 94/1378 [6.8%] p<0.0001 for trend), as well as with FRS (low: 83/2399 [3.5%]; intermediate: 73/1532 [4.7%]; high: 55/1279 [4.3%]) and p<0.0001 for trend) and CAC-score categories (CAC=0: 45/1381 [3.3%]; 1–100: 79/1532 [5.2%]; ≥100: 41/1279 [3.2%]; p<0.001 for trend). ECF were associated with ACM (Hazard Ratio (HR): 2.55 [95% Confidence Interval (CI): 1.86; 3.49] p<0.0001), which remained increased after adjustment for CACVF (HR: 1.82 [1.33; 2.51] p=0.0002). Even after further adjusting for CAC-score, ECF remained independently associated with ACM (HR: 1.82 [1.32; 2.51] p<0.0002).

Conclusion: Clinical relevant ECF on cardiac CT are common in the general population and their predictive value on ACM is substantial. Evaluation of those findings may improve individual diagnostic strategies, particularly in subjects at high cardiovascular risk.

2105 | BEDSIDE
Does coronary CTA provide sufficient image quality in heart transplant recipients with supposing rate during scan?


Aims and objectives: Cardiac allograft vasculopathy (CAV) is the leading cause of death after the first year of heart transplantation (HTX). According to the current guidelines, cardiac CTA is recommended as a non-invasive alternative to ICA during the follow-up exams for CAV. Does cardiac CT angiography (CTA) in heart transplant recipients with suboptimal heart rate during scan satisfy the current recommendations?

Methods: Between 2009 and 2012, we analyzed 281 coronary segments in 282 heart transplant recipients (HTX) who underwent coronary CTA. The median HR was 70/min [IQR: 66–76] in HTX group and 70/min [IQR: 66–76] in the control group (p=0.265). We have analyzed 282 coronary segments in 282 HTX patients, which seems to be beneficial for coronary CTA imaging. Coronary CTA imaging was performed with 64-slice and 128-slice CT scanners during the same time to compare with the MRI considered the gold standard.

Results: The median HR was 70/min [IQR: 66–76] in the control group (p=0.265). We have analyzed 282 coronary segments in 282 HTX patients, which seems to be beneficial for coronary CTA imaging. Coronary CTA imaging was performed with 64-slice and 128-slice CT scanners during the same time to compare with the MRI considered the gold standard.

Conclusion: Does coronary CTA provide sufficient image quality in heart transplant recipients with supposing rate during scan?
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.

Methods: 137 patients were prospectively examined by clinically indicated cardiac imaging methods (n=69 CTA, n=29 SPECT, n=39 ICA), with 10 controls. ICA is associated with a significant increase in DSB levels compared to a control group with no testing (Figure 1c). There were no differences 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. ICA demonstrated the lowest radiation dose, with no observed difference in DSBs between CTA and SPECT despite higher radiation exposure with CTA. This may reflect differences between radiation sources, and requires further study.

Figure 1

Conclusion: ICA is associated with a significant increase in DSB levels compared to CTA and SPECT, attributed to increased radiation exposure. ICA demonstrated the lowest radiation dose, with no observed difference in DSBs between CTA and SPECT despite higher radiation exposure with CTA. This may reflect differences between radiation sources, and requires further study.

Figure 1

Conclusion: ICA is associated with a significant increase in DSB levels compared to CTA and SPECT, attributed to increased radiation exposure. ICA demonstrated the lowest radiation dose, with no observed difference in DSBs between CTA and SPECT despite higher radiation exposure with CTA. This may reflect differences between radiation sources, and requires further study.
with SSS standard right atrium appendage pacing prolongs atrioventricular conduction resulting in higher percentage of ventricular pacing.

**P2112 | BEDSIDE**

ECG criteria for right ventricular lead positioning. An analysis from the right pace study

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**Introduction:** Pacing on right ventricular (RV) septum could allow more physiological activation than RV apical pacing. Recently, ECG criteria were proposed to accurately define RV lead position. The aim of this study was to assess the agreement between fluoroscopic and ECG criteria for RV lead positioning in a population of patients who underwent RV lead implantation.

**Methods:** The RIGHT PACE study enrolled patients with indications for cardiac pacing. Following device implantation, fluoroscopic radiographs were recorded in 3 views (posterior-anterior, 40°RAO, 40°LAO) and analyzed by an independent observer who categorized lead position. A 12-lead ECG was performed during ventricular pacing and following criteria for RV septal positioning were considered: a negative or isoelectric QRS in lead I; a paced QRS duration <140ms; an absence of notching in the inferior leads; early precardial QRS transition (earlier than V4). An agreement between fluoroscopic and ECG criteria for RV lead positioning in a 37% and 63%, the absence of notching in the inferior leads with 59% and 44%.

**Results:** Complete data were available for 409 patients. The analysis of radio-graphs confirmed septal placement of the lead in 170 patients (17 high-, 65 mid-, 88 low-septum) and apical placement in the remaining 239 patients. According to ECG analysis, a negative or isoelectric QRS in lead I identified septal leads with sensitivity of 11% and specificity of 89%, a paced QRS duration <140ms with 38% and 76%, the absence of notching in the inferior leads with 59% and 44%.

**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. Measurements were simulated in virtual human models of various lead pathways in commercial scanners. Electric fields were extracted at both normal operation mode and 1st level control mode. Single lead testing was used as it typically experiences higher heating than that from dual lead testing. Clinically relevant lead states of various levels of fluid ingress were studied, and the lead transfer function (TF) with the highest ingress heating was selected. The TF was validated through ED2 Annex M pathways. It was then integrated with the extracted electric fields to estimate in-vitro temperature rises. A validated thermal model scaled the in-vitro temperature estimates to in-vivo results. The thermal model simulated the worst case conditions using an extreme level of tissue encapsulation of the generator with cardiac tissue. Uncertainties from measurements, TF, and in vivo simulations were assessed with the Monte Carlo (MC) method. Safety was assessed based upon the accepted 43 °C standard (Meshorer, 1983) for cardiac tissue interface with the lead tip helix electrode and lead MRI filter inductor.

**Results:** Over 400 different patient and MRI system permutations were simulated. When combined with exhaustive lead pathways, and MC analysis, over 14 million simulations were performed. The risk associated with MRI scans was based upon the number of these 14 million simulations exceeding the safety criterion. For 2 W/kg scans, none of the 14 million scans exceeded the safety criterion at the lead tip helix or the MRI filter inductor, and so is estimated as <1 in 14 million. For 4 W/kg scans, the risk was <1 in 15,000 at the lead tip helix and <1 in 14 million at the MRI filter inductor.

**Conclusions:** Our results indicate that the risk associated with MRI scans of patients with an Accent MRI pacemaker system due to cardiac damage at the lead helix and introduct MRI filter inductor is extremely low for 4 W/kg scans, and miniscule for 2 W/kg scans, even taking into account worst case considerations into every modeling step.

**P2114 | BEDSIDE**

Clinical impact of new-onset left bundle branch block after aortic CoreValve implantation: long term follow-up


**Background and purpose:** New-onset rhythm conduction disturbances are frequently observed after transcatheter aortic valve implantation (TAI). The most frequently observed is the left bundle branch block (LBBB). The clinical impact of the new-onset LBBB (NO-LBBB) after TAVI remains controversial. The aim of this study was to determine the impact of new-onset LBBB in terms of mortality and morbidity (need for pacemakers and admissions for heart failure) at long-term follow-up.

**Methods:** From April 08 to December 14, 220 patients with severe aortic stenosis were treated by implantation of a CoreValve prosthesis. Sixty-seven were excluded for analysis: 22-patients with preexisting LBBB and 45-patients with permanent pacemaker, whether it was implanted before or immediately after implantation of CoreValve prosthesis. The remaining 153 patients were divided into two groups: those with persistent NO-LBBB and those without conduction disturbances after treatment (WCDAT). Patients were followed-up at 1-month, 6-month, 12-month, and yearly thereafter.

**Results:** Persistent NO-LBBB occurred in 83-patients (37.7%) immediately after TAVI, and 70-patients (31.8%) did not develop any conduction disturbances. The mean follow-up time of both patient groups was 32±22 months (range 3 to 82). There were no differences in mortality rate between the NO-LBBB and WCDAT groups (39 vs. 34%, p=0.59). There were no differences between groups in re-hospitalizations for heart failure (31% vs. 32%, p=0.55). The NO-LBBB group did not require more frequently late implantation of permanent pacemaker at follow-up (31% vs. 26%, p=0.38).

**Conclusions:** New-Onset-LBBB was not associated with a higher incidence of late need of pacemaker after CoreValve implantation. In addition, there was not a higher risk for late mortality or rehospitalization rates.

**P2115 | BEDSIDE**

Time course of detection of new atrial fibrillation (AF) and AF burden in patients with cardiac implanted electronic devices


**Background:** In patients with a cardiac implantable electronic device (CIED), continuous monitoring, through an atrial lead, allows detection and quantification of new atrial fibrillation (AF). New onset AF is associated with an increased risk of stroke. Several different thresholds of AF burden (5 minutes, 1, 6, 12 and 23 hours) have been studied to quantify the increase in stroke risk, which has been observed is the left bundle branch block (LBBB). The clinical impact of the new-onset LBBB (NO-LBBB) after TAVI remains controversial. The aim of this study was to determine the impact of new-onset LBBB in terms of mortality and morbidity (need for pacemakers and admissions for heart failure) at long-term follow-up.

**Methods:** From April 08 to December 14, 220 patients with severe aortic stenosis were treated by implantation of a CoreValve prosthesis. Sixty-seven were excluded for analysis: 22-patients with preexisting LBBB and 45-patients with permanent pacemaker, whether it was implanted before or immediately after implantation of CoreValve prosthesis. The remaining 153 patients were divided into two groups: those with persistent NO-LBBB and those without conduction disturbances after treatment (WCDAT). Patients were followed-up at 1-month, 6-month, 12-month, and yearly thereafter.

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**Conclusions:** New-Onset-LBBB was not associated with a higher incidence of late need of pacemaker after CoreValve implantation. In addition, there was not a higher risk for late mortality or rehospitalization rates.
Elderly were defined for age 70 years old. Advanced age and high-residual platelet reactivity in patients receiving dual antiplatelet therapy with clopidogrel or ticagrelor. Elderly still represent a challenging subset of patients for the management of antithrombotic strategies, due to the complex balance between the risk of bleeding and the occurrence of high- residual on treatment platelet reactivity (HRPR).

Purpose: Among the three compared antiplatelet agents, aspirin was associated with a lower prevalence of major CV events and mortality. Baseline characteristics were matched by propensity score (PS).

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 anti-platelet agent and 11,259 non-users were included. Compared to the non-users, those using an antiplatelet agent were significantly associated with fewer CV events and mortality. Baseline characteristics were matched by propensity score (PS).

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.

Impact of intravenous lysine acetylsalicylate versus oral aspirin on percutaneous coronary intervention: results of a prospective, randomized, crossover study

Discussion: In conjunction with other risk factors of ST, WBV as the major determinant of ESS, seems to be an independent predictor of ST after acute STEMI and may obtain additional data for risk categorization.

Impact of intravenous lysine acetylsalicylate versus oral aspirin on percutaneous coronary intervention: results of a prospective, randomized, crossover study

Purpose: In dialysis patients, an antiplatelet agent usage is significantly associated with fewer CV events and mortality. Baseline characteristics were matched by propensity score (PS).

Methods: Among the three compared antiplatelet agents, aspirin was associated with a lower prevalence 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 anti-platelet agent and 11,259 non-users were included. Compared to the non-users, those using an antiplatelet agent were significantly associated with fewer CV events and mortality. Baseline characteristics were matched by propensity score (PS).

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.

Efficacy of antiplatelet agent usage for primary and secondary prevention in dialysis patients: a nation-wide data survey and propensity analysis

Purpose: In dialysis patients, an antiplatelet agent usage is significantly associated with fewer CV events and mortality. Baseline characteristics were matched by propensity score (PS).

Methods: Among the three compared antiplatelet agents, aspirin was associated with a lower prevalence 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 anti-platelet agent and 11,259 non-users were included. Compared to the non-users, those using an antiplatelet agent were significantly associated with fewer CV events and mortality. Baseline characteristics were matched by propensity score (PS).

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.

Whole blood viscosity predicts the definite stent thrombosis after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction

Methods: Between 2010–2015, 2663 patients with acute STEMI who were performed primary PCI were included and followed up median 34.6 months. 96 patients were re-admitted to hospital with acute coronary syndrome and diagnosed as “definite” ST according to ARC criteria. The patients were classified into tertiles according to WBV. WBV for low shear rate (LSR) and high shear rate (HRR) were calculated from hematocrit and total plasma protein with validated equations.

Results: The prevalence of stent thrombosis, were higher in third WBV tertiles at LSR (p<0.001) and HSR (p<0.001). In Cox regression analysis, WBV at LSR (OR=1.998, 95% CI: 1.323–3.019) and WBV at HSR (OR=2.183, 95% CI: 1.445–3.299) were demonstrated as independent predictors of long term ST. In ROC analysis for prediction of ST, a cut-off value of 67.1 WBV for LSR had a 73% sensitivity and 67.7% specificity for prediction of (AUC: 0.775) and a cut-off value of 16.79 WBV at HSR had a 62.5% sensitivity and 70.5% specificity (AUC: 0.676).

Conclusion: Whole blood viscosity predicts the definite stent thrombosis after primary percutaneous coronary intervention for ST-segment elevation myocardial infarction.
administration of oral prasugrel and intravenous LA versus prasugrel and aspirin orally on platelet aggregation.

**Methods:** This was 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 450 mg plus oral prasugrel 60 mg, or LD of aspirin 300 mg plus prasugrel 60 mg orally in a crossover fashion after a 2-week washout period between treatments. Platelet function was evaluated at baseline, 30 min, 1 h, 4 h, and 24 h using light transmis-
sion aggregometry and vasodilator-stimulated phosphoprotein phosphorylation.

**Results:** The primary endpoint of the study, inhibition of platelet aggregation af-
after arachidonic acid (AA) 1.5 mm 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 at 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 in-
hibition faster and greater than oral aspirin.

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**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 in-
farction (MI) have not been characterized in detail. The present study aimed to investigate temporal trends in incidence of MI with or without ST-segment eleva-
 tion (STEMI) and the effect of prior cardioprotective medication on the initial clinical presentation.

**Methods:** Using individual-level linkage of data from Danish nationwide reg-
isteries, 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 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 likeli-
hood 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 medicad-
tion use increased in both groups, i.e. for statins from 9.8 to 25.6%, angiotensin-
converting enzyme inhibitors/angiotensin receptor blockers (ACEIs/ARBs) from 21.5 to 31.9%, beta-blockers from 16.9 to 22.0%, aspirin from 23.7 to 26.8%, 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 1.2 to 7.0% to 13.7%); OR 1.27 (CI 1.19–1.36) with beta-blockers, OR 1.16 (CI 1.05–1.28) with ACEIs/ARBs (15.2 to 20.9%, p=0.001), and thienopyridines from 0.6 to 1.5%; p<0.001, 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.

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**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 contribu-
tors 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 evalu-
ated Rac-1 in the enhanced platelet aggregation in DM.

**Purpose:** We investigate whether Rac-1 inhibitor, named NSC23766, could re-
duce human platelet hyperaggregation induced by high glucose stimulation, and also whether it could modulate vascular and platelet functions in vitro and in a in vivo mouse model of DM.

**Methods and results:** Mesenteric arteries (n=4 for each group) from C57BL/6 mice were exposed to low (5mM) and high (25mM) glucose concentrations. At high glucose levels arteries showed a significant reduction to acetylcolline-
evated vasorelaxation (p<0.01 vs. Glu 5mM), which was restored by pretreat-
ment with NSC23766 (30 μM). To evaluate the in vivo effects of hyperglycemia on Rac-1 regulation of vascular function, diabetes was induced in C57BL/6 mice with single intraperitoneal injection of streptozotocin (STZ - 40 mg/kg). Vascular studies revealed the abolition of endothelial dysfunction up to 96 hours after a single injection of Rac-1 inhibitor. Studies on human platelets revealed that high glucose levels (25mM) induced the activation of Rac-1 and the reduction of nitric oxide (NO) release, which was restored after the treatment with NSC23766. Treatment with NSC23766 also restored vasorelaxation evoked by supernatant from stimulated platelets close to basal condition. Aggregation induced by type I collagen (0.8 μg/ml) was significantly increased when platelets were pre-
incubated with glucose (25 mM) while RAC1 inhibitor (30 μM) reduced platelet aggregation, and this effect was improved at highest glucose concentrations. Fi-
nally, platelets from diabetic patients (n=20) showed higher levels of Rac-1, corre-
lated to percentage of glycated hemoglobin, when compared to control subjects (n=11); consistently, a higher dose of NSC23766 (60 μM) was necessary to obtain a significant reduction in DM platelets aggregation compared to control subjects. NSC23766 treatment was also able to potentiate antplatelet 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.

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**P2122 | BEDSIDE**

**Class effect of beta-blockers in survivors of ST-elevation myocardial infarction: a nationwide cohort study using insurance claims database**

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**Introduction:** Beta-blockers reduce mortality after acute myocardial infarction (MI). Whether beta-blockers exert a class effect in the era of coronary reperfu-
sion therapy is unknown.

**Methods:** We identified patients with the first hospitalization for ST-segment elevation MI through January 2003 to December 2010 from the National Health Insurance claims database, Taiwan. Patients receiving carvedilol, bisoprolol or propranolol were analyzed. Treating the carvedilol group as the common reference, simul-
taneous three-group comparison approach usings among three different beta-
blockers. Cox regression model with adjustment for propensity score was used to compare the relative risks of outcomes included all-cause death, cardiovascular death and recurrence of MI.

**Results:** Among 16836 patients, 7591 were prescribed with carvedilol, 5934 with bisoprolol and 3311 with propranolol. The mean follow-up was 1.0 years. After ac-
counting for baseline differences, patients treated with bisoprolol (adjusted hazard ratio [HR] 0.87, 95% confidence interval [CI] 0.72–1.05, p=0.14) or propranolol (adjusted HR 1.07, 95% CI 0.84–1.36, p=0.68) had a similar risk of all-cause death in comparison with those with carvedilol. There was also no significant dif-
fERENCE among three beta-blocker groups in risks of cardiovascular death and recurrence of MI.

**Conclusions:** Beta-blockers have class effect in the modern era of acute MI treat-
ment.
CARDIOVASCULAR MAGNETIC RESONANCE – TRANSLATIONAL

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) improved ejection fraction as compared to baseline but was not better than that of moderate 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±3 (35°C) and 28±2 (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 35°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 relative to baseline was less affected in the 32°C group only (−30%±16, −24%±7, −17%±18, p<0.01) as well as in histological HE staining (p<0.001).

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 thienopyridin-class antiplatelet agents on IR injury in an in vivo mouse model with an innovative molecular MR 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 GPIIIb/IIIa (LIBS-MPIO). In comparison, a control antibody was applied (control-MPIO). Necrosis was depicted via late gadolinium enhancement (LGE). All imaging results were correlated to findings in histology for platelets, platelet-neutrophil-complexes (PNCs), and necrosis. Ejection fraction and infarct size of the area at risk in wildtype vs. P2Y12/−/− mice were quantified by echocardiography and Monolite blue/TTC staining.

Results: In MRI short axis images a significant signal decrease in the area of LAD occlusion occurred after injection of LIBS-MPIO in WT mice, whereas in P2Y12/−/− mice no signal decrease was found. In parallel, gadolinium allowed the detection of myocardial necrosis in both groups. The extent of necrosis was significantly lower in P2Y12/−/− mice quantified by LGE (p<0.01) as well as in histological HE staining (p<0.001). Significantly less accumulation of microthrombi in P2Y12/−/− mice was counted in the reperfused myocardium (p<0.001). The amount of bound MPIOs was significantly reduced to the level of WT mice (p<0.01). Moreover, the amount of PNCs was reduced in P2Y12/−/− 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 toward an elevated preserved EF in P2Y12/−/− compared to WT mice was found in echocardiography (p<0.1).

Conclusions: A simulated therapy with P2Y12-receptor inhibitors leads to reduced inflammation and myocardial necrosis after coronary vessel occlusion and reperfusion in mice. This was evident in histology and echocardiography as well as in a novel dual in-vivo MR imaging technique and is of great clinical and prognostic interest.

P2126 | BEDSIDE
Presence of myocardial scar does not prevent improvement in myocardial perfusion and left ventricular function in refractory angina patients undergoing intramyocardial bone marrow cell injection
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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) >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
Ultrasound superparamagnetic particles of iron oxide-enhanced magnetic resonance imaging in the assessment of cellular inflammation after myocardial infarction

Background: Optimal levels of early “proinflammatory” and late “reparative” macrophages after myocardial infarction (MI) are crucial to the recovery of cardiac function. Ultrasound superparamagnetic particles of iron oxide (USPIO) are engulfed by resident macrophages in 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 was performed immediately before and 24 hours after USPIO (ferumoxytol, 4 mg/kg) administration at 2±1, 5±2, 13±3, 21±4, and 89±11 days. Regions of interest (ROIs) were categorised into infarct, peri-infarct, and remote myocardial zones by co-registration with late gadolinium enhancement (LGE). R2* values (1/T2*) within ROIs were determined to assess the duration of USPIO uptake.

Results: Compared to remote myocardium, increased USPIO uptake in the infarct zone is seen at days 21±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).

Figure 1: Compared to remote myocardium, increased USPIO uptake is seen in the infarct zone at days 21±1 (p=0.001), days 52±2 (p=0.01) and days 133±3 (p=0.01). There is no difference in uptake at later time points; days 21±1 and 89±11 (both p>0.05, 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.

**P2129 | BEDSIDE**

**Non-invasive estimation of pulmonary vascular resistance by cardiovascular magnetic resonance in systolic heart failure:**

**Prognostic implications beyond late gadolinium enhancement**

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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 (6.93±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 risk of adverse events at 9 months follow-up (HR 2.98; 95% CI 1.12–7.88; p<0.03).

**Conclusions:** 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 late gadolinium enhancement or LVEF.
holesterol modifies HDL and its potential to induce cardioprotection during MI. Increased extent of infarct size and worsening of cardiac perfusion and performance are major findings in this study. Hypercholesterolemia induces HDL remodeling and shifts HDL towards a less anti-oxidant profile.

P2131 | BEDSIDE
Association between epicardial fat thickness and circulating endothelial progenitor cell levels in patients with coronary arterial disease.

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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 inured endothelial monolayer is regenerated by circulating bone marrow derived-endothelial progenitor cells (EPCs), and levels of circulating EPCs reflect vascular repair capacity. However, the relation between EFT and EPC remains unclear. Here, we tested the hypothesis that patients with thicker EFT might have decreased EPC levels and attenuated EPC function.

Methods: A total of 101 consecutive patients undergoing elective coronary angiography because of suspected coronary artery disease (CAD) were screened and received examinations of echocardiography between November 2013 and November 2014. Flow cytometry with quantification of EPC markers (defined as CD34+; CD34+/KDR+; and CD34+/KDR+/CD133+) in peripheral blood samples was used to assess circulating EPC numbers. The adhesion function, migration, and tube formation capacities of EPCs were also determined. Syntax scores were calculated according to the coronary angiography.

Results: Patients with thicker EFT (>5mm) had significantly decreased circulating EPC levels (table), attenuated EPC functions, and enhanced systemic inflammation compared to patients with thinner EFT. In addition, higher Syntax score was found patients with thicker EFT (31.23 vs 24.69, p=0.009).

Conclusions: Patients with CAD and thicker EFT have decreased circulating EPC numbers and functions and higher syntax score than those with thinner EFT.

P2132 | BENCH
ATF3 regulates high fat diet induced adipocytes hypertrophy and obesity by repressing the ChREBP signaling pathway.

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Background: Obesity is a severe and complicated health issue related to lifestyle and dietary modifications, and is highly associated with metabolic syndrome and diabetes. Activating transcription factor 3 (ATF3) is a member of the ATF/cAMP response element-binding protein family of transcriptional factors. It can be induced by stress condition in a variety of tissues, including the adipocytes. However, the physiology and mechanism of ATF3 in adipocytes and obesity regulation are not clear. ever, the physiology and mechanism of ATF3 in adipocytes and obesity regulation are not clear. Nevertheless, ATF3 expression and suppressed inflammatory marker ICAM-1 and serum resistin levels thus rescue the obesity phenotype seen in these mice. We further investigate the role of ATF3 in 3T3-L1 adipocytes. ATF3-overexpressing adipocytes exhibited less lipid accumulation (Oil red O staining) with diminished expression of adipogenic markers (including C/EBPa, PPARg, adiponectin, leptin and resistin), and lipogenic markers (including ACC1, ACC2, FAS, DGAT1 and DGAT2) as compared to the control cells. Inflammation-related genes like ICAM1, IL-6, MCP1 and TNFa, and lipid droplet coat protein, perilipin, were found downregulated in ATF3-overexpressing adipocytes. Mechanistically, we found that expression of ATF3 repressed the ChREBP promoter activity of the p(−2980)/Luc reporter in 3T3-L1 adipocytes, whereas the expression of ATF3 did not repress both PPARg and FABP4 promoter activities.

Conclusions: These results suggest that ATF3 inhibits 3T3-L1 preadipocyte differentiation and lipid droplet formation in murine adipocytes through attenuating cellular inflammation and inhibiting both adipogenic and lipogenic processes; likely through repressing the ChREBP-ACC1 pathway. Therefore, our results confirm that ATF3 regulates high-fat diet-induced adipocytes hypertrophy and lipid metabolism in mice via ChREBP repression.

P2133 | BEDSIDE
Arginase inhibition improves endothelial function in patients with familial hypercholesterolemia.

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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 35±3) on lipid-lowering medication and twelve healthy subjects (age 30±2) were recruited. Venous occlusion plethysmography with intra-arterial infusion of serotonin and nitroprusside was used to assess forearm endothelium-dependent (EDV) and –independent (EIDV) vasodilatation, respectively, before and after 120 min administration of the arginase inhibitor (L-arginine hydroxy-nor-L-arginine, 2 mg/min 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 2.9±0.3 mmol/l. Baseline EDV and EIDV did not differ between the examination and the groups. Arginase inhibition enhanced EDV both in control subjects and FH patients. However, the improvement in EDV evoked by arginase inhibition was significantly higher in FH patients with high LDL-C levels as compared to the respective control group.

Conclusions: Arginase inhibition results in greater improvement in endothelial function in patients with FH 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 flavonoids on endothelial function and hemodynamics. In a subsequent study following a 30-day ingestion period, we studied the effects of flavonols on hemodialysis-mediated vascular dysfunction as compared to a nutrient-matched control. Primary and secondary outcome measures included safety and changes in FMD and plasma flavanol metabolites, respectively.

Results: 57 patients with ESRD were included (mean±SD, 42% male, age 65±13 years, BMI 29±5 kg/m², dialysis vintage 41±32 months). Flavonol ingestion was safe and well tolerated. Acute ingestion was associated with an increase in circulating epicatechin metabolites and increased FMD by 53% (p<0.0001) with no effects on blood pressure or heart rate. A 30-day ingestion of flavonols led to an increase of baseline FMD by 18% (p<0.001) with increased heart rate (70±2 vs 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 flavonols during hemodialysis alleviated hemodialysis-induced vascular dysfunction (Delta FMD flavonols 0.71±0.1 vs. placebo 1.48±0.1, p<0.001).

Conclusions: Flavonol ingestion resulted in increased FMD, systemic vascular resistance and plaque stiffness in hemodialysis patients. Dietary flavonol ingestion is associated with improved endothelial function and improved hemodynamics. Flavonol supplement significantly improves vascular function in ESRD patients. Further studies are warranted to confirm these promising findings.
Conclusion: Dietary flavanol ingestion mitigates hemodialysis-induced endothelial dysfunction in an acute and chronic fashion. Flavanols may thus have the potential to ameliorate vascular dysfunction in this high-risk population.

P2135 | BENCH Occurrence of coronary lipid deposits and myocardial fatty dystrophy in dabigatran etexilate-treated diabetic rats

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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=6), diabetes (D; n=6), and diabetes treated with DE (DD; n=6). In D and DD, 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 wk. At 38 wks of age, all rats were euthanized; blood and tissue samples were collected. Atherosclerotic lesion formation in aorta, coronary, and myocardial lipid deposits were evaluated with Oil Red staining. A 3-point scoring system was used to assess lipid burden within the 3 examination sites.

Results: Three D and 2 DD rats died during the study and were excluded from the analysis. In D and DD, dilated plasma thrombin time revealed relevant anti-coagulation. Blood glucose, total cholesterol, and triglycerides were significantly higher in D and DD rats compared to C and CD rats (all p<0.01). In DD, plasma triglycerides were significantly lower than in D rats (p<0.01). In D and DD, diabetes was associated with atherosclerotic lipid deposits in the thoracic aorta, coronary, and myocardial lipid deposits were evaluated with Oil Red staining. A 3-point scoring system was used to assess lipid burden within the 3 examination sites.

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 rats. 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 interference with thrombin availability by direct thrombin inhibition in diabetic rats may promote coronary atherosclerosis and myocardial fatty dystrophy.

P2136 | BEDSIDE HDL functionality in children with type 1 diabetes

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Background: The prognosis for childhood-onset type 1 diabetes (T1D) remains poor. Apart from poor glycaemic control, microalbuminuria is considered as an early risk marker for the development of cardiovascular (CV) disease in T1D patients. HDL dysfunction has been reported in adults with diabetes and this seems to further increase their CV risk. However it remains unknown whether similar changes can be seen in T1D adolescents.

Methods: We examined HDL function in 40 children (aged 10–16 years) with T1D and 20 age matched controls in relation to Albumin/Creatinine ratio (ACR) in the urine. T1D adolescents were divided into two groups (high ACR and low ACR). HDL endothelial properties were assessed by measuring Nitric Oxide and superoxide production in aortic endothelial cells using ESR spectroscopy. Serum paraoxonase (PON-1) activities were measured by UV spectrophotometry.

Results: Children with high ACR had higher HDL levels than those with low ACR and normal controls (beta per group 0.12 (95% CI 0.025 to 0.22), p-trend: 0.017). HDL from the high ACR group showed reduced Nitric Oxide bioavailability compared to controls (beta +0.73 (95% CI –12.7 to –1.8), p: 0.001) and the low ACR group (beta +0.71 (95% CI –12.6 to –1.7), p: 0.012). Similar trends but no significant differences 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 normal controls (beta per group 0.12 (95% CI 0.025 to 0.22), p-trend: 0.017).

Conclusion: In this study we demonstrated that T1D adolescents with high ACR had impaired HDL endothelial properties compared to controls. These disturbances in HDL 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: 0.001) and the low ACR group (beta +0.71 (95% CI –12.6 to –1.7), p: 0.012). Similar trends but no significant differences 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 normal controls (beta per group 0.12 (95% CI 0.025 to 0.22), p-trend: 0.017).
Relation between exercise capacity and skeletal muscle metabolism during exercise in patients with repaired tetralogy of Fallot

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Background: Peak oxygen uptake (VO2) is affected by central haemodynamics and by peripheral factors although the relative contribution is still debated. The correlation of cardiac output 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, could play a role in patients with CHD.

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 index (TOI), from the right vastus lateralis muscle. Patients also underwent cardiac magnetic resonance imaging (MRI). Patients had lower peak VO2 in patients with CHD are very scarce. Peripheral factors, which affect oxygen extraction, including reduced physical activity and fitness, could play a role in patients with CHD.

P2140 | BEDSIDE Ascending Aorta dilation late after tetralogy of Fallot repair: an intrinsic aortopathy?

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Background: Histological abnormalities of the ascending aorta (AAo) have been described in tetralogy of Fallot (ToF) but the clinical implications are not well known.

Purpose: To determine the extension, prevalence and predictors of aortic dilatation late after ToF repair (rToF) and to assess the aortic strain and stiffness in this context.

Population and methods: Eighty-six consecutive adults after rToF were included and were compared with a sex- and age-matched healthy volunteer group (n=46). The inner diameters of the sinuses of Valsalva (SOV), sinotubular junction (STJ) and AAo were measured using transthoracic echocardiography, in parasternal long-axis view. We defined aortic dilation as an aortic z-score (AoZ) >2. The aortic deformation was assessed by two-dimensional speckle tracking (2D-ST) global peak circumferential ascending aortic strain (CAAS). The aortic stiffness index was calculated according to ln (Ps/Pd)/CAAS and the arterial stiffness as 0.9*Ps/SV (Ps and Pd stand for systolic and diastolic blood pressure, respectively and SV for stroke volume).

Results: The overall cohort mean age was 30±9 years, 55% were males, with a mean Ps 116±11.3 mmHg. SV 58±8.16 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±0.1 vs 1.79±0.21 m², P=0.01) but bigger aortic diameters (SOV 33.6±4.5 vs 28±3.2 mm, STJ 32.0±4.2 mm, AAo 33±4.7 vs 25±3.2 mm, all P<0.001), with efferentation of the STJ in 43% of cases. The prevalence of aortic dilation (AoZ >2) in this cohort was 28%. The global peak CAAS was lower in ToF patients (7.5±4 vs 7.4±6, P=0.036) with a higher aortic stiffness index (17.7±3.7 vs 11.1±5.9, P=0.048). By multivariate reanalysis the AAo dilation was predicted by gender (β=0.18), P=0.029) 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.

P2141 | BEDSIDE Infective endocarditis following pulmonary valve intervention in patients with repaired congenital heart disease; a comparison of surgical and percutaneous procedures

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Background: Percutaneous pulmonary valve implantation (PPVI) avoids the additional heart surgery, improves heart function, allows for better quality of life and improves survival outcomes. It reduces both short and long-term risks. However, it is still associated with a high risk of infective endocarditis (IE) which is a major cause of death in CHD patients. The incidence of IE is described in following both pulmonary homografts and percutaneous valves.

Purpose: To quantify the incidence and define the clinical course of CHD patients undergoing 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, 393 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 was 140±273 days in the PPVI group (261–273 days) and 116±309 in the PPVI group (58–2500 days, p<0.0001). Three patients in the surgical PVR-IE group were successfully treated with antibiotic therapy, three required early PVR due to failure of medical treatment and two underwent elective PVR following a period of antibiotic sterilization. In the PPVI-IE group, one patient was successfully treated with antibiotic therapy; seven required urgent PVR and one underwent elective surgical PVR. We did not perform repeat PPVI in any patients. There was one death in PPVI-IE group. Three patients in surgical PVR-IE group had recurrent IE after repeat PVR despite antibiotic therapy.

Conclusion: PPVI is significantly safer 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 cadaveric remodelling post-pulmonary valve replacement in patients with repaired tetralogy of Fallot

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Background: Despite the reported strong prognostic significance of LV filling pressures, there are scarce data on the rate of right ventricular (RV) volumes, there are scanty data on the rate of ventricular mechanical and biological adaptation. We aimed to assess early and late post-operative RV volume and function in adult patients with repaired ToF. Therefore, the current data suggest that elevated RV 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.

Methods and results: 80 consecutive adults after rToF were in-
Conclusions: Cardiac remodelling is generally regarded as a gradual process post-PVR but RVEF monastere for the first time that major improvement in RV volumes seen at mid-term follow-up has 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 146 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 assessed using multivariate Cox proportional hazard model. Receiving operating characteristics (ROC) curves were used for discrimination. Internal validation in subgroups of patients with tetralogy of Fallot (N=81) and patients with severe pulmonary regurgitation as hemodynamic indication for PVR were also performed.

Results: Median age at intervention was 23 years old. There were 60 reinterventions due to PPVF (41%). Median event-free survival was 14 years (95% CI 12–16 years). The only independent risk factor was the age at intervention (hazard ratio 0.93; 95% CI 0.90–0.97; p=0.001; area under the ROC curve 0.95; 95% CI 0.92–0.98; p<0.001). Freedom from re-intervention because of PPVF 15 years after surgery was 70% when it was performed at age >20.5 years compared with 33% when age at intervention was ≤20.5 years (p<0.004) (figure). Internal validation in patients with tetralogy of Fallot (area ROC 0.98; 95% CI 0.98–1.0; p<0.001) or severe pulmonary regurgitation (area ROC 0.94; 95% CI 0.86–1.02; p<0.001) was excellent.

Conclusion: Re-intervention risk due to PPVF after 15 years of follow-up is more than two-fold when PVR is performed before the age of 20.5 years.

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 7.3% in 1997 to 30.7% in 2007. The overall CHD event rate declined from 1.35 per 100 patient-years of follow up in the pre-statin cohort to 1.20 in the post-statin cohort. The average baseline LDL-C in CHD cases was lower in the post-statin cohort compared with the pre-statin cohort (140 mg/dL vs 132 mg/dL, p=0.001). Despite these differences, the association between LDL-C and new 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=0.28). The population attributable risk of CHD due to elevated LDL-C was also numerically lower in the post-versus pre-statin era (18.3% (10.8–25.8%) vs 22.7% (13.2–32.1%), 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 new CHD remains unchanged in the modern era despite the use of statins in more than 30% of adults. 13.2% of CHD cases in the post-statin era are still attributable to elevated LDL-C.
Model: HR 2.19, 95% CI 1.19–4.02, P < 0.01; fully adjusted model: HR 2.21; 95% CI: 1.20–4.08, P < 0.01.

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 multivariable adjustment, however, 5-year mortality was even 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 (n=3,101) and without (n=3,171) relocation (Rel) due to residential property destruction.

Results: Body weight and lipoprotein cholesterol levels at Phase 1 (baseline) were similar between the two subgroups with and without Rel. However, changes in body weight between Phase 1 and Phase 2 were significantly greater in the subgroup with Rel compared to that without Rel. (+0.4 vs. −0.2 kg, p<0.001: Fig-left). There was a greater decrease in high density lipoprotein cholesterol (HDLc) level in the subgroup with Rel than in the subgroup without Rel (−0.9 vs. −0.1 mg/dl, p<0.001: Fig-right). Changes in other ACV risk factors such as systemic blood pressure, smoking status, non-HDLc and 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.

Sex-age adjusted changes in BW and HDLC

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 Lp(a) < 110 mg/dl. 

Conclusion: 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.

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% success 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 < 1% in Asian population (1000 Genomes 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 (c.7173C>A or p.P2077H/c.6223G>A or p.S2046L, and c.2842G>A or p.G948V/c.1130C>T or p.P377L).

Conclusion: WES combined with integrated variant annotation prediction successfully identified asymptomatic Tangier disease with novel ABCA1 mutations for the first time even where DNA is available for only one affected individual. Such comprehensive approach is useful to determine true causative variants, especially, in recessive form of inherited cardiovascular diseases.

CURRENT STATUS AND FUTURE DIRECTIONS OF CORONARY ARTERY BYPASS GRAFTING

P2151 | BEDSIDE

Long term follow-up following total arterial versus conventional and hybrid myocardial revascularisation: a propensity-match analysis

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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 transaortic revascularisation of non-LAD vessels in addition to the LIMA-LAD graft.

Purpose: To evaluate the impact of the revascularization technique (by means of conventional, total arterial or hybrid myocardial revascularization) in patients with mCAD: primary end-point was overall survival while secondary end-points were cardiovascular mortality, cardiac death, stroke and repeated target vessel revascularization.

Methods: Among 593 consecutive patients undergoing myocardial revascularisation between January 2000 and December 2002, 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 (LIMA/LAD plus PTCA on non-LAD vessels (Group 3, G3, n=489). Matching criteria were: age, sex, left ventricular ejection fraction, number of diseased vessels, NYHA-III, logistic EuroSCORE, peripheral vascular disease, chronic obstructive pulmonary disease, previous stroke, chronic renal failure, dyslipidemia, recent STEMI/STEMI.

Results: Early mortality was 0% in all groups. At a mean follow-up of 6±2 years, the use of total arterial myocardial revascularization was associated with a significantly improved overall survival (G1=90.4±3.5% vs G2=82.3±4.2% vs G3=82.1±5.9%, p=0.049) as well as freedom from MACCEs (G1=95.2±2.4% vs G2=93.8±6.4% vs G3=96±6.9%, p<0.001) while the survival free from cardiac-related death was similar among the groups (G1=97.7±1.6% vs G2=95.1±2.4% vs G3=89.5±5.4%, p=0.08). Finally, at 10 years follow-up, patients undergoing total arterial myocardial revascularisation had a significantly higher freedom from MACCEs (G1=78.9±8.6% vs G2=72.4±5.7% vs G3=62±9.7%, p<0.001)

Conclusions: The use of total arterial revascularization is associated with improved outcomes at mid and long term follow-up compared with conventional or hybrid revascularization. In particular, the use of a hybrid strategy is associated with a significantly higher incidence of myocardial infarction and repeat revascularisation, thereby underlying the need for a careful patients’ selection.

P2152 | BEDSIDE

An evaluation of the incidence and prognosis of post coronary artery bypass grafting myocardial infarction according to different definitions in the CORONARY trial

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Background: Over the years, clinical studies in cardiac surgery have used different diagnostic criteria for post coronary artery bypass grafting (CABG) myocardial infarction (MI). These diagnostic criteria, even though widely accepted, are based on arbitrary biomarker thresholds sometimes in association with ECG signs of cardiac necrosis (new pathologic Q waves or new left bundle branch block). The validation of these diagnostic criteria in terms of their association with clinical events is limited.

Methods: Using data from the CORONARY trial (n=4,752), a randomized controlled trial evaluating on-pump versus off-pump CABG, we evaluated the incidence of MI according to five different post CABG MI definitions. To evaluate the clinical relevance of the definitions, we calculated the associated hazard ratio (HR) for 30-day mortality adjusted for the EuroScore.

Results: Depending on the diagnostic criteria used, the incidence of MI after CABG surgery varied from 0.6 to 19% and the associated HR for 30-day mortality ranges from 2.7 to 6.9. On-pump versus off-pump surgery was not a significant interaction term.

Discussion and conclusion: A clinically relevant post CABG MI definition should be independently associated with mortality. Diagnostic criteria that are associated with a 4.0 to 6.9 fold increase in 30-day mortality may lack sensitivity to identify patients at substantial risk of short-term mortality. Our results illustrate the need for a validated post CABG MI diagnostic criteria formulated from its independent association with important clinical outcomes, especially with the movement towards the use of high sensitivity troponin assays.

P2153 | BEDSIDE

Impact of preexisting cerebral ischemia detected by magnetic resonance imaging on clinical outcomes after coronary artery bypass grafting in patients without history of stroke

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Purpose: We sought to assess the impact of preexisting ischemia detected by brain magnetic resonance imaging and angiography (MRI/MRA) on clinical outcomes after coronary artery bypass grafting (CABG).

Background: Limited data existed for long-term clinical outcomes of asymp-tomatic CABG.

Methods: From January 2003 to May 2009, 3,071 patients underwent CABG in our center. Preoperative brain MRI/MRA was performed in 2,417 patients. Patients with history of stroke were excluded and a total of 2,119 patients were evaluated. Ischemia was detected by brain MRI in 253 patients (group A), but not in remaining 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: 1) The incidence of MACCE (HR) for 30-day mortality adjusted for the EUROscore.

Abstract P2152 – Table 1. MI incidence and 30-day mortality

<table>
<thead>
<tr>
<th>Definition</th>
<th>Criteria</th>
<th>Incidence</th>
<th>HR for 30-day mortality (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Universal Definition</td>
<td>CK-MB &gt;5xULN with ECG abnormalities</td>
<td>50 (1.1)</td>
<td>5.1 (2.2–11.4)</td>
</tr>
<tr>
<td>Universal Definition</td>
<td>CK-MB &gt;10xULN with ECG abnormalities</td>
<td>29 (0.6)</td>
<td>5.3 (2.0–14.2)</td>
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<tr>
<td>Moussa Definition</td>
<td>CK-MB &gt;5xULN or 3xULN with ECG abnormalities</td>
<td>127 (2.7)</td>
<td>6.9 (4.3–11.5)</td>
</tr>
<tr>
<td>CORONARY Definition</td>
<td>CK-MB &gt;5xULN</td>
<td>328 (6.9)</td>
<td>4.0 (2.6–6.2)</td>
</tr>
<tr>
<td>SIRS Study Definition</td>
<td>CK-MB mass &gt;6xULN or activity ≥40</td>
<td>902 (19.0)</td>
<td>2.7 (1.9–4.0)</td>
</tr>
</tbody>
</table>

ULN: 99th percentile upper limit of normal; ECG abnormalities: new pathologic Q waves or new left bundle branch block. *Adjusted for EuroScore.

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Undergoing CABG were related to death, stroke, and MACCE. Conclusion: Further studies are needed to validate these findings, which needs confirmation in a larger clinical trial powered to assess clinical endpoints. 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 11,891 patients (mean age 65.5±9.3 years, 2202 females) who underwent CABG (OPCAB, n=6133; ONCAB, n=5858).

Survival data was complete in 99.2% of patients, with a median follow-up duration of 8 years (interquartile range: 4.8 to 11.8 years; maximum 17.3 years). Both groups were similar in terms of baseline characteristics and intraoperative variables. Euroscore (3.7 (0.03) vs 3.8 (0.03), SMD=0.038) was similar between OPCAB and ONCAB groups and mean number of distal anastomoses performed were 2.5 (0.81) in the OPCAB group and 2.9 (0.78) in the ONCAB group (SMD=0.505). Long-term survival was similar between patients undergoing OPCAB and ONCAB (log-rank test for equality of survivor functions (χ² (1) =2.93; Pr>χ²=0.087); HR for death: 0.94, 95% CI [0.87, 1.01], p=0.087).

Conclusion: In patients undergoing CABG surgery, long term survival is similar using OPCAB and ONCAB strategies.

P2156 | BEDSIDE
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 bypass 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 hsTnT was 616 [396–988] pg/ml in the colchicine group versus 1613 [732–2587] pg/ml in controls (p=0.002). Maximal CK-MB was 44.6 [36.6–68.8] ng/ml and 93.0 [48.0–182.3] ng/ml respectively (p=0.002). The median AUC for hsTnT was 40,755 [20,868–79,176] pg.h/ml in controls versus 20.363 [13.891–31.661] pg.h/ml in the colchicine group (p=0.002). AUCs for CK-MB were 2552 ng.h/ml [1564–4791] in controls and 1586 ng.h/ml [1159–2073] in the colchicine group (p=0.003).

Conclusion: Pre-existing cerebral ischemic findings on brain MRI in patients who undergoing CABG were related to death, stroke, and MACCE.

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 ratio (SMR) and the χ²-test.
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 (epifluorescence microscopy. Fura 2) were analyzed in freshly isolated human myocardial cardiomyocytes (CM). In HF, Ca spark frequency (CaSpF) was increased by 99±25% compared to Hy (n=148/3 vs. 45/5, P <0.05). An inhibition of PP1 and PP2a in Hy using ouabain (OA, 100μM) resulted in an increased CaSpF (by 163±49%, n=36/4 vs. 28/4) and Ca spark frequency (CaSpF) was increased by 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 inhibition increased SR Ca load and amplitude of systolic Ca transients in Hy (P <0.05).

In CCl4-treated and to 157±18% in aortic-ligated RKIP−/− mice per mm2, decreased migration capacity in a modified Boyden chamber by 23%. RKIP-deficient adult cardiac fibroblasts demonstrated increased SR Ca load and amplitude of systolic Ca transients in Hy (P <0.05) in comparison to untreated mice (n=9–10 per group). RKIP−/− mice were treated with CCl4 (0.7 mg/kg, 12 i.p. injections, 6 weeks) to induce cardiac and systemic fibrosis. The cardiac QTLs linked to collagen accumulation were screened for potential candidates by expression QTL analyses, availing of transcriptomic data of CCH-treated BDXs (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 BDX 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 (WT) and C57Bl/6-RKIP-deficient mice (RKIP−/−) were subjected to transverse aortic constriction (TAC, 360 μm) or sham-operation or treatment with CCH4 (6 weeks), untreated mice served as controls (n=9–10 per group). RKIP-deficiency reduced both CCH4-induced interstitial- and TAC-induced replacement fibrosis. In CCH4-treated RKIP−/− and to 61±12% in TAC-operated RKIP−/− compared to the respective control groups. Collagen I and mRNA were reduced by approximately 50% both in TAC and CCH4-treated RKIP−/− mice. RKIP-deficiency increased the number of CD31/CD34-positive cells in TAC mice to 118±5% in CCH4-treated and to 157±18% in aortic-ligated RKIP−/− mice per mm2, decreased the number of fibroblasts per mm2 assessed by immunostaining for intracellular fibronectin in TAC mice by 20±5%, the percentage of cycling Ki-67-positive fibroblasts in CCH4-treated mice to 23±18% and the percentage of CXCR4-positive fibroblasts in TAC mice to 74±8%. RKIP-deficient adult cardiac fibroblasts demonstrated increased migration capacity in a modified Boyden chamber by 23%. RKIP-deficiency diminished cardiomyocyte apoptosis in CCH4-treated mice to 39±13% and in aortic-ligated mice to 31±10%. Heart weight to tibia length ratio, cardiomyocytes across-sectional area and the percentage of Ki-67-positive cardiomyocytes were decreased in RKIP-deficient aortic-ligated mice. All effects were significant with p <0.05.

Conclusions: These data identify Raf Kinase Inhibitor Protein as an important regulator of interstitial and replacement cardiac fibrosis.
the underlying cause of heart failure, with benefit of EX after myocardial infarction (MI) but not during aortic stenosis. Here we tested the hypothesis that the balance between nitric oxide (NO) and superoxide (O2-) is responsible for these divergent effects of EX, and is due to differential effects of EX on endothelial NO synthase (eNOS) function.

**Methods:** Mice were exposed to 8 wk of voluntary wheel running EX or sedentary housing (SED) after MI, transverse aortic constriction (TAC), or sham (SH). Left ventricular (LV) function was measured by echography. Picro-sirus Red staining was used to assess collagen content. Total and NOX-dependent LV O2- production was studied using lucigenin-enhanced chemiluminescence without or with NOX inhibitor L-NAME. Peroxynitrite (ONOO-) formation was studied using luminol-enhanced chemiluminescence. eNOS uncoupling was measured by western blot. eNOS-S-glutathionylation was measured by coimmunoprecipitation. Results: Increased LV dysfunction and fibrosis in MI but not TAC (Table). Strikingly, O2- generation was blunted by EX in MI, but exacerbated by EX in TAC, which was largely NOX-dependent. eNOS uncoupling was corrected by EX in MI but aggravated in TAC mice, in parallel with attenuation and exacerbation of both NOXO- levels and glutathionylation of eNOS by EX in MI and TAC, respectively.

**P2162 | BENCH**

Regulation of fetal gene reprogramming by the early-onset myocardial infarction associated PHACTR1 gene in the heart

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**Background:** Phosphatase and actin regulator 1 (PHACTR1) locus is one of the most often identified genome-wide association studies hit for coronary artery disease and myocardial infarction (MI). However, the function of PHACTR1 in the heart is still unknown.

**Purpose:** We characterized the mechanisms regulating Phactr1 expression in the heart and investigated the effects of Phactr1 gene delivery on cardiac function. Moreover, we investigated whether delivery into the heart 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 < 0.001 vs corr. SED). When the direct myocardial effects of Phactr1 were studied, 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 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 cardiac function (n=1550).

**Conclusions:** Phactr1 regulates reprogramming of cardiac gene expression, particularly skeletal to cardiac α-actin isoform ratio.

**P2165 | 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 remodeling accompanied by accumulation of collagen is known to be important for scar formation. Excessed collagen production leads to cardiac fibrosis and impaired cardiac function. As matrix-degrading enzymes matrix-metalloproteinases (MMP) are key mediators during these cardiac remodeling processes. The MMP-13 is considered to be the major metalloproteinase collagenase in MI.

**Methods and results:** In this study, we induced MI in wild type and MMP13 knock-out mice. Five days after MI mice deficient for MMP13 showed an aggravation in survival and hemodynamic function compared to wild type animals. In both mice strains a clear scar formation with an accumulation of collagen could be 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 remodeling processes. As MMP13 deficient mice had isolated pronounced 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 ECTs derived from MMP13 deficient fibroblasts were less functional.

**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**

**P2164 | BENCH**

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. Even ambulatory central blood pressure monitor 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 could be assessed by 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 120 patients undergoing elective coronary angiography in
this study. Brachial and central BP values 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 brachial/aortic BP (ccSBP, ccBP) and calibration with carotid/aortic BP (CcBP). Mean central pulse pressure (MPP) as aortic systolic BP minus mean arterial BP and fractional pulse pressure (FPP) as pulse pressure over mean BP.

Results: In CcBP, Central systolic BP (ccSBP), cPP and FPP values did not significantly differ between low and normal EF group (ccSBP: low EF: 154±29 mmHg, normal EF: 145±21mmHg, P=0.11; cPP: low EF: 63±21mmHg, 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 ones in both groups, whereas mean difference in ccSBP was markedly better in normally contracting patients (ccSBP: normal EF group: low EF r=0.76, difference-7.15±19.7mmHg, normal EF r=0.71, difference-0.15±16.8; cPP: low EF r=0.69, difference10.1±18.0mmHg, normal EF r=0.70, difference14.7±14.4mmHg; FPP: low EF r=0.56, difference0.09±10.15, normal EF r=0.56, difference0.14±0.14). CcBP consistently showed inferior accuracy compared to CcBP 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 arterial BP consistently shows better data accuracy.

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 2576 patient with no use of beta blocker and less than 400Ng/m 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 80bpm) 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: 17.8–21.6] vs. 15.1 [13.7–16.6]mg/gcre, P<0.001). PWV in the top quintile (174 [1745–180]cm/s) was significantly higher than in the lowest (in the 1572 [1543–160]cm/s, P<0.001) and second quintile vs 1543–160)cm/s, P<0.001) and second quintile (vs 1543–160)cm/s, P<0.001) and second quintile (vs 1543–160)cm/s, P<0.001) and second quintile (vs 1543–160)cm/s, P<0.001.

Conclusion: Increased resting pulse rate is associated with organ damage, but is negatively associated with arterial pulse volume overload.

P2167 | BEDSIDE
Broad P wave is associated with brain natriuretic peptide, left atrial dimension, length of hypertension history and hypertensive medication in hypertensive patients

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Purpose: High P wave duration is a predictor of atrial fibrillation. The aim of this study was to clarify the associations among P wave duration, left atrial dimension and brain natriuretic peptide (BNP) in hypertensive patients.

Methods: We enrolled 3,511 patients who had at least one cardiovascular risk factor. We conducted electrocardiography and measured the serum BNP levels.

A significant higher percentage of males (82% vs. 45%, p<0.001), significantly higher BNP (median BNP 21.8 vs. 17.6 pg/ml, p<0.006), significantly longer histories of hypertension (10.0±9.7 vs. 8.2±8.7 years, p<0.001) and significantly longer durations of hypertension medication (5.8±6.4 vs. 6.5±7.8 years, p<0.001) compared to the narrow P wave group (maximum P wave duration <120 ms, n=3,236). Office systolic and diastolic blood pressure values were similar in both groups. The left atrial diameter was significantly larger in a broad P wave group (n=89) compared to a narrow P wave group (n=1,165) (39.6±5.5 vs. 37.0±5.4 mm, p<0.001). Broad P wave was a significant independent predictor of BNP and left atrial diameter (BNP: p=0.08, p<0.001; left atrial diameter: p=0.10, p<0.001) after adjusting for age and gender.

Conclusions: Broad P wave in hypertensive patients was associated with the length of their hypertension history, left atrial dimension and BNP level.

P2168 | BEDSIDE
Aortic pulsatility assessed by a brachial cuff-based oscillometric 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 Mobil-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 (FPP) 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 FPP (PP: brachial 48±15.2 vs 55.0±16.2mmHg, aortic 51.7±19 vs 62.3±19.9mmHg; FPP: 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±2.3mmHg; p<0.05), Pb (21.7±7.8 vs 26.7±6.5mmHg; p<0.05) and lower value of PPA (0.65±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 FPP, aortic PP, aortic PWV, PPA and Pb were associated with the presence of CAD. Among them, when aortic FPP was entered into the multivariate logistic regression model, each with hemodynamic index, only aortic FPP remained an independent predictor for the presence of CAD. When brachial FPP was entered into the model instead of aortic FPP, brachial FPP remained a significant predictor independent of PPA and PWV (see table).

Conclusions: Aortic FPP is most strongly associated with the presence of CAD among indices derived from a brachial cuff-based oscillometric device. Even brachial FPP could be a superior predictor over PWV and PPA.

P2169 | BEDSIDE
Aortic-to-upper arm pulse wave transit time ratio can predict the risk of coronary artery disease and stroke better than pulse wave velocity

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Background: The major limitation of carotid-femoral pulse wave velocity (cPWV) is the less accurate measurement of pulse wave travel length (PWTL). We evaluated the usefulness of carotid-femoral to carotid-radial pulse wave transit time (PWTT) ratio in the risk prediction of cardiovascular disease, not using PWTL.

Methods: Patients with coronary artery disease (CAD, n=80, 62±8.6 years), and stroke (Stroke, n=62, 65±9.1 years) were compared to individuals without history of cardiovascular or cerebrovascular disease (Control, n=104, 52±9.8 years). PWTT ratio was measured with pulse waves which were obtained from carotid, femoral and radial arteries, simultaneously. Carotid-femoral PW (cf-PWV) was calculated.

Results: Patients with cardiovascular disease (CAD + Stroke) had higher cfPWV ROC curves comparison

<table>
<thead>
<tr>
<th>Variables</th>
<th>Brachial FPP</th>
<th>Aortic FPP</th>
<th>PWV</th>
<th>PPA</th>
<th>Pb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic FPP</td>
<td>3.11 (1.02–9.46)*</td>
<td>4.74 (1.43–15.8)*</td>
<td>2.10 (1.04–4.24)</td>
<td>3.23 (1.53–6.81)**</td>
<td>3.83 (1.39–10.59)**</td>
</tr>
<tr>
<td>Brachial FPP</td>
<td>–</td>
<td>2.15 (0.71–6.53)</td>
<td>0.62 (0.15–2.51)</td>
<td>2.93 (1.23–6.98)*</td>
<td>1.96 (0.98–3.91)*</td>
</tr>
</tbody>
</table>

Abstract P2168 – Table 1. Odds ratios of aortic/brachial FPP

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(9.5±4.95 vs 7.67±2.96 mmHg, p < 0.001) and lower PWTT ratio (0.79±0.15 vs 1.01±0.19, p < 0.001) compared to control group. A significant difference of cf-PPW (p<0.038) and PWTT ratio (p<0.003) between groups were present in adjudicted analysis. In a multivariate logistic analysis, after controlling for age, gender, body mass index, diabetes, hypertension, hyperlipidemia, smoking, and eGFR, the middle and lowest tertile of PWTT ratio were associated with increased risk of CAD or stroke (OR 3.542, 95% CI 1.299–9.733, p=0.014; OR 6.090, 95% CI 1.790–20.715, p<0.004, respectively), but the highest tertile of cfPWV was not associated. Area under the curve of PWTT ratio was higher compared to that of cfPWV (AUC 0.823 vs 0.790, p=0.001).

Conclusion: Our study is suggesting that PWTT ratio is better than cfPWV in the risk prediction of cardiovascular disease.

P2170 | BEDSIDE
Abdominal adiposity distribution quantified by ultrasound and incident hypertension in a general population
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Background: Abdominal obesity is a major risk factor for hypertension. However, different distributions of adipose tissue may affect hypertension risk differently. Subcutaneous adipose tissue (SAT) is located beneath the skin and is relatively metabolically inactive. Visceral adipose tissue (VAT) is located around the internal organs and is highly metabolically active.

Purpose: To explore the association of SAT and VAT with both prevalent and incident hypertension in a population-based setting. We hypothesized that VAT, rather than SAT, would be independently associated with both prevalent and incident hypertension.

Methods: SAT and VAT 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 further followed for a median of five years. We constructed multiple logistic regression models to compute standardized odds ratios (ORs) with 95% confidence intervals (CIs) per standard deviation (SD) increase in SAT and VAT.

Results: We recorded 1,027 persons with prevalent hypertension and 203 persons with incident hypertension at the five-year follow-up examination. Mean SAT was 3.0 centimeters and mean VAT was 6.5 centimeters. SAT and VAT were significantly linearly associated with systolic and diastolic blood pressure. However, in models including both SAT and VAT, and adjusting for overall adiposity (BMI and waist circumference), and traditional risk factors for hypertension such as age, sex, smoking status, diabetes mellitus, family history of hypertension and in the incident model also baseline blood pressure, only VAT was significantly associated with prevalent and incident hypertension; OR 1.32 (95% CI 1.16–1.51, p<0.0001) and OR 1.33 (95% CI 1.01–1.74, p<0.040) per one SD increase, respectively (P for SAT: 0.61).

Conclusion: VAT, but not SAT, as a measure of abdominal adiposity, is independently associated with both prevalent and incident hypertension in a random sample of Danish adults. Thus, ultrasonic VAT measurements provides thephysician an easy and non-invasive method to pinpoint those individuals in greater risk of becoming hypertensive.

P2171 | BENCH
Haemodynamic effects of adenosine adsorbed on silica nanoparticles
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Introduction: A promising vehicles for targeted drug delivery (TDD) to the ischimic myocardium are silica nanoparticles (SNP). TDD achieves higher drug concentration in target organs and minimizes side effects. According to our hypothesis, the adsorption of adenosine (ADN) on SNP may reduce the negative side effects of ADN, particular, arterial hypotension. The purpose of this study was to evaluate the effects of intravenous infusion of SNP-adsorbed ADN on blood pressure as compared to the effects of free ADN in the equivalent volume.

Materials and methods: Experiments were performed on male Wistar rats weighing 200–250 g anesthetized with sodium pentobarbital (80 mg/kg i.p.). To register mean arterial pressure (MAP) we used the software and hardware PhysExp. Carotid artery was cannulated for MAP measurement. The samples were injected into the femoral vein during 10 min. The animals were randomized into middle and at volume of 1 ml, 2) ADN+SNP2 - the same dose of ADN adsorbed on SNP at a concentration of 2 mg/ml, 3) ADN+SNP2+T80 - the same as in group ADN+SNP2, but with the addition of stabilizer Tween 80 (polyethylene glycol sorbitan monolaurate). The amount of cross-linking, LOXL2 and hemodynamic function were studied after 10 weeks. Histological function was performed invasively and by echocardiography. The amount of collagen, collagen cross-linking and LOXL2 were studied in endomyocardial biopsies. Transcardiac constriction (TAC) was performed in mice and an anti-LOXL2 antibody was administered 2 weeks after TAC. The amount of collagen, cross-linking, LOXL2 and hemodynamic function were studied after 10 weeks. Furthermore, the effects of LOXL2 inhibition by knockdown of the LOXL2 gene was studied on isolated murine cardiac fibroblasts stimulated with TGF-β.

Results: Patients with HPFEF showed a significantly higher amount of collagen I and total collagen compared to healthy controls. LOXL2-expression was 2.5 times higher in HPFEF patients and was correlated with significantly higher collagen amount and collagen cross-linking compared to controls. Higher LOXL2 levels, total collagen and collagen cross-linking were associated with higher filling pressures and increased left ventricular stiffness. Mice showed a significant cardiac hypertrophy, increased interstitial fibrosis, collagen cross-linking and LOXL2 amount, as well as progressive diastolic and systolic dysfunction 10 weeks after TAC. Administration of an anti-LOXL2 antibody decreased the degree of cardiac fibrosis and significantly improved hemodynamic function.

Isolated cardiac fibroblasts showed an increased migratory capacity after TGF-β treatment, which was reduced after LOXL2-knockdown. Furthermore, LOXL2-knockdown significantly inhibited intracellular TGF-β signaling by decreasing downstream mediators of TGF-β.

Conclusions: Myocardial LOXL2 is increased in clinical and experimental HFPEF and leads to higher myocardial fibrosis, collagen cross-linking and LV stiffenss. Inhibition of LOXL2 ameliorated myocardial fibrosis and LV stiffness by decreasing total collagen amount, collagen cross-linking and activation of cardiac fibroblasts. Inhibition of LOXL2 might be a novel therapeutic target in patients with HPFEF and progressive myocardial fibrosis.

2205 | BENCH
Lysyl oxidase-like-2 inhibition decreases cardiac fibrosis and improves diastolic dysfunction in experimental and clinical heart failure with preserved ejection fraction
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Purpose: Lysyl oxidase-like-2 (LOXL2) promotes cross-linking of fibrillar collaegene fibrosis. Chronic inhibition of LOXL2 prevents progression fibrosis. Hence, inhibition of LOXL2 would be associated with both prevalent and incident hypertension.

Methods: We investigated 41 HPFEF and control patients. Assessment of diastolic function was performed invasively and by echocardiography. The amount of collagen, collagen cross-linking and LOXL2 were studied in endomyocardial biopsies. Transcardiac constriction (TAC) was performed in mice and an anti-LOXL2 antibody was administered 2 weeks after TAC. The amount of collagen, cross-linking, LOXL2 and hemodynamic function were studied after 10 weeks. Furthermore, the effects of LOXL2 inhibition by knockdown of the LOXL2 gene was studied on isolated murine cardiac fibroblasts stimulated with TGF-β.

Results: Patients with HPFEF showed a significantly higher amount of collagen I and total collagen compared to healthy controls. LOXL2-expression was 2.5 times higher in HPFEF patients and was correlated with significantly higher collagen amount and collagen cross-linking compared to controls. Higher LOXL2 levels, total collagen and collagen cross-linking were associated with higher filling pressures and increased left ventricular stiffness. Mice showed a significant cardiac hypertrophy, increased interstitial fibrosis, collagen cross-linking and LOXL2 amount, as well as progressive diastolic and systolic dysfunction 10 weeks after TAC. Administration of an anti-LOXL2 antibody decreased the degree of cardiac fibrosis and significantly improved hemodynamic function.

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Conclusions: Myocardial LOXL2 is increased in clinical and experimental HFPEF and leads to higher myocardial fibrosis, collagen cross-linking and LV stiffenss. Inhibition of LOXL2 ameliorated myocardial fibrosis and LV stiffness by decreasing total collagen amount, collagen cross-linking and activation of cardiac fibroblasts. Inhibition of LOXL2 might be a novel therapeutic target in patients with HPFEF and progressive myocardial fibrosis.

2206 | BENCH
Chronic inhibition of Na+/Ca2+ exchanger (NCX) with SEA0400 improves cardiac function in a model of heart failure with preserved ejection fraction
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Background: Heart failure with preserved ejection fraction (HFpEF) is increasingly common but there are currently no established therapeutic strategies, mostly because the underlying cellular mechanisms are not well understood. We have previously shown in a rat model of HPFEF with chronic kidney disease that left ventricular (LV) cardiomyocyte Ca2+ transient decay is slowed, possibly related to altered function of the Na+/Ca2+ exchanger (NCX). Therefore we investigated the effects of chronic inhibition of NCX with SEA0400 on cardiac function in this HPFEF model.

Methods: Young male Wistar rats were subjected to subtotal nephrectomy (NXT) or sham operation (SOP). 8 weeks after intervention chronic treatment for 16 weeks with the NCX inhibitor SEA0400 (1mg/kg body weight) was started. At 24 weeks non-invasive blood pressure measurements, echocardiography, pressure-
In cardiac biopsies, both TIMP-1 (73.2±13.4 ng/ml vs. 13.6±2.2 ng/ml; p<0.001) and TIMP-2 (22.2±2.5 ng/ml vs. 14.5±1.2 ng/ml; p<0.001) were much higher in the border that in the remote zone, indicating higher inhibition of MMP-related extracellular matrix degradation.

At follow-up, SVR was associated with a significant reduction of LV volumes (EDVI from 225±11 to 198±11 ml/m²; p<0.01) and a significant increase of LVEF (8±4% vs. 11±2%; p<0.01). By multivariate analysis, risk factors for PGF were donor age (OR: 1.02; 95% CI: 1.01–1.03; p<0.001) and cardiopulmonary bypass time (OR: 1.02; 95% CI: 1.01–2.10; p<0.01) and cardioplegia (OR: 1.01; 95% CI: 1.01–2.01; p<0.01) and cardioplegia (OR: 1.01; 95% CI: 1.01–2.10; p<0.01) and cardioplegia (OR: 1.01; 95% CI: 1.01–2.01; p<0.01) and cardioplegia (OR: 1.01; 95% CI: 1.01–2.01; p<0.01). The combination of TIMP-1 and TIMP-2 was a powerful predictor of PGF (AUC: 0.81; 95% CI: 0.76–0.87; p<0.001).

Conclusions: The combination of TIMP-1 and TIMP-2 is a powerful predictor of PGF. This might be a useful tool to identify patients at higher risk for PGF.
which included TAPSE <1.60m (1 point), RV S' <5 cm/sec (2 point), LAD >45mm (1 point) and E/E' < 20 (1 point). The Echo-RVF score was significantly associated with RVF development post-LVAD (odds ratio [OR] 2.19, 95% CI [confidence interval] 1.50–3.46, p < 0.001). The ROC curve analysis identified the Echo-RVF score of 2, 3, and 4 can discriminate patients in RVF group from those in non-RVF group with sensitivity and specificity of 92.0 and 42.8% (score=2), 84.0 and 65% (score=3), and 72.0 and 86.4% (score=4), respectively (ACU=0.78836).

Conclusions: The Echo-RVF score, which included parameters reflecting right ventricular systolic impairment and left ventricular diastolic dysfunction before LVAD surgery, can effectively risk-stratify patients who may develop RVF following LVAD.

2211 | BEDSIDE
Diastolic dysfunction is prognostic of long-term mortality in liver transplant recipients

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Background: Diastolic dysfunction is the commonest finding among cirrhotic patients with subclinical cardiac cardiomyopathy. However its prognostic value after liver transplant (LT) has not been evaluated.

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 diseases were excluded. Only 1,248 LT recipients with ejection fraction (EF) ≥ 55% were included in this analysis. Diastolic dysfunction in cirrhosis was defined as a ratio of the early to late ventricular filling velocities (E/A) ratio value <1, according to the World Congress of Gastroenterology consensus.

Results: The prevalence of diastolic dysfunction was 20% in cirrhotic patients with EF ≥ 55%. Patients with diastolic dysfunction were older (59±7 vs 51±11 years; p<0.0001) and had greater preexisting cardiovascular comorbidities compared to those with normal diastolic function (p<0.05). During 5.9 years follow-up after LT, the mortality of patients with diastolic dysfunction was 5.0% vs. 3.6% per person-year in those without diastolic dysfunction (HR 1.4, 95% CI 1.1–1.8; p=0.02) (Figure). Other traditional cardiovascular risks including preexisting cardiovascular comorbidities, hypertension, hyperlipidemia and obesity were also independently associated with the mortality (p<0.05 for all).

Conclusion: Among cirrhotic patients with normal ejection fraction, diastolic dysfunction independently predicts post-liver transplant mortality during long-term follow-up.

2212 | BEDSIDE
Clinical significance of elevated diastolic pressure gradient in heart failure with preserved ejection fraction

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Background: Pulmonary hypertension due to heart failure with preserved ejection fraction (PH-HFpEF) is common in elderly patients and is associated with poor outcome. A subset of affected individuals has a combined pre- and postcapillary PH (Cpc-PH). Pathophysiological mechanisms cannot be explained by a simple backward transmission in left-sided filling pressures. The diastolic pressure gradient (DPG) with a cut-off of 7mmHg has been recently suggested to distinguish between patients with isolated postcapillary PH (Ipc-PH) and Cpc-PH.

Purpose: The clinical significance and predictive value of DPG remains to be elucidated in this specific disease entity.

Methods: Patients with HfPEF diagnosed according to current ESC guidelines were enrolled in our prospective registry. Borderline PH was defined as a mean pulmonary arterial pressure (mPAP) between 21–24mmHg, and manifest PH was defined as a mPAP ≥25mmHg. DPG was calculated as the difference between diastolic PAP and mean pulmonary arterial wedge pressure. Hospitalization for heart failure and death for cardiac reason were defined as the primary study endpoint.

Results: Between December 2010 and December 2014, 193 HfPEF patients were registered. 19 patients refused right heart catheter and were excluded. Of the remaining 174 patients, 11 (6.3%) had no PH, 15 (8.6%) had borderline PH and 148 (85.1%) a manifest PH. PH patients (66% females, mean age 70±7 years) were further sub-classified into Ipc-PH (n=126) and Cpc-PH (n=22).

Patients with a Cpc-PH had a shorter six-minute walk distance (253.5±128.7 m versus 318.4±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 ventricles (42.1±8.9 mm versus 37.4±7.1 mm, p<0.010) and a lower capillary oxygen partial pressure (63.4±9.8 mmHg versus 73.3±11.6 mmHg; p<0.001) compared to patients with Ipc-PH. During a median follow-up time 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 p<0.001).

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 ejection fraction: are factors associated with all-cause and heart failure rehospitalization different?

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Background: Rehospitalization in heart failure is frequent and is associated with worse outcome and increased health-care costs. Many of the studies that have analyzed factors associated with readmission have studied patients from randomized controlled trials or patients with heart failure with reduced ejection fraction (HFrEF). Therefore, the aim of this study was to identify factors associated with readmission in a real-world heart failure cohort and analyze whether differences exist between HFrEF and heart failure with preserved ejection fraction (HFpEF).

Methods: Post-hoc analysis of a single-center prospective cohort of 1072 patients with reduced (n=559) and preserved (n=513) chronic heart failure. HfPEF was defined as an ejection fraction >45%. The association of all-cause rehospitalization (ACR) and heart failure rehospitalization (HFR) with baseline characteristics was assessed using a χ2 and t-test, both in HfPEF and HFpEF. Multivariable Cox proportional hazard regression models to evaluate the effect of ejection fraction (HFrEF vs. HfPEF) on all-cause (ACR) and heart failure rehospitalization (HFR) were developed.

Results: During a median follow-up of 10 [5.5–15.8] months, ACR and HFR rate were 47% and 29%, respectively. Four factors were independently associated with HFR in Cox analysis both in HfPEF and HfPEF: previous hospitalization due to heart failure the last year (HR 2.2; 95% CI 1.2–3.9) in HfPEF and HR 2.8; 95% CI (1.5–5.5) in HfPEF, chronic obstructive pulmonary disease (COPD) (HR 1.8, 95% CI (1.2–2.5) and HR 1.4, 95% CI (1.0–2.0), respectively), NYHA functional class III-IV (HR 1.5, 95% CI (1.1–2.1) and HR 1.6, 95% CI (1.1–2.2), respectively) and heart rate >70 beats per minute (HR 1.5, 95% CI (1.1–2.1) and HR 1.4, 95% CI (1.0–1.9), respectively), all p<0.05. Anemia (HR 1.4, 95% CI (1.1–1.9), p=0.044) and log-Nt-proBNP (HR 1.4, 95% CI (1.1–1.9), p=0.048) were associated with HFR in HfPEF but not in HfPEF. The presence of COPD, anemia, history of heart failure the previous year, heart rate >70 beats per minute and log-Nt-proBNP were independently associated with ACR in both HfPEF and HfPEF. In HfPEF, NYHA class III-IV was also associated with ACR.

Conclusions: Heart failure hospitalization the previous year, COPD and heart rate >70 beats per minute are independently associated with ACR and HFR both in HfPEF and HfPEF. Other factors frequently associated with ACR and HFR are NYHA functional class III-IV, log-Nt-proBNP and anemia. These factors allow the identification of patients at high-risk of readmission.

2214 | BENCH
The Cardiac Protease-Activated Receptor 2 expression is crucial for the maintenance of the cardiac function in the aged heart


Purpose: Elderly patients often suffer from left ventricular hypertrophy and di-
astolic dysfunction with preserved systolic function resulting from ongoing cardiomyocyte 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 examine 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 microconductance 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 immunofluorescence assay on adult cardiac fibroblasts. The PAR2 gene expression was determined in myocardial biopsies from HFPEF patients.

**Results:** 1 yr 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/gelatin III ratio revealed a fibrosis in PAR2ko mice but not in wt mice (p<0.05). Moreover, adult cardiac PAR2ko fibroblasts also showed an increased collagen I release into the supernatant compared to wt fibroblasts. Furthermore, the TGFβ-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 yrs old mice pointed also to an increased oxidative stress in PAR2ko mice compared to wt mice (wt vs PAR2ko: 8.3±1.59 vs. 4.8±1.53, p<0.05). These results indicate that the loss of PAR2 is associated with elevated oxidative stress, which leads to fibrosis and an impaired heart function. In HFPEF patients a decreased PAR2 expression was associated with severe diastolic dysfunction and vice versa.

**Conclusion:** The cardiac PAR2 expression is essential for the maintenance of the heart function in the aged heart. The loss of PAR2 results in increased oxidative stress, an age-dependent cardiac fibrosis and a left ventricular diastolic dysfunction.

**OBESITY – THE GLOBAL THREAT!**

**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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**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.

**Results:** 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 different intervention periods and doses.

**Conclusion:** Increased %VAT is independently associated with the incident of MACE, indicating that adipose tissue composition is a useful predictor of cardiovascular outcome.
green tea supplementation duration of 8 weeks (WMD: 0.029 mg/L, 95% CI: −0.229–0.288, p<0.028) and >8 weeks (WMD: 0.099 mg/L, 95% CI: −0.555–0.754, p<0.766). Likewise there was no significant effect in subgroups of studies with total catechins doses <400 mg/day (WMD: 0.073 mg/L, 95% CI: −0.251–0.398, p=0.658) and >400 mg/day (WMD: 0.213 mg/L, 95% CI: −0.148–0.574, p=0.247). The effect size were not significant after stratification of studies to those recruiting healthy subjects (WMD: −0.028 mg/L, 95% CI: −0.216–0.160, p=0.769), and those recruiting subjects with cardiometabolic diseases (WMD: 0.260 mg/L, 95% CI: −0.815–1.334, p=0.636).

Conclusions: The results of this meta-analysis did not indicate a significant effect of supplementation with green tea catechins on plasma CRP concentrations. Further, well-designed trials are necessary to validate these results.

2230 | BEDISE
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 eliminate the dependence of QT on HR.

Purpose: This study aimed to validate the association of obesity with QT-prolongation and to verify that changes of a period of low-calorie diet and physical training are similar in uncorrected QTc (QTc) in obese patients using different methods for QT correction.

Methods: In a prospective longitudinal study QT was determined in 318 severely obese subjects (BMI 41±23 kg/m²) participating in a multimodal weight reduction program and in 45 healthy lean controls (BMI 22±5 kg/m²). The HR corrected QTc was calculated using 8 established methods.

Results: The uncorrected QT was similar in obese and healthy lean subjects (389±32 vs. 399±33 ms; ns, p<0.130). As expected obese had a significantly higher HR than lean subjects (72±15 vs. 64±12 bpm; p<0.001). Obese had a higher HR corrected QTc when using Bazett’s and Ashman’s formulae, and Karajalainen’s nomograms, but 5 alternative correction methods, including Friderica, Sages-Frameingham, Hodges, Rautaharju and Pfeifer, revealed comparable QTcs in obese and lean subjects. Analogue 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 (15,9±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 is clearly relevant changes in the QT interval. The BMI should be considered when using Bazett’s HR correction.

Acknowledgement/Funding: This study was supported by internal funds from the University of Regensburg

2231 | BEDISE
Nutritional state predicts long-term survival in heart failure
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Introduction: NICE recommends screening for malnutrition. We hypothesize that the unassessed NUTRITION STATUS INDEX (CONUT) score predicts all-cause mortality in heart failure patients.

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 female. 1131 males, office blood pressure (BP)=143/89 mmHg) free of cardiovascular disease (CAD) in a cohort of patients with heart failure (position 1). Median survival time was 40 months (21,86). 1660 (45%) had preserved systolic function (EF >50%) and 88% had preserved systolic function (EF <50%).

Results:

<table>
<thead>
<tr>
<th>Malnourishment degree</th>
<th>Normal</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>73 (64, 79)</td>
<td>75 (68, 80)</td>
<td>76 (70, 81)</td>
</tr>
<tr>
<td>Sex, % female</td>
<td>698 (52%)</td>
<td>574 (35%)</td>
<td>402 (27%)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25 (4, 33)</td>
<td>27 (14, 42)</td>
<td>32 (17, 51)</td>
</tr>
<tr>
<td>NT pro BNP, ng/L</td>
<td>871 (372, 1835)</td>
<td>1305 (552, 2931)</td>
<td>3882 (1665, 7890)</td>
</tr>
<tr>
<td>Preserved systolic function (%)</td>
<td>546 (33%)</td>
<td>518 (31%)</td>
<td>88 (40%)</td>
</tr>
<tr>
<td>LVMI, g/m²</td>
<td>43 (33, 55)</td>
<td>43 (32, 52)</td>
<td>40 (29, 51)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>672 (46%)</td>
<td>726 (44%)</td>
<td>133 (40%)</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>125 (127, 148)</td>
<td>131 (12, 143)</td>
<td>118 (10.6, 12.9)</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L</td>
<td>96 (81, 117)</td>
<td>102 (84, 129)</td>
<td>118 (91, 155)</td>
</tr>
</tbody>
</table>

Conclusions: Our findings suggest that the nutritional state, independent of age, sex and NTproBNP, can be used to predict survival in patients with heart failure.

2232 | BEDISE
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 patients with essential hypertension.

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 the 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. Waist to hip ratio (WHR) was also calculated. Adiposity index (BMI) and LVMI were obtained after statistical analysis. Receiver Operating Characteristic (ROC) analysis determined the critical values that optimally discriminated between patients with or without CAD. Logistic regression analysis was used to examine the association between the risk factors and the endpoints.

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), LVMI (117±26.8 vs 103.3±27 g/m², p<0.001) and prevalence of LVH (43% vs 26%, p<0.014). No difference was observed between hypertensives with 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 LVMI (HR 1.012, p=0.003) were independent predictors of CAD.

Conclusions: In essential hypertensives 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 | BEDISE
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 2001–2002 and included 3042 participants free of CVD at baseline (48.6%, 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 hyperlipidaemia under statin therapy that had uncharacteristically dietary habit (coast tertile) had 75% increased CVD risk than normalipidemic 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 64 were monozygotic (MZ) pairs (age: 55.7±9.7 years) and 42 were dizygotic (DZ) pairs (age: 58.1±18.7 years). All subjects were investigated by using 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, intra-pair correlations were calculated. With the use of structural equation models these correlations were broken down to additive genetic (A), common (C) and unique (E) environmental correlation components.

Results: The EFV was 98.1±45.2 cm³, the WC was 98.0±14.1 cm, and the BMI was 27.8±5.6 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; MWCr=0.70, rDZWCr=0.40; rMzBMI=0.67, rDZBMI=0.16; all p<0.05), which implies a strong genetic dependence of these parameters. The structural equation models confirmed these findings: AEFV=78%, AWC=71%, ABMI=66%; EEFV=25%, EWC=39%, EBM=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 independently with two times higher frequency of overweight and obesity. “Prescription to eat” reduces the overweight and obesity rate by 32%.

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. Cholera-toxin-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 characterise 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 choleratoxines 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 chimeras generated by fusion of the cAMP reporter to Tnpl (part of the troponin complex at the sarcomere), AKAP18d (part of the SERCA/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 isoproterenol the cAMP response is significantly smaller at the sarcomere than at Tnpl complexes, but it is bigger compared to AKAP79 and AKAP18d. In contrast, the cAMP increase generated on application of the non-selective phosphodiesterases (PDEs) inhibitor, IBMX 100 μM was identical in the three subcompartments, indicating a key role of PDEs in the local regulation of cAMP. Myocytes treated with
Isolating 0.3nM of IBMX 100uM to generate the same amount of global cAMP an increase in contractility with both treatments but interestingly the increase was significantly higher than βAR stimulation than on PDEs inhibition. Such difference is calcium independent as both treatments elicited an identical increase in the calcium transient. These findings highlight 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/10/75/282537, RG/12/3/29423 and PG/15/5/31110

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 Ca2+ release via cardiac ryanodine receptor (RyR2) and therapeutic effects of RyR2 stabilization by inhibiting phosphorylating activity, or by dantrolene, which stabilizes RyR2 structurally, in transgenic mouse (TG) model with FHC–related TnT mutation (delta160E).

Methods and results: 6-months-old 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)

ISO 0.3nM or IBMX 100

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 (42.1%; vs ISO-treated–non-TG 14%), whereas it was again attenuated by KN-93 (15.8%), but not significantly by H-89 (33.0%). The events of aberrant Ca2+ release through RyR2 in ISO-TG were reproduced by adding ETYA-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 sCaT (5.4±0.3; p<0.05 vs ISO-TG) and sCaT (25.9% in TG).

Conclusions: In FHC–linked cTnT 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 growing 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, FF-0646609, FF-0646667) on cardiac contractility were tested in non–falling 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, GLP-1R-agonists depressed on isolated 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, FF-0646667. 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 force in human atrial trabeculae, whereas GLP-1(9–36)NH2 had no effect. Exendin (9–39)NH2, a GLP-1R–partial agonist, and H-89 blunted the positive inotropic 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 increased 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 myocaradial function and remodeling.

RESISTANT HYPERTENSION

2264 | BEDSIDE

Prevalence and comorbidity of resistant hypertension in community patients with treated uncontrolled hypertension

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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±11.3 years, and 1502 (48.3%) of the participants were female. 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 in patients with RH were 8.1%. 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 multicomorbidity (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

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Background: Prevalence and comorality of resistant hypertension (RH) with respect to its severity is limited.

Purpose: We investigated the cardiovascular risk of severe RH 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/or 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 RH. Three groups were identified depending on presence of RH (office–based uncontrolled hypertension under at least 3 drugs including a diuretic) and levels of office systolic BP 118 patients (70%) without RH, 313 (18%) with not–severe RH (systolic BP 160mmHg) and 200 (12%) with severe RH (systolic BP>160mmHg). Endpoint of interest was cardiovascular morbidity set as the composite of coronary heart disease and stroke.

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 RH, 12.4 cases per 1,000 person–years in the group with not–severe RH and 16.5 cases per 1,000 person–years in the severe RH group. Unadjusted analysis showed that compared to uncontrolled patients without RH, patients with not–severe RH exhibited a similar risk but patients with severe RH had a significantly higher risk by 2.5 times (CI: 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 RH remained as an independent predictor of the cardiovascular outcome, (OR: 2.57, CI: 1.27–5.19, P=0.008).

Excitation-contraction coupling on the road of translation / Resistant hypertension
Purpose: Among treated yet uncontrolled hypertensive patients, severe RHT exhibits a significantly higher cardiovascular risk indicating the need for prompt management.

Conclusions: Among treated yet uncontrolled hypertensive patients, severe RHT exhibits a significantly higher cardiovascular risk indicating the need for prompt management.

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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Introduction: MultiPoint Pacing (MPP) allows delivery of cardiac resynchronization therapy via low-energy high-frequency pacing from multiple electrodes. The aim of this study is to evaluate the influence of MPP on QRS duration and on LV ejection fraction.

Methods: Data from 386 patients (pts) (80% male, LVEF 28±8% QRS 162±26ms) were collected in 67 Italian hospitals. After CRT implantation, device programming was optimized per center standard practice and electrical measurements were performed. QRS and Ejection Fraction (EF) data were available at follow-up (fup) in 88 pts.

Results: Implant procedural was 114±47 min. The lead was implanted in 16% antero-lateral, in 50% lateral, in 34% in a postero-lateral vein. The LV cardiac thresholds (CTs) were measured in at least 2 out of 10 available configurations with different cathodes. The mean of CT (at 0.5ms) was <3V in all the pacing configurations. The MPP was programmable in 96% of the pts with CT <5V for both cathodes and without PNS issues. In pts optimized by QRS (86 pts) the Delta QRS (relative percentage change from bas QRS) was significantly greater in the optimized MPP compared to best conventional biventricular mode (BiV) (17±21 vs 12±22, p<0.001). At fup, among 48% pts programmed in MPP, the Delta QRS in MPP mode was greater than in BiV (20±21 vs 13±24, p=0.16). Whilst bas EF didn’t differ significantly between the two groups, after 6 month, EF increased significantly in the MPP group vs BiV group (+121±10% vs +73±9%, p<0.01). Patients with an EF increase of at least 5% were considered as CRT Responders; only 82% of the pts programmed in BiV were responders vs 76% in MPP group.

Conclusions: MPP was programmable in 96% of the pts; it could ensure greater QRS shortening and EF improvement, compared to conventional CRT

2271 | BEDSIDE

Relation of QRS duration to clinical benefit of cardiac resynchronization therapy in mild heart failure patients without left bundle branch block MADIT-CRT sub-study

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Background: There are conflicting data on the efficacy of cardiac resynchronization therapy (CRT) in heart failure (HF) patients without left bundle branch block (LBBB) morphology. Current US and European guidelines do not negate implant-
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=0.034), 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 LVD patients (1.31, 95% CI: 0.89–1.93, p=0.172).

Conclusions: Our findings suggest that mild HF patients without an LBBB ECG pattern do not derive clinical benefit from CRT-D, not even during long-term follow-up. Instead of, there appears to be a significant increase in HF or death in those with non LBBB and QRS duration >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 strain 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 present 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 parameter in a controlled experimental setting. A standardized measurement setup and ii) to investigate the influence of afterload on this new parameter is lacking. The aim of the present 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.

Results: An experimental validation of this novel parameter is missing. The aim of this 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.

Conclusions: The slope of the relationship between left ventricular (LV) segmental strain 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 present 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.

2284 | BENCH

Strain and strain rate by speckle-tracking echocardiography reflect the effects of exercise training and detraining in a rat model of athlete’s heart


Recently our working group provided detailed morphologic and hemodynamic characterization on exercise-induced left ventricular (LV) hypertrophy in a rat model, confirming increased contractility. In the current study we aimed to assess whether strain parameters by speckle-tracking echocardiography (STE) are able to describe the effects of training and detraining on LV function.

Rats were divided into trained (n=12) and control (n=12) groups. Trained rats swam 200 min/day for 12 weeks, then remained sedentary for 8 weeks. Echocardiography was performed at baseline, 12 and 20 weeks using a 13MHz linear transducer to obtain LV long- and short-axis recordings for STE analysis. Global longitudinal and circumferential strain (GLS, GCS) and systolic strain rate (LSr, CSr) were measured. After the detraining period, LV pressure-volume (P-V) analysis was performed to calculate contractility indices (i.e. slope of the end-systolic P-V relationship). STE echocardiography showed the development of LV hypertrophy in the trained group (trained vs. control; LV mass index: 2.4±0.1 vs. 2.0±0.1 g/kg, p<0.05). This difference disappeared after detraining (2.3±0.1 vs 2.4±0.1 g/kg, NS), which was confirmed by post-mortem measured heart weight and histological morphometry. GCS, CSR and LSr were all increased after the training period (GCS: Figure; CSR: -5.6±0.3 vs -4.0±0.3; LSr: -4.6±0.2 vs -3.9±0.2Hz, p<0.05). After detraining, non-parametric values reversed to the control level and ESPVR did not differ either (1.8±0.1 vs 1.8±0.2 mmHg/L, NS).

Morphologic and functional properties of exercise-induced LV hypertrophy completely regressed after the detraining period. Both changes induced by exercise training and effects of detraining reflected by STE, allowing a consecutive evaluation of LV function in rat models.

Cardiac resynchronisation therapy: strategies for improving response / New advances in cardiac imaging

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ENDOCARDITIS – EVALUATING RISK AND IMPROVING OUTCOME

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=426) and validation (n=247) samples. The primary endpoint was in-hospital mortality. We also analyzed the predictive performance of Euroscore I in our cohort of 672 patients.

Results: In-hospital mortality was similar in the derivation and validation samples (29.2% vs 28.1%; p=0.723). In the derivation sample, a univariable analysis for in-hospital mortality was performed. Those variables found to be statistically significant and, clinically relevant were used to develop a multivariable prediction model. The variables included in the final model were: age>70 years, prosthetic infection, vegetation detection, perianular complications, Staphylococcus aureus infection, acute renal failure before surgery, septic shock before surgery, acute heart failure or cardiogenic shock, and platelet count <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, perianular complications, sepsis manifestations) beside the universal ones (age, hemodynamic conditions), independently predicted mortality in IE surgery. Our model had a superior predictive accuracy than Euroscore I.

2319 | BEDSIDE
Incidence, pathogenesis and outcome of patients developing infective endocarditis after transfemoral transcatheter 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 about the occurrence, pathogenesis, treatment and outcome of IE in patients 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 treatments options were analysed. 30-day and 1-year mortality after diagnosed 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±14.0. According to Duke criteria, 59% and 41% of the patients had definite or probable IE, respectively. Early IE occurred in 70% and late IE in 30%. Clinically, all patients except one had fever >38.0°C, all had a predisposition, and a sepsislike event occurred in 24%. Blood cultures (positive in all cases) included staphylococci in 44%, enterococci in 29%, streptococci in 7%, and others in 20%. Transesophageal echocardiography was performed in 38 patients. There was no typical endocarditis in 25% of those patients. IE affecting another valve than the prosthetic was evident in 11%. Lead endocarditis alone occurred in 11%. The remaining 53% had echocardiographic evidence of PVE alone or in combination with multilocular IE.

Treatment included antibiotics in 78%, antibiotics and operation in 15%, and no treatment due to death immediately after admission in 7%. Overall 30-day and 1-year mortality after diagnosis of IE was 54.3% and 71.7%, respectively. Definitive and probable IE did not differ in 30-day (51.9% vs. 57.9%, p=0.69) and 1-year mortality (74.1% vs. 68.4%, p=0.68). No difference in 30-day (42.1% vs. 47.4%, p=0.74) and 1-year mortality (68.4% vs. 63.2%, p=0.73) was detectable in patients with echocardiographic evidence of PVE compared to those without.

Conclusion: IE after TF-AVI occurred in 2.7% and was associated with a high mortality. Echocardiographic evidence of PVE was only evident in 53%. However, there was no difference in mortality between patients with echocardiographic evidence of PVE compared to those without, underlining the necessity of aggressive therapy in all TAVI patients with bacteremia.

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 potential role 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<0.02) 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 common in G-II. Perianular complications were found similarly in both groups. During hospitalization, patients with A-IE 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, early surgery was still associated with lower mortality (66% vs 89%, p=0.002).

Conclusion: IE after TF-AVI occurred in 2.7% and was associated with a high mortality. Echocardiographic evidence of PVE was only evident in 53%. However, there was no difference in mortality between patients with echocardiographic evidence of PVE compared to those without, underlining the necessity of aggressive therapy in all TAVI patients with bacteremia.

VASCULAR BIOLOGY – NEW MOLECULAR AND GENETIC FINDINGS

2334 | BENCH
Inhibition of FGF signaling with PD173074 ameliorates monocrotamine-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 monocrotamine-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 monocrotamine. And then a daily intraperitoneal injection of PD173074 (20 mg/kg)
Vascular biology – New molecular and genetic findings

3235 | 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 a circulating half-life than CNP-22. However, it remains unknown if CNP-53 possesses biological actions through GC-B and cGMP activation and if CNP-53 is a vascular remodeling. Based on its structural similarity to CNP-22, we hypothesized that CNP-53 would: 1) have cGMP activating actions in human vascular smooth muscle cells (hVSMCs), specifically through GC-B and 2) lower blood pressure in an experimental model of hypertension.

Methods:
HEK293 cells over-expressing GC-A and GC-B and hVSMCs, which expresses GC-B, were stimulated with CNP-53 for 10 minutes at a dose of (10−8M) and cGMP was measured. Two groups of anesthetized spontaneously hypertensive rats (SHRs; n=8) received a 75-minute infusion of Vehicle (V: saline) or CNP-53 (cGMP dose of 0.264 μg/kg/min; a therapeutic dose of CNP-22). We then assessed the absolute change in mean arterial pressure (MAP), glomerular filtration rate (GFR), sodium (Na+) excretion, plasma CNP-53 and plasma and urinary cGMP. Data are means±SE, *p<0.05.

Results:
CNP-53 significantly activated cGMP in hVSMCs (0.09±0.1 vs. 0.000±0.0 pmol/well*) and in GC-B HEK cells (75±9 vs. 0.4±0.1 pmol/well*) compared to no treatment. In contrast, CNP-53 failed to generate cGMP in GC-A HEK cells. In SHRs, CNP-53 infusion (compared to vehicle) significantly elevated plasma CNP-53 (CNP-53: 1232±281, V: 10±3 pg/ml) as well as cGMP in aorta. In addition, activated ERK1/2 has been described in SHRs in response to CNP-53 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.

3237 | BENCH
The role of macrophage STAT3 signaling in pathogenesis of aortic dissection

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Aortic dissection (AD) is a common disease with sudden onset and high mortality, caused by the disruption of the intimomedial layer. Recent studies showed that IL-6, a JAK/STAT3-activating proinflammatory cytokine, plays an important role in AD. In addition, activation of JAK/STAT3 has been described in human AD tissue. However, it is unclear exactly how IL-6 and STAT3 participate in pathogenesis of AD, or how they are related to cell cycle activation. In this study, we 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 monocyte/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 (CaAngII) 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 CaAngII. In WT, the microscopic injuries healed with fibrosis in 6 weeks. However, the injuries progressed to AD in 6 weeks in mSOCS3-KO. Transcriptome analysis showed the activation of cell cycle and inflammatory genes at the stage of microscopic injury in mSOCS3-KO compared to WT before the development of AD. Flow cytometric analysis revealed the proinflammatory M1-skewed differentiation of mSOCS3-KO macrophages compared to WT. In 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. Deciphering such molecular events during the development of AD will be essential to develop a new diagnostic and therapeutic strategies for this lethal disease.

3238 | BENCH
Excessive sodium intake worsens aortic dissection via IL-17 pathway

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Excessive sodium intake is an established risk factor of cardiovascular events,
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-aminopropionitrile (BAPN), an inhibitor of a collagen/elastin 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 as 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 that excessive sodium intake activates the T17L1 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. Transcriptome analysis of aortae before the onset of AD showed that strong induction of proinflammationary genes and suppression of ECM genes precede the AD development in this model. Although IL-17 is central to inflammatory response in general, alteration of inflammatory response was not prominent in IL-17 knockout aorta. Instead, genes of ECM were upregulated in IL-17 knockout at the baseline. Furthermore, excessive sodium intake resulted in the up-regulation of ECM genes in IL-17 knockout mice, which was not observed in wild type mice. With BAPN+AngII and excessive sodium intake, expression of ECM genes were higher in IL-17 knockout compared to wild type aorta. From these findings we propose that IL-17 suppresses ECM gene expression in all conditions 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.

2339 | BENCH
Endothelial mesenchymal transitions do not contribute to the development of pulmonary arterial hypertrophy caused by a VEGF receptor inhibitor in mice
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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 cells in plexiform lesions derive from mesenchymal cells.

Methods: To generate reporter mice, tdTomato and Tie2-Cre double transgenic mice, with a marker for endothelium-derived cells, mice homozygous for a conditional floxed tdTomato allele (Gt(ROSA)26Sor-CAG-tdTomato) were crossed with Tie2-Cre+/- reporter mice. Adult 8 week-old male reporter mice were injected subcutaneously with either SUs416, a vascular endothelial growth factor (VEGF) receptor inhibitor at 20 mg/kg, or a vehicle, once a week for three weeks and were simultaneously exposed to chronic normobaric hypoxia (10% O2) in a ventilated chamber. Control mice were kept in the same room and the same light-dark cycle under normoxia. Each mouse was intubated through the mouth and anesthetized with isoflurane. Right ventricular (RV) systolic pressure was measured by right catheterization directly through right ventricle wall. After hemodynamic measurements, each animal was sacrificed by cervical dislocation, and lung and heart tissue samples were collected for histological and molecular profiling.

Results: The expression of tdTomato was recognized specifically in pulmonary artery endothelial cells in Tie2-Cre and tdTomato-floxed double Tg mice under normoxia. Compared with control mice, mice treated with SUs416 and hypoxia showed higher RV systolic pressure (44.3 versus 21.6 mmHg; n=6, P<0.01). Histological examination showed vascular remodeling with the development of neointimal occlusive lesions. Immunofluorescent staining of frozen sections showed thickening of medial layer of arterioles that highly expressed alpha smooth muscle actin but did not express tdTomato in the mice treated with SUs416 under hypoxia.

Conclusions: These results indicate that, in mice, endothelial mesenchymal transitions did not contribute to the development of plexogenic lesions associated with pulmonary artery hypertensive response caused by the combination of SUs416 and chronic hypoxia.

2340 | BENCH
Diastolic dysfunction in mice lacking nuclear factor (erythroid-derived 2)-like 2
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Background: The transcription factor Nr2f2 is a key master switch controlling the expression of antioxidant and protective. In this study we aimed to investigate the cardiac and vascular phenotype and systemic hemodynamics in Nr2f KO mice, generated by crossing Nr2f cre/cre mice to littermates.

Methods: Male Nr2f KO mice and WT mice 6 month of age were studied for global changes in cardiac and vascular function and changes in biochemical parameters including redox state, eNOS/cGMP expression and NO bioavailability in the aorta and the heart. Echocardiography and Flow-Mediated-Dilation was measured. High resolution ultrasound in aorta and iliac artery, perfusion was assessed by calculation of pulse wave velocity. Coronary vascular function and cardiac response to β-adrenergic stimulation by isoproterenol, was assessed in Langendorff hearts by measuring reactive hyperemia and changes in increase of cardiac contractility. Mean adventitial pressure measurement was performed with a Millar catheter and responses to cardiac glycocalyx ouabain were detected. Expression of eNOS in the aorta and the heart was assessed by western blot analysis. The circulating NO pool was analyzed by HPLC and chemiluminescence detection; cGMP levels in plasma and aorta were measured.

Results: We found that Nr2f KO mice show an impaired left ventricular diastolic function, as demonstrated by prolonged isovolumic relaxation time, E-wave deceleration time and increased myocardial performance index. Accordingly, isolated perfused Nr2f KO hearts showed an impaired response to β-adrenergic stimulation by isoproterenol, as shown by lower developed pressure and dp/dt/min as compared to WT mice, while systolic left ventricular function was preserved. Administration of the cardiac glycocalyx ouabain in vivo increased dp/dtmax and dp/dt/min in WT mice, but failed to increase diastolic or systolic left ventricular function in the KO mice as assessed by Millar catheter. Surprisingly, blood pressure in Nr2f KO mice was significantly decreased, and endothelial function of arterial conductance and coronary reserve 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: Nr2f 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 Nr2f-dependent pathways play a central role in preserving cardiac diastolic function in mice.

2341 | BENCH
Casein kinase 2 beta is a critical player in platelet activation, arterial thrombosis and ischemic stroke
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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 ser(in)/thr(eon) 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 (ck2β+/−) and wildtype littermates (ck2β+/+) 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 ck2β+/−+ platelets in response to activation with collagen-related peptide (CRP) or thrombin. Fura-2 AM spectrophotometric Ca2+ measurements pointed to a significant reduction in activation-dependent cytosolic Ca2+ increase due to a defective Ca2+ influx in ck2β+/−+ platelets upon stimulation with CRP or thrombin in consequence, in vitro thrombus 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 arterioles were significantly diminished in ck2β+/−+ mice compared to ck2β+/+ mice. Furthermore we show that ck2β+/−+ mice were protected against progressive P2Y12-mediated response when subjected to occlusion of the middle cerebral artery (MCAO). CK2β+/−+ mice displayed drastically reduced cerebral infarct volumes and developed significantly fewer neurological deficits (grip test, Bederson score) following MCAO compared to ck2β+/++ mice while tail bleeding time was only mild prolonged in ck2β+/−+ mice. Finally, we identified potent CK2β selective downstream 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.

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Background: Adenosine to inosine (A-to-I) RNA editing is catalysed by ADARs (adenosine deaminases acting on RNA) and is an important posttranscriptional regulator of RNA metabolism. Its role though in cardiovascular system remains unknown. The goal of the present study was to evaluate the role of RNA editing in human endothelial cells in vitro and in patients with coronary artery disease. Further, we addressed the role of ADAR1 in vascular development and homeostasis in mice.

Methods and results: Next generation RNA sequencing of human endothelial cells revealed that ADAR1 is the main RNA editor inducing A-to-I RNA editing events in almost 25% of transcripts, mostly in introns followed by 3′-untranslated regions (3′UTR). Among the highest ADAR1 edited targets was cathepsin S (CTSS), an extracellular matrix degradation enzyme with an established role in cardiovascular disease. RNA editing of CTSS 3′UTR was increased after hypoxia or LPS and evaluated the clinical relevance 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 compared to controls (P <0.001). Of interest, the extent of RNA editing in single nucleotide positions was strongly associated with cathepsin S mRNA expression (r=0.8, P<0.001) in our cohort. In order to investigate the underlying mechanism, we studied the role of ADAR1 in CTSS mRNA expression, silencing of ADAR1 profoundly reduced RNA editing of the 3′UTR of CTSS mRNA and inhibited CTSS mRNA and protein expression by 60% (P=0.001 for all). In a similar manner, ADAR1 regulated endothelial cell CTSS mRNA expression under hypoxic or inflammatory conditions. Mechanistically, RNA editing alters CTSS mRNA secondary structure and stability by regulating the binding of the stabilizing RNA-binding protein HuR to CTSS 3′UTR (P<0.05 for all). The importance of RNA editing in vascular system was further highlighted in mice by a retinal angiogenesis defect after postnatal endothelial cell ADAR1 ablation. In adult mice, deletion of ADAR1 in endothelial cells leads to a lethal phenotype.

Conclusion: This study is the first to assign a vascular function to ADAR1 and RNA editing, and it may serve as a prototypical example for the evaluation of RNA-based mechanisms in patients with cardiovascular disease.
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, 1.02-10.6 ms), a longer corrected QT-time (1.02, 1.00-1.03 ms) and wider angle between the frontal axes of the QRS complex and the T-wave (1.02, 1.01-1.03 degree).

Conclusion: Routine 12-lead ECG provides useful information in directing the diagnostic work-up of a young stroke patient. In addition to AF, particularly PTF had statistically strong association with final etiology of cardioembolism from a high-risk source.

P2347 | BEDSIDE
Dabigatran and rivaroxaban versus warfarin in patients with high risk of stroke and embolism undergoing electrical cardioversion with persistent and long-acting atrial fibrillation

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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 despite high CHA2DS2VASc risk, HASBLEED and AF duration. The aim of this study was to compare the use of dabigatran and rivaroxaban versus warfarin when compared to the same period in 2013 (p<0.0001).

Methods: We have analysed the data collected before and after ECV in 1742 patients (pts) undergoing ECV. All pts had AF, 1313 persistent and 429 defined as long-lasting, CHA2DS2VASc score ≥ 2.0–3.0. 110 mg twice were prescribed for pts ≥ 75 year, HASBLEED score ≥ 4 and kidney problems. Transesophageal echocardiography (TEE) was encouraged before ECV in all pts with CHA2DS2VASc score ≥ 4, left atrial (LA) dilatation and AF duration ≥ 6 months. ECG and Echo-kg data were analysed 30 days and 90 days after ECV.

Results: ECV was successful after first shock in 1602 (92%) pts, total success ECV 1709 (98.1%) pts. LA thrombi were detected on TEE before ECV in 36 pts in NOAC group and 32 pts in warfarin group, so, pts continued OAC therapy for two months, and TEE had been performed again. After 10 days in dabigatran (150 mg twice), 8 pts in rivaroxaban (20 mg) group and 7 pts in warfarin group were free of thrombus and have been referred to ECV. Average time before ECV was significantly lower for NOAC (25 days) vs warfarin (48 days, p<0.01). Stroke and systemic embolism rates at 90 days were lower in NOAC group (0.1%) vs warfarin group (1.5%), but the event in NOAC group was documented after discontinuation of the drug while 10 warfarin events were detected under the time of use of OAC. There was no difference in analysis of events between TEE and non-TEE pts in dabigatan and rivaroxaban. NOAC pts had significantly lower clinical relevant bleeding rate vs warfarin (D 110 mg 0, D 150 mg 0.4%, R 0.39% vs W 2.87%, p=0.01).

Conclusions: Rivaroxaban 20 mg daily and dabigatran 150 mg and 110 mg twice are a safe, effective and reasonable alternative to warfarin for patients undergoing ECV despite high CHA2DS2VASc risk, HASBLEED and AF duration. The frequency of LA thrombi in NOAC group was lower in dabigatran 150 mg and 110 mg and rivaroxaban 20 mg versus warfarin with lower major bleeding within 30 and 90 days after ECV. Patients undergoing NOAC’s have shorter time before procedures.

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 significant numbers of elective DCCV admissions and, more relevantly for patients, longer periods of time spent in atrial fibrillation.

Aim: To establish if changing trends in novel oral anticoagulant (NOAC) prescriptions reduce waiting times for elective DCCV.

Methods: A review of an electronic database of elective DCCV admissions at our institution was performed. Data included recorded, including age, sex, booking date, procedure date, OAC prescribed and procedure outcome.

Results: There were 653 DCCV admissions from 01/01/2010 to 30/09/2014. In 2010-2011 (pre-NOAC), 377 DCCV admissions (57%) proceeded to DCCV and of these, 512 (88%) were successfully cardioverted to sinus rhythm. Age at admission ranged from 27–86 years (mean of 63 years). 509 (78%) of patients were male. On average, female patients attending for DCCV were older than their male counterparts (Mean of 66 vs. 62 years, p<0.001). Warfarin was the prescribed OAC in 470 admissions (72%). Waiting time for admissions on warfarin was significantly longer than those on NOACs (Mean of 60 vs. 35 days, p=0.000). Of the 183 admissions on NOAC, rivaroxaban was the most commonly prescribed (102), followed by dabigatran (68) and apixaban (13). There was no significant difference in the age of patients on warfarin compared to NOAC (Mean 62.66 years vs. 62.93 years) and the trend towards older mean age in female patients was consistent in both groups. The proportion of female patients on warfarin (23.4%) was higher than in those on NOACs (18.58%) however this was not statistically significant (p=0.198). 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 the previous year.

Conclusion: Mean waiting time for elective DCCV was significantly shorter for patients on NOACs than on warfarin (35 days vs 60 days). With the increasing trend in prescribing NOACs, there has been a corresponding reduction in average waiting times which likely leads to improved patient outcomes.

BEST POSTERS IN MYOCARDIAL ISCHAEMIA

P2350 | BENCH
Continuous erythropoietin receptor activation reversal 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 reverse the I/R injury.

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/2-h reperfusion. Level of serum creatinine was higher in SNx than in Sham (0.82±0.06 v. 0.34±0.02 mg/dl), confirming development of CRF in SNx. Hemoglobin level was lower in SNx than in those in Sham (14.2±2.0 v. 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±4.0% v. 43.9±2.2% of risk area, p<0.05). CERA significantly reduced infarct size in SNx (36.9±3.9%), though the effect of CERA in Sham was modest (31.6±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 CERA-induced renal protection. Immunohistochemical analysis revealed a clear decrease in phosphorylation levels of Akt and PHLPP-1-mediated dephosphorylation of Akt at Ser473 in the myocardium under baseline conditions. The phosphorylated ratio of Akt at Ser473 was increased in SNx regardless of treatment with CERA. However, expression level of PHLPP-1, a phosphatase specifically regulating phosphorylation of Akt at Ser473, was higher in SNx than in Sham. CERA restored Akt-Ser473 phosphorylation in SNx.

Conclusions: Continuous erythropoietin receptor activation reverses increased myocardial susceptibility to I/R injury in CRF presumably by attenuation of PHLPP-1-mediated dephosphorylation of Akt at Ser473.
Methods and results: We determined that SGLT1 was highly expressed in both human autopsied hearts and murine perfused hearts, as assessed by immunostaining and immunoblotting with membrane fractionation. To test the functional significance of the substantial expression of SGLT1 in the heart, we studied the effects of a non-selective SGLT inhibitor, phlorizin, on the baseline cardiac function and its response to IR using the murine Langendorff model. Although phlorizin perfusion did not affect baseline cardiac function, its administration during IR significantly impaired the recovery in left ventricular contractions (%recovery of baseline: 67±3.4% vs 89.7±5.6%, n=5 each, P<0.05) and rate pressure product, associated with an increased infarct size, as demonstrated by TTC staining (%MII: 22±1.2.7% vs 11.1±1.3%, P<0.01) and CPK activity released into the perfusate (19.0±5.4 versus 9.0±3.3 U/Ig, 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 IR by replenishing ATP stores in ischemic cardiac tissues via enhanced glucose availability. The present findings provide new insight into the essential role of SGLT1 in optimizing cardiac energy metabolism, at least during the acute phase of IR.

BEST POSTERS IN CARDIOVASCULAR MAGNETIC RESONANCE

P2355 | 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 the heart remains 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: Plasma concentrations of hs-cTnT increased (>10%) after stress test in 90/125 cases. Overall, hs-cTnT significantly increased from 17.5±4.16 ng/L before the test to 25.5±27.90 ng/L 6-hrs afterward (p<0.0001), without significant changes in CK-MB. Increments in hs-cTnT were documented after ECG/echo-exercise test (from 15.87±11.90 ng/L to 19.47±13.65 ng/L, p<0.0001), after echo-dipyridamole test (from 17.71±19.12 ng/L to 24.38±35.74 ng/L, p<ns) and after echo-dobutamine test (from 20.63±20.80 ng/L to 37.83±31.07 ng/L, p<0.0006), without significant changes in CK-MB according to each stress type. Out of 125 tests, 84 were negative and 41 positive for myocardial ischemia. Significant increments in hs-cTnT were detected after both negative (from 18.6±21.21 ng/L to 27.11±32.07 ng/L, p<0.0018) and positive stress tests (from 15.2±10.8 to 22.3±16.22, p<0.0005), without significant changes in CK-MB according to the test result.

Conclusions: Plasma concentrations of hs-cTnT increase in the vast majority of patients undergoing a cardiac stress tests, irrespective from the result of the test. These data suggest that plasma release of hs-cTnT is caused not only by myocardial necrosis but also by other mechanisms, such as reversible ischemia and myocardial stretching secondary to increased heart rate and inotropism.
Background: They are a common finding in MRI scans of the brains of elderly subjects and are more frequent in clinical practice. Cardiovascular magnetic resonance imaging (CMRI) 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, the prognostic utility of CMRI 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 CMRI) in this patient group. 2. Establish the degree of concordance between clinical panel and CMRI diagnoses. 3. Demonstrate the incremental diagnostic and prognostic value of CMRI.

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 CMRI. The only exclusion criteria was the presence of CMR contraindications. A panel of three experienced cardiologists (>5 years) consulting cardiologists unaware of the CMR diagnosis and blinded to each other's assessment, each provided a clinical diagnosis based on clinical, biochemical, ECG, echocardiographic and angiographic findings. A consensus panel diagnosis was defined as two or more cardiologists sharing the same clinical diagnosis. Findings were classified into: Acute myocarditis, Takotsubo Cardiomyopathy, Non-ST elevation myocardial infarction (NSTEMI) or indeterminant.

Results: Median troponin value was 500ng/L (IQR 183,840). Consensus panel diagnosis of WML and CMR were concordant in 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 67% 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 diagnosis in majority of these patients. 3. Although concordance between CMR diagnosis and clinical diagnosis without CMR is poor, the overall incidence of major adverse cardiovascular events in these patients is low.

Table 1. Linear regression for the association of WML with traditional cardiovascular risk factors

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Beta-estimate (95% CI)</th>
<th>p-value</th>
<th>Beta-estimate (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.073 (0.061–0.085)</td>
<td>&lt;0.001</td>
<td>0.068 (0.055–0.087)</td>
<td>0.007</td>
</tr>
<tr>
<td>Gender male</td>
<td>0.355 (0.174–0.535)</td>
<td>&lt;0.001</td>
<td>0.265 (0.117–0.413)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>0.002 (0.000–0.005)</td>
<td>0.049</td>
<td>0.002 (0.000–0.004)</td>
<td>0.021</td>
</tr>
<tr>
<td>Diabetic nephropathy (y/n)</td>
<td>0.010 (0.011–0.020)</td>
<td>0.003</td>
<td>0.003 (0.003–0.012)</td>
<td>0.005</td>
</tr>
<tr>
<td>BMI</td>
<td>0.041 (0.002–0.062)</td>
<td>0.001</td>
<td>0.014 (0.003–0.032)</td>
<td>0.129</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.342 (0.173–0.512)</td>
<td>&lt;0.001</td>
<td>0.185 (0.044–0.327)</td>
<td>0.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>-0.096 (-0.220–0.028)</td>
<td>0.128</td>
<td>-0.093 (-0.211–0.023)</td>
<td>0.866</td>
</tr>
</tbody>
</table>

Conclusion: WML are associated with traditional cardiovascular risk factors and CM-sc. Our results suggest that the degree of subclinical atherosclerosis may predict WML volume a few years later.
Obesity-related metabolic and myocardial dysfunction. The strong anti-diabetic effects observed with 
p21 deficiency might open a new therapeutic research avenue in metabolic cardiomyopathy.

**P2361** | **BENCH**

The SR influences mitochondrial ATP production via IP3 mediated Ca release

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**Background:** The mechanisms in cardiac myocytes to distinguish between general Ca release for contraction and local Ca signaling e.g. for metabolic adaptation still need to be elucidated.

**Hypothesis:** Mitochondrial Ca uptake is influenced by Ip3-mediated Ca release from the SR. Through this mechanism myocytes are able to adapt mitochondrial metabolism to the ATP demand of the cell.

**Methods:** Isolated adult mice ventricular myocytes were examined using confocal microscopy. X-Rhod was used for Ca measurements, mitochondria membrane potential (ΔΨm) and ROS were measured using TMFR and mitoSOX, respectively.

**ATP concentration was measured indirectly using mag fluo-4 and directly using a luciferase assay.**

**Results:** The stimulation of myocytes with the IP3 agonist endothelin-1 (ET-1, 10 nM) resulted in a strong increase of mitochondrial Ca by +29±13% after 20 min (n=27, p<0.01). The observed increase could be blocked completely by the IP3R antagonist 2-APB as well as in functional IP3 i.ko 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 (+15%, n=8).

As a consequence of the cellular stimulation with IP3 agonists, the mitochondrial ATP production, measured indirectly by using the dye mag fluo-4, was increased significantly by 25±2% (n=9). ATP production was markedly decreased in the presence of 2-APB.

Interestingly, the stimulation of mitochondria with the beta agonist 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 unipporter (mCU) using Ru360. This did not influence mitochondrial Ca uptake following cellular stimulation with ET-1 (+31±7% after 20 min, n=11) but prevented iso induced mitochondrial Ca uptake (+15±2%, 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±3%, n=9).

**Conclusion:** IP3 mediated Ca release from the SR results in mitochondrial Ca uptake via the mRyR1. This Ca uptake is followed by an increase in mitochondrial ATP production. 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.

**P2362 | BENCH**

TIMP3 acts through apelin to maintain cardiac metabolic flexibility

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At the myocardial level, we found histological signs of lipotoxicity in-
Efficacy and safety of first-line oral triple upfront combination therapy in severe pulmonary arterial hypertension patients

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Background: Severe pulmonary arterial hypertension (PAH) is still devastating disease in modern PAH treatment. The efficacy and safety of first-line oral triple upfront combination therapy including long-acting oral prostacyclin analogue for severe PAH has not been investigated.

Methods: We retrospectively reviewed 22 patients who received oral combination therapy (oral long-acting prostacyclin analogue, endothelin receptor antagonist, phosphodiesterase 5 inhibitor) from 2008 to 2013. They were divided into two groups; 11 patients were treated with oral upfront combination therapy, 11 patients were treated with oral sequential combination therapy. We evaluated NYHA, 6MWD and hemodynamics before and after treatment. And we examine the duration free from death, transplantation or epoprostenol induction between upfront and sequential group.

Results: The hemodynamic and exercised capacity was evaluated 6.6±7.3 months after oral triple combination therapy medication. WHO-FC improved from 3.0±0.9 to 2.2±0.6 in upfront group (P<0.001), and 3.1±0.3 to 2.4±0.6 in sequential group (P=0.002), 6 minutes walking distance improved from 334±89 to 450±122 meters in upfront group (P<0.05), and 346±77 to 380±57 meters in sequential group (P=0.3). Mean pulmonary arterial pressure decreased from 47.1±8.9 to 34.7±6.9 mmHg in upfront group (P=0.0003), and 47.1±10.4 to 39.1±13.7 mmHg in sequential group (P=0.02), cardiac index increased from 1.97±0.67 to 2.87±0.54 L/min/m2 in upfront group (P=0.012), and 2.89±0.56 L/min/m2 in sequential group (P=0.05). After mean follow-up of 39.0±17.4 months, all patients initiated with oral triple upfront combination therapy were still alive and free from epoprostenol therapy, the other side, five patients were dead or induced epoprostenol therapy in sequential group (three were started epoprostenol therapy and two were dead) (P<0.05). One patient experienced adverse event (headache), needing medical switch sildenafil to tadalafil in upfront combination therapy group. No new adverse effect was observed during the follow-up period in the whole patients.

Conclusions: First-line oral triple upfront combination therapy improved symptoms, exercise capacity and hemodynamics and significantly reduced mortality and induction of epoprostenol therapy for PAH patients without severe adverse effect.

Efficacy and safety of cardiac rehabilitation initiated just after balloon pulmonary angioplasty in patients with inoperable chronic thromboembolic pulmonary hypertension

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Purpose: We have recently shown that balloon pulmonary angioplasty (BPA) ameliorates exercise intolerance and ventilatory inefficiency early after the procedure (even within 1 week) relative to haemodynamic improvements in patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH), with minimal postprocedural deconditioning. However, little is known about the effects of cardiac rehabilitation (CR) on remaining exercise intolerance after BPA. Thus, the aim of this study was to determine safety and efficacy of CR in patients with inoperable CTEPH, who suffered from remaining exercise intolerance after BPA.

Methods: We prospectively enrolled 12 consecutive patients (mean age, 69±13 years) (men) with inoperable CTEPH who underwent a series of BPA (3.6±1.7 procedures) with resultant improved haemodynamics (mean pulmonary arterial pressure, 36.1±11 to 24.6±16 mmHg) and remaining exercise intolerance (peak oxygen uptake, 69±11% of predicted). They were divided into the follow-up groups just after the final BPA (6.7±2.4 days); patients with CR (n=6) or without (non-CR, n=19) participating in CR program, which included walking, bicycle ergometer, and resistance training and consisted of 1-week in-hospital training and following 11-week outpatient program under supervision. Cardiopulmonary exercise testing (CPX), right heart catheterisation, and quality of life were assessed at the beginning and end of CR program.

Results: At baseline, there were no significant changes in age, sex, haemodynamic-, or CPX-related parameters between 2 groups. At 3 months, percent increase in peak VO2 (V02peak) (%), was significantly larger in non-CR group (+10.5±9.8 vs. +1.2±9.6%, P<0.05). Moreover, peak VO2 (71.4±27.2 to 19.3±3.6 mL/min/kg), normalised peak VO2 (71±9 to 79±13%), peak work load (86±24 to 98±28 W), and WHO
Coronary CT angiography was performed in asymptomatic sportsmen aged ≥45 years whose routine sports medical examination, including exercise testing, was normal. Those with a coronary artery calcium score of ≥100 and no plaques on CT angiography were considered to have perfect coronaries. Lifestyle exercise was defined as having trained at least 2 hours per week from adolescence onward. Ideal cardiovascular health (CVH) was defined as fulfilling at least 5 out of 7 criteria: physical activity (≥5000 steps per day), healthy diet, untreated total cholesterol ≤200mg/dL, untreated blood pressure ≤120/80 mmHg, and untreated fasting glucose ≤100mg/dL.

Results: Among fit sportsmen ≥45 years with a low ESC SCORE risk, lifelong exercisers with ideal cardiovascular health are most likely to have perfect impact on RVF remains unknown. This observation may help tailor preparticipation screening strategies in senior athletes.

Background: The aim of this prospective, randomized and controlled training study was to assess the molecular effects of physical training in exercising 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 non-CR group (control) or three training interventions: 1) aerobic endurance training (AET), continuous running; 2) high-intensive interval training (IT, 4x4 method) or 3) strength endurance training (SET; circle training on 8 devices).

Results: Telomerase activity and mRNA expression (real-time PCR) of telomere repeat-binding factor 2 (TRF2) and senescence marker p16 were measured. Telomerase activity increased in all three training groups, however the activity of the enzyme telomerase (TEP) on the treadmill at a pulse of 150/min (control: 0.23±0.1; AET: 4.74±0.8; IT: 4.22±1.1; SET: 2.44±1.2 ml/kg*min), which was higher in endurance compared to strength training. Quantification of telomerase activity (TRAP assay, compared to HEK cells as positive controls) in MNC revealed a significant 4–5-fold increase in both endurance exercise groups, but not in strength training (Δ pre/post: control 45±6; AET 287±150; IT 225±85; SET −15±52 HEK cell equivalents).

Conclusion: The study is the first prospective randomized, controlled trial showing 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.

Background: Most exercise-related cardiac arrests occur in men aged ≥45 years and are caused by coronary artery disease (CAD). Traditional cardiovascular risk scores and exercise testing do not reliably identify CAD in asymptomatic sportsmen. Lifelong physical activity and “ideal” cardiovascular health are key in preventing cardiovascular events.

Purpose: To determine the impact of lifelong exercise and ideal cardiovascular health on the occurrence of CAD in 283 asymptomatic sportsmen aged ≥45 years with a low ESC SCORE risk.

Methods: Coronary CT angiography was performed in asymptomatic sportsmen who have participated in organized competitive sports from childhood or adolescence to adulthood. Screening included a physical examination, lifestyle questionnaire, and traditional cardiovascular risk factors. The study population included 30,542 individuals aged 14–35 years who were evaluated by a cardiologist at a cost of €44 per person with HPV and an ECG interpreted in line with 2010 ESC recommendations.

Introduction: Right ventricular failure (RVF) is the most common cause of death in patients with pulmonary arterial hypertension (PAH). Growing evidences suggest that exercise training (ExT) is safe and beneficial for this population but its exact impact on RVF remains unknown. This observation may help tailor preparticipation screening strategies in senior athletes.

Conclusion: Among fit sportsmen ≥45 years with a low ESC SCORE risk, lifelong exercisers with ideal cardiovascular health are most likely to have perfect impact on RVF remains unknown. This observation may help tailor preparticipation screening strategies in senior athletes.

Conclusion: Among fit sportsmen ≥45 years with a low ESC SCORE risk, lifelong exercisers with ideal cardiovascular health are most likely to have perfect impact on RVF remains unknown. This observation may help tailor preparticipation screening strategies in senior athletes.
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
**Nanotechnology enabled rapid endothelialisation of stent-grafts**


1 Mayo Clinic, Cardiovascular Diseases, Rochester, United States of America; 2 Mayo Clinic, Engineering, Rochester, United States of America; 3 University of Durham, Medicine, Pharmacy and Health, Durham, United Kingdom.

**Background:** Clinically used synthetic vascular grafts are limited to diameters greater than 5 mm due to thrombosis, restenosis and incomplete endothelialisation. Stent-grafts used for emergency treatment of vascular perforations consist of bulky dual stents with a fabric sandwiched in the middle, and have high rates of reocclusion. Conduits for small caliber peripheral, coronary and neurovascular applications are currently unavailable.

**Purpose:** To demonstrate that a small caliber magnets-enabled 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 neointima (>200 μm thick) along with confluent endothelium. Fluorescence microscopy (Fig 1B) demonstrated the presence of delivered endothelial cells within the neointima.

**Conclusions:** Magnetic endothelialisation may enable the development of small caliber synthetic vascular conduits, thereby enabling additional therapeutic revascularisation options for smaller vessels.

#### P2377 | BEDSIDE
**Reduction of radiation exposure with a quality control system and influence of technological progress - comparison of a German coronary angiography and angioplasty registry and single centre data**

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**Introduction:** Exposure to radiation is of general concern as there is an increasing number of CT scans, procedures in interventional radiology, and interventional cardiology. Whenever possible patients and physicians exposure to radiation should be minimized. The reduction of radiation exposure can be driven by operator experience or technological progress. Can experienced interventionists still improve and reduce radiation when using a system of quality control although cases have become more complex? And which role does technological progress play, as for instance flat panel detectors and image data processing in comparison of a German coronary angiography and angioplasty registry and single centre data?

**Methods:** The completed randomized two arm (1:1) study (NANOM-PCI) with parallel assignment (n=62) assessed (NCT01436123) the safety and feasibility of the delivery technique for nanoparticles (NP) using micro-injection catheter (with intravascular intramural injection of allogenious stem cells carrying NP after MSC, IVUS and OCT-guided mapping of the vessel), and 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).

**Conclusions:** Plasmmonic resonance-mediated therapy using noble-metal NP associated with significant regression of coronary atherosclerosis below a 40% PB and minimal nanotoxicity.
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 data of a single centre with the values of the whole registry over a period from 2002 to 2013. The radiation dose area product (DAP) was measured as Gy cm², the fluoroscopy time (T) as minutes (min) and the contrast medium (dye) consumption as ml.

Results: In the selected centre two cardiologists perform their procedures in the catheterization laboratory continuously for more than 20 years. Each of them has done about 10,000 coronary angiographies or interventions. In 2012 a new X-ray unit was installed, allowing the assessment of the influence of technological progress significantly contributes to this positive effect with a substantial reduction of the radiation dose area product (DAP) (~32% as dye consumption (~37%) declined significantly in the whole registry from 2002 to 2013, but not fluoroscopy time. We found the same development in the selected centre (DAP: −30%, dye: −33%). Compared to the whole registry, the centre shows significantly smaller values for DAP (% −9) and T (% 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 interventionalists can still reduce the amounts of radiation and contrast medium when using a system of quality control, although severity of PCI cases has been increasing over time. Furthermore technological progress was measured using individual electronic radiation dosimeter badges positioned externally on the sternum. Radioprotection materials and equipment were available to everyone.

Purpose: We sought to compare the operator radiation exposure by right femoral (RFA), right radial (RRA) and left radial (LRA) access during percutaneous catheterization for diagnostic coronary angiography (CA) with or without coronary angioplasty (PCI).

Methods: From September 2014 to February 2015, all consecutive patients (n=692) undergoing elective or emergency CA +/- PCI, performed at our hospital, Switzerland, were prospectively included. The selection of the percutaneous access site was left to the discretion of the interventional cardiologist. Operator radiation exposure was measured using individual electronic radiation dosimeter badges positioned externally on the sternum. Radioprotection materials and equipment was similar for all procedures. The primary endpoint was operator radiation exposure quantified as cumulative dose (CD) per dose area product (DAP), in order to adjust for the differences in total radiation dose. Results: A total of 692 consecutive procedures (386 [56%] CA and 306 [44%] PCI) were performed, of which 380 (55%) were realized via the RFA, 232 (34%) via the RRA and 80 (11%) via the LRA. The cumulative dose of radiation received by the operator in the selected centre was lower in the RFA (6.9±11.8 μSv) as compared to the RRA (26.4±54.1 μSv, p<0.001) or the LRA (9.9±18.5 μSv, p<0.001). The latter approach showed a significantly lower cumulative dose compared to RRA (p<0.001). There was no difference in the DAP between LRA (34.4±23.5 Gy cm²) and RRA (40.29±28.6 Gy cm², p=0.13). The fluoroscopy time (T) was significantly lower in the RFA compared to the RRA (0.30±0.36 cm² vs. 40.29±28.6 Gy cm², p=0.001) or the LRA group (0.30±0.36 cm²) and RRA (40.29±28.6 Gy cm², p=0.13). The RFA however demonstrated the adjusted operator radiation exposure was significantly lower in the RFA compared to the RRA (p<0.01) or the LRA (p<0.001). The adjusted operator radiation exposure was significantly lower in the RFA (0.17±0.27±0.71 Sv/Gy cm²) compared to the RRA (0.62±0.69±0.86 Gy cm², p<0.001) or the LRA group (0.30±0.36±0.71 Sv/Gy cm², p<0.001). Operator radiation exposure was lower for the LRA compared to the RRA (p<0.001).

Conclusions: The RFA in percutaneous coronary angiography and percutaneous coronary intervention is associated with significantly lower operator radiation exposure when compared to the RRA or LRA. The LRA is associated with significantly lower operator radiation exposure when compared to the RRA.

BEST POSTERS IN NEUROHORMONES

P2378 | BEDSIDE Radiation exposure of the operator during coronary interventions: comparison of right radial, left radial and right femoral approach

Background: Because of a presumably increased incidence of long-term malignant cardiologists, radiation exposure of the operator during coronary interventions is of rising concern. A few studies concerning the operator radiation exposure comparing femoral to radial or radial to left radial access have previously been published, but no data comparing the three access sites are available to our knowledge.

Purpose: Our study aimed to compare the radiation exposure of the operator during coronary interventions by right femoral (RFA), right radial (RRA) and left radial (LRA) access during percutaneous catheterization for diagnostic coronary angiography (CA) with or without coronary angioplasty (PCI).

Methods: From September 2014 to February 2015, all consecutive patients (n=692) undergoing elective or emergency CA +/- PCI, performed at our hospital, Switzerland, were prospectively included. The selection of the percutaneous access site was left to the discretion of the interventional cardiologist. Operator radiation exposure was measured using individual electronic radiation dosimeter badges positioned externally on the sternum. Radioprotection materials and equipment was similar for all procedures. The primary endpoint was operator radiation exposure quantified as cumulative dose (CD) per dose area product (DAP), in order to adjust for the differences in total radiation dose. Results: A total of 692 consecutive procedures (386 [56%] CA and 306 [44%] PCI) were performed, of which 380 (55%) were realized via the RFA, 232 (34%) via the RRA and 80 (11%) via the LRA. The cumulative dose of radiation received by the operator in the selected centre was lower in the RFA (6.9±11.8 μSv) as compared to the RRA (26.4±54.1 μSv, p<0.001) or the LRA (9.9±18.5 μSv, p<0.001). The latter approach showed a significantly lower cumulative dose compared to RRA (p<0.001). There was no difference in the DAP between LRA (34.4±23.5 Gy cm²) and RRA (40.29±28.6 Gy cm², p=0.13). The RFA however demonstrated the adjusted operator radiation exposure was significantly lower in the RFA (0.17±0.27±0.71 Sv/Gy cm²) compared to the RRA (0.62±0.69±0.86 Gy cm², p<0.001) or the LRA group (0.30±0.36±0.71 Sv/Gy cm², p<0.001). Operator radiation exposure was lower for the LRA compared to the RRA (p<0.001).

Conclusions: The RFA in percutaneous coronary angiography and percutaneous coronary intervention is associated with significantly lower operator radiation exposure when compared to the RRA or LRA. The RFA is associated with significantly lower operator radiation exposure when compared to the RRA.

P2381 | BEDSIDE Hyponothyroidism predicts the mortality of idiopathic dilated cardiomyopathy
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Background: Previous studies showing 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 influence the mortality in patients with HF.

Methods and results: The original cohort consisted of 572 consecutive patients with idiopathic dilated cardiomyopathy (IDCM), and 458 patients remained at the end of follow-up. All the patients took thyroid function test and other regular examinations in hospital. The risk of mortality was evaluated based on FTC3, 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 (HF-troph). Fourteen patients were in NYHA III-IV. During the follow-up (17±8 months), there were 111 cumulative deaths. Hyponothyroidism 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: 1.556–6.355) and subclinical hypothyroidism (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.

P2382 | BENCH Myocardial gene expression of osteopontin is higher in idiopathic than ischemic end-stage dilated cardiomyopathy
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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 (<50% EF) as well as ICM patients (EF >50%). 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: 1.127±0.26; DCM: 1.29±0.22; ICM: 1.00±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** 

Pro-ADM is a strong prognostic biomarker in acute heart failure with preserved ejection fraction: data from the ACE 2 Study 

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**Background:** There is a need for improved patient management in heart failure with preserved ejection fraction (HFrEF). Mid-regional pro-adrenomedullin (MR-proADM) levels are reflective of left ventricular (LV) remodeling, but the prognostic utility of MR-proADM in HFrEF is unknown. 

**Methods:** We measured MR-proADM levels on hospital admission in 141 patients with preserved ejection fraction (HFrEF). We determined if MR-proADM was affected by etiology of heart failure in the presence of similar LVEF. 

**Results:** MR-proADM levels were higher in HFrEF compared to HFpEF (4800 ± 2600 vs. 2160 ± 1190 pmol/L (p<0.0001), adjusted for established risk indices, including NT-proBNP levels, MR-proADM levels discriminated between patients with a poor and favorable prognosis. 

**Conclusion:** Measuring mid-regional pro-adrenomedullin (MR-proADM) in patients with heart failure with preserved ejection fraction is important for patient management. 

**Acknowledgement/Funding:** Thermo Fisher Scientific supported the study by providing reagents.
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.

P2387 | BENCH
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 sympathetic 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) underwent RSD. All patients had a stable antihypertensive drug regimen of 3 agents including a diuretic. All RSD procedures were performed using the Symplicity Flex Catheter. Aortic PWV was assessed invasively by simultaneous pressure recordings in the ascending aorta and femoral artery. PWV was calculated from distance between pressure recordings and wave transition time. PWV was assessed in all patients before RSD and in 29 patients before and 6 months post RSD.

Results: Mean age of the patient population was 62±10 years. There was a significant reduction in mean daytime systolic ABPM from 154.3±11.4 to 146.2±13.0 mmHg (p<0.0001). Patients with baseline PWV below the median (14.4 m/s) displayed a significantly greater reduction in mean daytime systolic ABPM as compared to patients with PWV above the median (PWV < median: -12.3±10.9 vs. PWV > median: -4.3±9.6 mmHg, p=0.005). Baseline PWV correlated significantly with changes in mean systolic ABPM 6 months after RSD (r=0.42, p=0.0008).

Conclusion: Increased aortic stiffness as assessed by PWV seems to be associated with unfavourable outcome after RSD and remains unaffected by RSD. These results warrant further study of PWV as a patient selection criterion for RSD.

P2388 | BENCH
The effectiveness of chemical renal denervation by vincristine depends on the flow rate of delivery
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Background: The effectivess of chemical renal denervation by vincristine depends on the flow rate of delivery.

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 (1.48±0.37 vs 1.70±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.

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.

Objective: To evaluate potential echocardiographic predictors related to super-response after CRT.

Methods: 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 predictor for CRT super-response (95% confidence interval [CI] 1.007–1.055; P=0.011). In ROC curve analysis LVPEP demonstrated sensitivity 73.7% and specificity 75% (AUC 0.753; P=0.002) in prediction of response to CRT.

Conclusion: Greater cardiac mechanical dyssynchrony is associated with super-response to CRT in patients with CHF: LVPEP can be used as an independent predictor of super-response.

P2394 | BEDSIDE Cardiac resynchronisation therapy: the importance of the interventricular depolarization time as a predictor of clinical response

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Purpose: To evaluate the impact of QRS duration changes with CRT in clinical outcomes such as symptomatic improvement, hospital admissions for cardiac causes and mortality.

Methods: Retrospective review of 139 consecutive patients evaluated in a specialized medical follow-up appointment with a CRT implanted (44% women, mean 66±9 years, 30% with ischemic cardiomyopathy). In each patient, QRS duration without pacing and with biventricular pacing was registered. We calculated a difference “delta” QRS duration between “baseline” (QRS duration without pacing “baseline”) and QRS duration with biventricular pacing (QRSpacing). Patients were randomized into 2 groups – patients with “delta” QRS <150ms and group 2 with “delta” QRS ≥150ms. The narrowest biventricular QRS can represent an optimal cardiac synchronisation. ECG is reproducible method for CRT optimization.

Results: There were no significant differences in cardiomyopathy etiology, baseline QRS, QRS between the groups. 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 of the 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: QRS duration optimization improves hemodynamic parameters in the long-term period. The narrowest biventricular QRS can represent an optimal cardiac synchronisation. ECG is reproducible method for CRT optimization.
spouse only amongst patients with QRS > 150ms 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 > 150ms, a simple variable (‘delta’ QRS) can be helpful in predicting clinical response to CRT implantation. In patients where baseline QRS was >150ms the clinical response occurred in over 75%, and “delta” QRS showed no benefit in predicting clinical response

P2395 | 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 modality for patients with chronic heart failure and a 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±9, NYHA class II/III/IV 69/64/6, ejection fraction 25±6, mean heart rate 75±15) receiving a CRT system who underwent a cardiac CT with measurement of LA size and function (Table). Patients alive, not hospitalized for heart failure, and improving >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).

<table>
<thead>
<tr>
<th>LA parameters</th>
<th>Clinical response</th>
<th>Echocardiographic response</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>CTR</td>
<td>CI</td>
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<tr>
<td>Maximum volume</td>
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<td>Active emptying volume*</td>
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<tr>
<td>Active emptying interval*</td>
<td>0.963</td>
<td>0.892–1.038</td>
</tr>
</tbody>
</table>
| OR, odds ratio; CI, confidence interval. Adjusting for gender, age, NYHA class, QRS duration, heart failure etiology, ejection fraction, and atrial fibrillation. Patients in sinus rhythm with a two-phased LA emptying (n=97).

Conclusion: 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.

P2396 | BENCH
The ratio of the neutrophil leukocytes to the lymphocytes predicts the outcome after cardiac resynchronization therapy
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Background: The low lymphocyte counts and high neutrophil leukocyte fractions have been associated with poor prognosis in chronic heart failure. We hypothesised that the baseline ratio of the neutrophils to the lymphocytes (NL ratio) would predict the outcome of chronic heart failure patients undergoing cardiac resynchronisation therapy (CRT).

Methods: The qualitative blood count and the serum levels of NT-proBNP (N-terminal of the prohormone brain natriuretic peptide) of 122 chronic heart failure patients and 122 healthy controls were analysed. We considered the 2-year mortality rate and the 2-year mortality (n=29, hazard ratio=2.14 [1.04–4.43], p=0.029) as outcome. 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 ventricular pacing.

Conclusions: Baseline ratio of neutrophils to lymphocytes is associated with clinical and echocardiographic response to CRT. Patients with a 2-year mortality rate and the 2-year mortality (n=29, hazard ratio=2.14 [1.04–4.43], p=0.029) as outcome. 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 ventricular pacing.
ELECTROCARDIOGRAPHY – CARDIOVERSION – DEFIBRILLATION

P2401 | BEDSIDE
Difference of mean ventricular fibrillation zone cycle length between appropriate and inappropriate therapy in patients with congenital heart disease

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, Cardiology, Seoul, Korea, Republic of Background: The implantable cardioverter defibrillator (ICD) is indicated in high risk patients with Brugada syndrome (BS), early repolarization 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±13.0 years, 35 males) with BS, ERS and IVF (24, 9 and 8 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 were detected by the ICD were measured.

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. Programming a single, high cut off rate VF zone of 270 ms in patients with BS, ERS and IVF would be associated with reduced inappropriate ICD therapy with very low risk of missing appropriate therapy.

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 these algorithms and that of the single criteria included in them. Interobserver agreement was evaluated.

Methods: A retrospective review of the arrhythmia in adult congenital heart disease database at our institution, from 1996 to 2015 was performed. All patients with WCT, a 12-lead electrocardiogram (ECG) available for review, and an electrophysiological study used as the gold standard for defining VT and SVT were included. Patients with a paced rhythm were excluded. Three blinded cardiologists independently analysed the ECGs according to the Brugada and Vercelli 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 tachyarrhythmia (SVT) and atrial fibrillation (AF) was noted in 78.2% and VT in 21.8% of the ECGs. The mean age was 38.5±21.6 years. 62.7% were male. The mean tachycardia cycle length was 418±215 milliseconds. CHD were: 21 tetralogy of Fallot, 6 atrial septal defect, 7 transposition of great arteries, 4 complex CHD, 4 Ebstein anomaly and 9 other CHD. The Brugada algorithm correctly predicted the diagnosis 72.7% of the time; the Vercelli algorithm correctly predicted the diagnosis 65.5% and the Pava criterion 98.2%. S, Sp, PPV and NPV of the algorithms 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.

Table 1. Results

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
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<tbody>
<tr>
<td>Brugada</td>
<td>66.7%</td>
<td>74.4%</td>
<td>42.1%</td>
<td>68.9%</td>
</tr>
<tr>
<td>Vercelli (aVF)</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 II ≤50ms)</td>
<td>100%</td>
<td>97.7%</td>
<td>92.3%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Conclusion: The Brugada and Vercelli 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.
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 IFV.

**Methods:** Patients with idiopathic VF (n=52, median age at event 37 [IQR 24] years, 62% male) were followed for a median time of 8 [IQR 11] years. Structural heart disease was excluded by echocardiography and/or cardiac MR. Channelopathies and ischemic heart disease were also ruled out. All patients received an ICD and subsequent follow-up included device-based data and clinical outcome. Pre-ICD implant ECGs were available in all subjects and were analysed independently by two electrophysiologists.

**Results:** A majority, 71%, had abnormal ECG findings at baseline. 3 patients developed reduced ejection fraction during follow-up, but no patients received any definite etiologic diagnosis. 9 patients (17%) had appropriate ICD therapy at a median of 1.5 (0–13) years after implant. 9 patients had inappropriate ICD shocks. One patient had a ventricular storm. All patients survived. Neither ECG nor imaging findings and clinical factors could predict appropriate ICD therapy (table).

**Conclusion:** Contrary to earlier reports, the vast majority of patients who survived idiopathic VF in our cohort had no VF recurrence during long-term follow-up. ECG abnormalities though common were unspecified 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 bradyarrhythmia after ablation.

**Results:** SND developed in 12 (5.9%) patients. There was no difference between the patients with and without SND in terms of the age (with SND: 67±9, and without: 66±10 years old, p=0.598) and sex (male: 52% vs. 79%, p=0.186). However, the patients with SND had a lower amplitude of the fibrillatory waves (0.15±0.086 vs. 0.176±0.077 mV, p=0.009) and larger left atrial volume index (LAVI: 66±31 vs. 34±13, p=0.007) than those without. A receiver operating characteristic curve identified a fibrillatory wave amplitude of 0.145 mV (AUC=0.742; sensitivity=65%; specificity=87%) as the optimal cutoff values for predicting SND. A multivariate analysis revealed that the amplitude of the fibrillatory waves (odds ratio=0.84 for 0.101mV increase, 95% CI: 0.71–0.98, 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.

**Conclusions:** A low amplitude of the fibrillatory waves and large LAVI were predictors of SND after restoration of sinus rhythm by ablation in patients with persistent AF.

**Acknowledgement/Funding:** Nothing

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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 62.1±13.1, 71% male with no significant differences among groups. 19 (7.4%) patients did not undergo EC in the DOAC group (sinus rhythm) and 18 (14.6%) in warfarin group (55.6% due to inadequate anticoagulation or LA thrombus). In patients naive to OACs (28%) time to EC was shorter in DOACs 31 (21–40) days vs 44 (7–70) days p=0.04. Mean CHADS2VASc Score was higher in warfarin group 3.0±0.9 vs 2.0±0.5 p<0.01. TE events occurred in 4 (1%) patients: 0 in DOACs 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 2012–14 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 (AAQRSV) 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, 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.

Results: Amongst the whole cohort (n=40), there was no difference in QT or TL before and after DCCV. However, patients who reverted to AF demonstrated significant prolongation of QT after DCCV (292±377 vs. 277±380 ms; P=0.001) and LVP increased at 1, 3, and 5 minutes (111±26 ms vs. 108±24 ms, P=0.002). There were no differences in OL between pre- and post-DCCV in those who maintained SR (1691±581s vs. 1480±786s; p=0.17). Between groups comparison showed significantly prolonged QT in those who reverted to AF compared to those who maintained SR after DCCV (289±173 vs. 147±192s; P=0.002). No change in QT was observed in between groups. There was no difference in baseline QT and baseline QRS duration 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 therapy. Larger studies are needed to confirm these findings and assess the role of endogenous thrombolysis from a native, non-anticoagulated blood sample. The groups were well matched for variables, including age, sex, OACs, and CHA2DS2-VASc score.

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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) without who had no evidence of acute ischemia or vascular diseases were evaluated and divided into two groups: 1) with early repolarization in inferior leads 2) without those findings. Baseline demographic, clinical and electrocardiographic characteristics were analyzed. Early repolarization was defined as ≥0.1mV J-point elevation of the ERS-ST junction in at least two leads in inferior leads as QRS slurring or notching, and was stratified according to the degree of J-point elevation (≥0.1mV or ≥0.2mV).

Results: ER was identified in 26 subjects. There was no significant difference in baseline characteristics between the two groups. However, 13 subjects with more than 0.2mV J-point elevation of Group 1 had markedly lower in survival time than the Group 2 (2.3±3.3 vs 9.7±19.1 days, P=0.02) and more than 5 days survival after resuscitation was significantly increased in Group 2 compared with those subjects in Group 1 (28 vs 15%, P=0.022).

Kaplan-Meier curve for cardiac arrest

Conclusions: Greater ascending of early repolarization in the inferior leads of ECG after resuscitation might suggest the poor outcome in the CA subjects.

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P2410 | BEDSIDE
Hyperkalemic induced 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 hypokalemia.

Objective: We aimed to describe the prevalence, clinical, electrocardiographic and arrhytmic 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 axial. Serious arrhythmias occurred more frequently (60%) in BP (1 high degree AV block and 2 VT) than in the rest of hyperkalemic p (25%) (7 high degree AV block, 3 VT and 1 VF).

Conclusions: Hyperkalemic induced Brugada phenocopy occurs more frequently than expected, often associated with severe hyperkalemia and is associated with more arrhythmias and serious arrhythmias compared to non BP p.

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<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Non-Brugada phenocopy (n=44)</th>
<th>Brugada phenocopy p value (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year, median (IQR)</td>
<td>72 (57–81)</td>
<td>57 (49–63) 0.03</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>20 (46%)</td>
<td>2 (40%) 0.82</td>
</tr>
<tr>
<td>Serum potassium, median (IQR)</td>
<td>6.9 (6.6–7.3)</td>
<td>8.2 (7.3–8.9) 0.04</td>
</tr>
<tr>
<td>Diabetes Mellitus, n (%)</td>
<td>20 (46%)</td>
<td>4 (80%) 0.02</td>
</tr>
<tr>
<td>Chronic kidney disease, n (%)</td>
<td>23 (52%)</td>
<td>7 (14%) 0.37</td>
</tr>
<tr>
<td>Critically ill, %</td>
<td>24%</td>
<td>0% 0.03</td>
</tr>
<tr>
<td>ECG RR segment, ms, median (IQR)</td>
<td>160 (120–180)</td>
<td>160 (120–130) 0.77</td>
</tr>
<tr>
<td>QRS width, ms, median (IQR)</td>
<td>100 (80–130)</td>
<td>130 (105–160) 0.08</td>
</tr>
<tr>
<td>QRS abnormal axis, n (%)</td>
<td>17 (39%)</td>
<td>4 (80%) 0.04</td>
</tr>
<tr>
<td>T wave height, mm, median (IQR)</td>
<td>4 (2.6–8)</td>
<td>9 (6.3–15.5) 0.01</td>
</tr>
</tbody>
</table>

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/163/434475/1163434215/434475 by guest on 14 March 2019
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 | BESIDE
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 aimed to follow PT, PAM and Ptf changes during 5-year follow-up (SFU) 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, SFU. The exclusion criteria were: arrhythmia other than AF, unsuccessful RSR, successful RSR but missing 12-leads ECG recording, previous ablation/operation within left atrium, no SFU. Consequently, 608 patients (52% male; median: age 65 years, CHADS2 2, CHA2DS2-VASc 3, EF 55%, LA 4.6 cm) were identified. PT, PAM 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 PTS (60 [40;100]), A2/PAM0 (0.075 [0.050;0.10]) and PAMS (0.1 [0.0;0.10]), A3/PT (4.75 [2.5;6.0]) and PHS (7.9 [6.0;10.0]); B/Correlations between: B1/changes of PT (PTS-PT0) and number of HOSP in SFU (HOSPS); r=0.28, p<0.00001; B2/changes of PAM (PAMS-PAM0) and HOSPS; r=0.25, p<0.00001; B3/changes of Ptf (Ptf5-Ptf0) and HOSPS: r=0.5, p<0.00001.

Conclusions: 1. The progression of atrial electrical remodelling can be observed with changes of PAM, PT, Ptf in standard 12-leads ECG. We describe significant SFU changes of PAM, PT, Ptf in standard 12-lead ECGs 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 | BESIDE
QT-TQ dynamics in long QT patients during a supine-standing ECG 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 (ΔR-TQ) during supine-standing tests may further improve the diagnostic possibilities.

Purpose: To evaluate QT-TQ dynamics in LQTS patients.

Methods: Age and gender matched subjects with LQTS1, LQTS2 and healthy relatives (controls) were studied (each group n=8). Continuous 12 lead ECGs were recorded over 2 minutes in supine position (baseline) followed by 3 minutes of standing. For analysis we used a custom-made program applying fiducial segment averaging. Beat-to-beat analysis of RR, TQ (ΔR-TQ), QT and TQ/TQ ratios and QT/TQ crossover (defined as a change in QT/TQ ratio from <1 at baseline to >1 at standing) was performed at baseline, during supine (first 30s of standing) and during standing (1 min following supine-stand).

Results: In all groups (mean±SD, 42±5 yrs, 63% male, before betablocker therapy, 347±36 beats per subject) QT significantly decreased during supine-stand, whereas QT hardly decreased (figure). It resulted in a significant QTc- prolongation during standing (QTc-stretching) in control (442±5 to 474±11) and LQTS (476±10 to 530±17), but not in LQT1 (495±9 to 524±25). In 6/8 controls QTc of several beats exceeded the previously established critical level of 490 ms during supine-stand. All four LQTS patients with a normal baseline QTc <465, and only 1 of 5 controls, demonstrated a QT/TQ crossover during standing (p<0.05).

Conclusions: QT/TQ ratio crossover during standing may add to diagnosis of LQTS, and identifies LQTS patients with otherwise normal baseline QTc.

P2413 | BESIDE
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 (IVLT), and evaluate ECG criteria for the differential diagnosis of wide QRS complex tachycardia (WCT) in this subset of arrhythmia.

Methods: Retrospectively, a total of 51 patients who underwent radiofrequency catheter ablation (RFCA) with ILVT verified by electrophysiological study between August 2012 and March 2014 were included in this study. The ILVTs were classified into three subgroups according to the origin verified by successful ablation. During the episodes of ILVT induced in the electrophysiology study (EPS), the atrioventricular and atriofascicular 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. VA conduction was observed in 29.4% induced ILVTs (ΔRIV 0.15-0.16s; 49.3% surface ECGs exhibited evidence for atioventricular 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±9.2ms, 3) Mean R/S interval was 57.6±9.5ms, 4) VVI=1 was observed in all preiral and aVR leads, 5) Mean R wave peak time at DII was 20.4±8.7ms, 6) Left axis deviation was observed in 64.4% ECGs while 35.6% exhibited axis of “no man’s land”, 7) Lead V1 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 anterior ILVTs, the ECG exhibited a right deviation of frontal QRS axis with qR pattern at lead V1 and Rs pattern at lead V6. Atrioventricular dissociation was observed in two of three ECGs in the subgroup of upper septal ILVT, leaving one case presenting 1:1 retrograde P wave.

Conclusion: WCT differential criteria related with conduction velocity fail to reliably predict the correct diagnosis of ILVT. Axis of “no man’s land” and morphology criteria are valuable in differentiating ILVT from wide QRS complex SVT. In addition, atrioventricular dissociation is frequently detected on the surface ECG of ILVT and represents the sole ECG finding to predict the presence of upper septal type ILVT.

P2414 | BESIDE
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 electrocardiogram (ECG) database was reviewed from 2013 to 2014 to identify patients with complete RBBB. ECGs recorded closest to the time of the echocardiogram were carefully reviewed and reviewed by two physicians to measure QRS and R’ wave duration. RV systolic dysfunction was defined as RV fractional area change (<35%), as indicated by echocardiography guidelines.

Results: Patients with RV dysfunction (n=241) showed more prolonged QRS duration (145.3±19.3 vs. 132.2±14.3 ms, p<0.001) predominantly due to R’ prolongation (84.8±14.0 vs. 102.9±12.0 ms, p<0.001) compared to the patients with normal RV function (n=123) (Table). R’ duration was significantly associated with RV FAC (r=-0.609, p<0.001), as well as RV systolic pressure (r=0.142, p=0.008), RV dimension (r=0.193, p<0.001) and RV myocardial performance index (r=0.199, p<0.001).

Conclusion: Prolonged R’ wave duration in lead V1 would be an indicator of RV dysfunction as well as pressure and/or volume overload in patients with RBBB.
The J-waves were recorded with ST-elevation in 18 patients (75%) during acute pericarditis. The J-wave was defined as terminal QRS notching or slurring with amplitude of >0.1 mV in at least 2 leads.

Results: The J-waves were recorded with ST-elevation in 18 patients (75%) during acute pericarditis (figure, A-D). The J-waves newly appeared in 16 patients, and the already existing J-waves were augmented in 2 patients. J-waves were more prevalently observed in the inferior leads (II, III, aVF) (83%). In the representative case, the notching type J-waves appeared with ST-elevation on Day 1 and changed to slurring on Day 2, and disappeared on Day 3 leaving with ST-elevation over AP at atrial pacing (unapparent PS); 24 patients had intermittent PS; 85 patients (14%) had a normal ECG in SR and anterograde conduction and 10 published EKGs of 8 Male, age 49±14 years, heart rate 115±14 min-1 and compared it to 443 patients with chronic LBBB, 160 Male, age 77±5 years, heart rate 77±5 min-1 (all data Mean±SD). Maximal precordial S/T wave ratio (S/T) was used as best approximation of the QRS/T vector ratio. Painful LBBB S/T was 1.48±0.16 (range 1.2–1.7) while chronic LBBB S/T was 3.92±0.05 (p<0.001 with painful LBBB). There was no overlap between chronic LBBB and painful LBBB at S/T cut-off of 2.4.

Conclusions: EKG pattern of the painful LBBB within seconds/minutes of onset is characterized by a very low (<1.7) precordial S/T ratio consistent with the “new LBBB” pattern. S/T ratio of 2.0 discriminated between acute onset and chronic LBBB. This finding confirms the validity of LBBB age determination based on QRS/T vector 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 by electrophysiological study (EPS) for palpitations.

Methods: ECGs of 617 patients in whom PS related to an atrioventricular accessory pathway (AP) was identified at esophageal and/or intracardiac electrophysiological study (EPS), were studied. All patients had symptoms that had led to EPS. Asymptomatic PS was excluded. PS was considered as malignant and at risk of sudden death when PS confers both intermediate AP (between preexcitation and right atrial activation = <250 ms in control state (CS) or >200 ms after isoproterenol during induced 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 (over PS). Gender and age (respectively 36±17, 38±19, 35±17.5) did not differ significantly. Accessory pathway (AP) was more frequently left lateral in patients with unapparent PS (62%) than in patients with intermittent PS (33%) (0.011) and overt PS (41%) (0.0003). Left 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 normal coronary arteries without CSF were included in this study. TP-e interval and QT duration were measured from the 12 derivation electrocardiogram (ECG), TP-e/QT ratio was calculated.

Results: Demographic, clinical, and electrocardiographic data of the study groups are listed in Table 1. TP-e interval (117±21 vs. 96±16, P = 0.001) and TP-e/QT ratio (0.30±0.06 vs. 0.27±0.06, P = 0.005) were significantly higher in CSF patients group than in the control group (Fig. 1).

Conclusion: Recently, TP-e interval and TP-e/QT ratio emerged as new electrocardiographic marker that predicts arrhythmia risk in different spectrum of diseases over AP. In our study, electrocardiograms demonstrated myocardial ischemia in 28-75% of patients with CSF having positive scintigraphic findings. Myocardial ischemia at the microvascular level may explain the increased TP-e interval and TP-e/QT ratio. Non-invasive techniques have been using to help determine the risk of life-threatening arrhythmias, and our study is the first to assess the utility of electrocardiographic assessment in this regard.

P2415 | BEDSIDE

Electrocardiographic characteristics of the painful left bundle branch block syndrome
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Background: Age determination of the left bundle branch block (LBBB) remains an unresolved issue of electrocardiography. T wave vector amplitude during continuous ST-elevation in patients with cardiac memory phenomenon of the QRS/T vector ratio have recently determined as the predictors of the development of malignant arrhythmias. The QRS/T vector ratio has been proposed to characterize LLBB morphology (QRS/T vector ratio) in the first seconds/minutes of its onset remains unknown. The “painless LBBB syndrome” is a chest pain syndrome coincidental with intermittent LBBB in the absence of myocardial ischemia commonly seen during an exercise stress test. Simultaneous onset of chest pain and LBBB during exercise stress test creates an opportunity for exact LLBB timing and accurate waveform measurement.

Objectives: To characterize LLBB morphology (in particular QRS/T wave ratio) in painful LBBB syndrome immediately after LBBB onset and compare it to the chronic LBBB.

Methods and results: We analyzed electrocardiograms (EKG) of 14 patients with painful LBBB syndrome (8 Male, age 49±14 years, heart rate 115±14 min-1) and compared it to 443 patients with chronic LBBB, 160 Male, age 77±5 years, heart rate 77±5 min-1 (all data Mean±SD). Maximal precordial S/T wave ratio (S/T) was used as best approximation of the QRS/T vector ratio. Painful LBBB S/T was 1.48±0.16 (range 1.2–1.7) while chronic LBBB S/T was 3.92±0.05 (p<0.001 with painful LBBB). There was no overlap between chronic LLBB and painful LLBB at S/T cut-off of 2.4.

Conclusions: EKG 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 vector ratio.

Figure 1. J-waves in acute pericarditis

Conclusion: The present study suggested that the J-waves manifested by acute pericarditis could be associated with electrophysiological abnormalities in the ventricular subepicardial region.
PS except the rate of malignant form higher in unapparent PS (23%) than in overt PS (14%) (P<0.03). Two patients with unapparent PS presented aborted sudden death. Patients with unapparent and overt PS differ significantly from intermittent 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 condition on AP (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 enlarge indications of EPS that is the only means compared to home event monitors to diagnose a PS and at opposite to eliminate an anterograde 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 pointing the depolarization or ionic channels alteration in the repolarization. A previous study reported the association between a wide frontal QRS-T angle and anterograde conduction 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 who underwent ICD implantation from 2008 to 2014 (66 males, 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 using univariate and multivariate Cox regression model.

Results: During follow-up, the event developed in 17 patients (18.5%). Patients with appropriate ICD therapy had wider QRS-T angle than those without ICD therapy (133° ± 42° vs. 75° ± 42°, P<0.001). The patients with frontal QRS-T angle ≥110° received more appropriate ICD therapy than those with QRS-T angle <110° (14.1% vs. 4.3%, P=0.001). Presence of frontal QRS-T angle ≥110° was the predictor of appropriate ICD therapy (hazard ratio 5.78, 95% confidence interval 1.95–17.60, 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 3.95, 95% confidence interval 1.78–8.94, P=0.003 and hazard ratio 5.05, 95% confidence interval 2.67–9.59, P<0.001 respectively). In multivari- ate 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 who underwent percutaneous ASD closure devices, to determine the effects of structural innovations on atrial electrical inhomogeneity.

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 10-lead surface electrocardiography, before the procedure and soon after the 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 18.3±2 mm. Pmax, Pmin and Pd were significantly decreased 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).

Conclusion: Pmax, P min 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: Electrocardiogram (ECG) finding characterized by J-point elevation and QRS notch or slurring in the inferior and/or lateral leads. Its prevalence in Southern Cone of Latin America is unknown.

Methods: CESCAS I study is an observational prospective cohort study with a multistage 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.

Purpose: To determine the prevalence of ERP according to the Nomenclature suggested by Macfarlane.

Prevalence of ERP was considered ERP if there was J-point elevation in ≥2 leads in the inferior (II, III, 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:

1. notch ≥0.1 mV and elevated ST amplitude ≥0.1 mV.
2. notch ≥0.1 mV and elevated ST amplitude <0.1 mV.
3. slr ≥0.1 mV and elevated ST amplitude ST ≥0.1 mV.
4. slr ≥0.1 mV and elevated ST amplitude <0.1 mV.
5. ST elevation ≥0.1 mV without notch or slr.

There was an important strength of agreement between the two initial interpreters (kappa test was used for inter-observer variation). There was an overall prevalence of ERP of 4.77%. The kappa test was used for inter-observer variability.

Results: A total of 1868 ECGs were analysed with a male proportion of 39.8% and a mean age of 54.2 years.

ERP prevalence was 4.77% (90/1886). The inferior territory was found in 70% of cases (63/1886). The most common type was the “slurring” appearance without ST elevation (type 4) represented 68.89% of cases. Type 2 was observed in 27.78% of cases (25/886).

Conclusions: Consistent with published estimates ranging from 1% to 13% we found an overall prevalence of ERP of 4.77%.

A novel formula to predict the QT interval during intrinsic atrioventricular conduction from the ventricular paced electrocardiogram
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Background: The QT interval is used to monitor drug safety and arrhythmia risk. Ventricular pacing (VP) alters the QT interval through immediate QRS prolongation and time-dependent repolarization remodeling. Normal QT interval limits during VP are unknown and there exists no consensus on its monitoring.

Purpose: We sought to develop a formula to predict the QT interval during intrinsic atrioventricular conduction (IC) from the ventricular paced electrocardiogram (ECG). We performed paired measurements in AAI (IC) and DDD (VP) modes at equal heart rates (HR) at baseline and after VP for 1 week. We fit a generalized estimating equation model to predict IC QT intervals from VP intervals.

Methods: In 38 patients (22 men, age 69±12.8 yrs, MtsSD) with cardiac devices and preserved atrioventricular conduction, we measured QRS, QT, QT peak (QTp), and T peak-T end (TpTe) intervals using custom-built software. We performed paired measurements in AAI (IC) and DDD (VP) modes at equal heart rates (HR) at baseline and after VP for 1 week. We fit a generalized estimating equation model to predict QT intervals from VP intervals.

Results: VP resulted in immediate QRS, QT, QTp, and TpTe prolongation compared to IC at baseline. After 1 week of VP, IC QT prolonged while VP QT shortened due to a decrease in the VP TpTe interval. QTp prolonged in both pacing modes at 1 week. A formula using VP QTp and HR: 0.861 x QTp [ms] – 1.21 x HR (beats per minute) + 205, predicted the IC QT interval with R²=82% (P<0.001 for model and coefficients).

Conclusions: One-week of VP results in repolarization remodeling as evidenced by prolongation of the QT interval during IC but shortening during VP. VP QT...
shortening occurs through a decrease in the TPTe interval, indicating reduced repolarization heterogeneity. In contrast, the QTp interval at 1 week trends in the same direction during IC and VP. In patients with ventricular paced rhythms, a formula using the VP QTp interval closely predicts the intrinsically conducted QT interval.

**P2423 | BEDSIDE**

Identification of the anatomic location of focal atrial tachycardias using synthesized 18 lead electrocardiography

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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 focal origin because of the many patterns depending on the anatomic location. Synthesized 18 lead ECG is well known and accepted as the detector of left ventricular posterior wall ischemia. However, it is not evident that it is useful for decision of local electrical activity. This study is to evaluate whether synthesized 18 lead ECG give us additional information to 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 roof area (n=1), right inferior pulmonary vein (RIPV) (n=2), 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.L 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 V7-9.

Conclusion: Synthesized 18 lead ECGs could be helpful to identify the origin of focal AT origins.

**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 arrhythmias, recurrent ischaemia, heart failure, and sudden cardiac death (SCD). Cardiac magnetic resonance (CMR) is still a gold standard which cannot be applied to every patient. A 12-leads electrocardiography (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 Verecieri criteria to differentiate wide complex tachycardia. The aim of this study is to evaluate the association of this criteria with myocardial scar presence.

Methods: This is a cross-sectional study. A consecutive subjects who underwent CMR during January 2013 and August 2014 were included. Myocardial scar were analyzed visually using late gadolinium enhancement CMR. Vi/vt on 12-leads electrocardiography with myocardial scar presence.

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 and left anterior descending (LAD) territory as the most common territory. General analysis of vi/vt in each contiguous leads shows significantly smaller vi/vt in myocardial scar presence with p value <0.001 in V1-V5 leads, p=0.006 in I, aVL, V6 leads, and p=0.004 II, III, aVF leads. Specific analysis of vi/vt in V1-V5 leads show significant difference of vi/vt in isolated and mixed scar in LAD territory, meanwhile vi/vt in I, aVL, V6 and II, III, aVF leads show significant difference of vi/vt only in mixed scar in each territory according to contiguous leads. A cut-off value ≥1.35 mV of vi/vt in V1-V5 leads with 71.4% sensitivity and 75% specificity and a cut-off value ≤1.20 mV of vi/vt in II, III, aVF leads with 69.4% sensitivity and 66.7% specificity were obtained by ROC analysis.

Conclusions: Vi/vt on 12-leads ECG associated with myocardial scar presence and location. A value of vi/vt 1.20–1.35 mV associated with myocardial scar presence in LAD territory and RCA territory with 69.4–71.4% sensitivity and 66.7–75% specificity.

**ANTIBRADYCARDIA PACING**

**P2425 | REDUCTION**

**REDUCTION in unnecessary ventricular pacing fails to affect hard clinical outcomes: A meta-analysis**

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Introduction: Several pacing modalities have been introduced to minimize unnecessary right ventricular pacing.

Purpose: We conducted a meta-analysis to assess whether ventricular pacing reduction modalities (VPRM) influence accepted hard clinical outcomes in comparison to standard dual-chamber pacing (DDD).

Methods: An electronic search was performed using Cochrane central database, PubMed, Embase, and Web of Knowledge. References were searched manually. Only randomized controlled trials (RCT) were included. Outcomes of interest were: percentages of ventricular pacing (VP), incidence of atrial fibrillation (AF)/atrial tachycardia (AT), all cause mortality (including cardiac death) and carotid (CV)/heart failure (HF) hospitalizations. Continuous variables were expressed as weighted means. Odds ratios (OR) were reported for dichotomous variables.

Results: Five RCTs involving 3470 adult patients were identified. VPRM were employed in 1737 patients (MVP Medtronic) in 1423 and SafeR (Sorin) in 314 patients. Baseline demographics and clinical characteristics were similar between VPRM and DDD groups (Age: 73±1.9 vs. 73±1.5 years, P=0.10; Male gender: 54% vs. 53%, P=0.9 and LVEF: 58±4.4% vs. 57±4.0%, P=0.7). Follow-up ranged between 12–36 months. VPRM showed significant reduction in VP in comparison to DDD groups (7% vs. 85%, P=0.001). The incidence of AF/AT was similar between both groups (14% vs. 15%, OR 0.98 [95% confidence interval [CI] 0.61; 1.30], P=0.56). VPRM showed no significant differences in comparison to DDD for all cause mortality or CV/HF hospitalizations (5% vs. 6%, OR 0.86 [95% CI 0.62; 1.19], P=0.35; 9% vs. 9%, OR 0.94 [95% CI 0.72; 1.22], P=0.64, respectively).

Conclusions: Novel VPRM significantly reduced VP in comparison to standard DDD. When actively programmed, VPRM did not improve clinical outcomes and were not superior to standard DDD programming in reducing incidence of AF/AT, all cause mortality or CV/HF hospitalizations.

**P2426 | BEDSIDE**

Health-related quality of life improvement following transcatheter pacing system implantation

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Background: Transcatheter pacing systems (TPS) provide a novel, less invasive approach in which a miniaturised, “leadless” pacemaker is implanted in the right ventricle using a percutaneous transfemoral route. Compared to conventional pacing systems, TPS mitigates complications related to the lead and pocket 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.

Purpose: To evaluate short-term HRQOL impact of TPS following implantation.

Methods: Between December 2013 and August 2014, 60 patients with an indication for a single chamber ventricular pacemaker were implanted with TPS and completed a 3-month follow-up visit in an ongoing global, multi-center, single-arm clinical trial. HRQOL impact of TPS was evaluated using SF-36 data collected at baseline (pre-implant) and at 3 months. Patient satisfaction with recovery, activity level, and aesthetic appearance at 3 months post-implant was assessed using a 3-item questionnaire.

Results: The mean age of the implanted cohort was 77 years (range: 21–94) and 66.7% were male. Of the 60 patients with a follow-up visit, 58 (97%) completed the SF-36 at baseline and at 3 months. Improvements were observed in all SF-36 domains including physical function, role function and mental health, and all attained statistical significance except for bodily pain (Table). In addition, 96.6%, 96.6% and 89.9% of patients were satisfied/very satisfied with their aesthetic appearance, recovery, and level of activity respectively.

Conclusion(s): TPS resulted in HRQOL improvements, and majority of patients experienced treatment satisfaction by 3 months post-implant.
Purpose: To identify perioperative electrocardiographic and electrophysiologic predictors of long term AVB.

Methods: Patients who underwent TAVR at our center between 2013 and 2014 were included. Patients with PPM at the time of TAVR were excluded. His bundle recording was performed before and after TAVR and repeated at day 2 for Edwards Sapien (ES) valves and day 5 for Medtronic Corevalve (CV). Indication for PPM was high degree AVB occurring before day 5 or prolonged HV interval (>80 ms at the last recording). Occurrence of high degree AVB after discharge was evaluated on pacemaker interrogation, clinical and electrocardiographic findings at 1 month and 6 months.

Results: Data was obtained in 86 patients (66% CV and 34% ES). PPM were implanted in 29 patients (34%) with documented AVB (n=18), 17.9%, or prolonged HV interval (n=8) or sick sinus syndrome (n=3). High degree AVB was observed after discharge in 12 patients (13.9%). The only preoperative predictive factor for AVB was the presence of RBBB (p<0.001). The occurrence of AVB during the procedure and the implantation of CV model were the other two periperaoperative factors associated with long term occurrence of high degree AVB on multivariate analysis (p<0.001 and p<0.003 respectively). Post-operative ECG findings were not associated with the occurrence of late AVB including post TAVR LBBB (p=0.8) and repeated EPS findings (last HV interval, p=0.91). The absence of AVB and narrow QRS at the end of the TAVR was correlated with an absence of delayed post-operative AVB.

Conclusion: Preoperative RBBB, the use of Corevalve model and peroperaoperative high degree AVB are the 3 independent factors for late AVB and should be considered for the decision making of PPM implantation.

P2430 | BEDSIDE
Left ventricular only pacing is a feasible and safe way to avoid tricuspid valve injury in patients with pre-existent tricuspid valve disease or surgery
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Background: Conventional right ventricular pacing is increasingly recognised to cause tricuspid valve (TV) injury or dysfunction, in part due to the need to pass the lead through the valve. This may be especially problematic in patients with pre-existing TV disease or prior TV surgery. Contemporary left ventricular (LV) pacing leads used in biventricular pacemakers or defibrillators have much reduced dislodgement rates and may be a viable alternative for ventricular pacing in these patients without having to pass a lead through the TV.

Purpose: We aimed to determine the safety and feasibility of implanting an LV lead in place of a conventional right ventricular pacing lead.

Methods: We report a series of 13 patients (age 69±10 years old, 7 female) who had moderate or severe tricuspid regurgitation (TR, n=10), TV repair or annuloplasty (n=3) or a bioprosthesis (n=1) or a bioprosthesis and TV replacement (n=1) and patients were followed for a median of 297 days (IQR 96-454 days) to determine lead performance.

Results: The LV lead was placed in the posterior (n=8), posterolateral (n=2), anterolateral (n=4) or middle cardiac vein (n=2) branches of the coronary sinus. LV lead sensed R wave amplitude was 11.8±7.1mV, impedance was 983±578 Ω and pacing threshold was 1.2±0.6mV (at 0.5ms at implantation). All leads were successfully positioned and remained in position at the last recording. No patient required repositioning due to lead dislodgement prior to discharge. At last follow-up, R wave amplitude was higher at 15.9±10.7mV (p<0.015) and pacing threshold (1.2±0.3V @ 0.4ms; p<0.048) were not submitted to prophylactic pacemaker implantation, 15 (35%) had the implant performed during follow up due to new onset cardiac conduction defects and the probability of being required pacemaker implantation reached 42% at 10 years follow-up. No patient remained free of pacemaker at 20 years after the LT.

Conclusion: LT does not prevent the progression of cardiac ventricular dysfunction. However, the prophylactic pacemaker implantation is not widely justified. Indeed, the probability of cardiac conduction dysfunction occurrence during the lifetime of the pacemaker generator (assuming a median battery longevity of 10 years) will be only 42%. Better risk markers are needed to identify FAP pts at risk of perioperative bradyarrhythmias.
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 pacing leads. It may reduce the risk of TV injury and does not appear to degrade LV function.

P2431 | BEDSIDE
Eight years experience in permanent pacemaker implantation after open heart surgery
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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 had its indication before surgery and those who underwent the implantation of other devices after surgery were excluded.

Results: Out of the hundred and thirty-five (0.33%) 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±6.26 days. Cross-clamp time and bypass time were 94.4±44.9 and 132.6±64.4 minutes, respectively. The latter group had a longer bypass time and medical history before surgery being its probable causes. Direct injury to the conducting system, cross-clamp time, bypass time, and waiting time for PPM implantation was similar between the CABG patients. Waiting time for PPM implantation was similar between the valvular surgery subgroups. In the valvular subgroups, there were no differences found in the acute study persist.

Conclusion: Prevalence of PPM implantation among patients who underwent open heart surgery and its predisposing factors.

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P2432 | BEDSIDE
Longitudinal strain and twist calculated by Cardiac MRI differs by open heart surgery
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Longitudinal strain and twist calculated by Cardiac MRI differs by open heart surgery

The ejection fraction was greater with the RVOT lead compared with the apical lead position, 58.4±10 vs 56.9±8.5%, P=0.02. Longitudinal strain in the 4 chamber view 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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P2433 | BEDSIDE
Minimum invasive hemodynamic assessment of right ventricular outflow tract septal wall pacing versus conventional right ventricular apex pacing
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Background: Previous studies suggest that right ventricular (RV) outflow tract wall (RVOT) pacing (p) may be superior to RV apex (RVA) conventional pacing. However, the study results differ mainly due to methodological heterogeneity, especially regarding lead position within the RVOT (septal or free wall). Little is known about the effects of right ventricular outflow tract septal pacing.

Purpose: We aim to compare the hemodynamic and electrocardiographic response to RVOTp, RVAp and LVp.

Methods: Prospective observational study in patients with permanent atrial fibrillation, with left ventricular ejection fraction <40%, undergoing cardiac resynchronization therapy implantation. One RV lead was implanted conventionally in the RVA and another in the RVOT under fluoroscopic guidance to ensure proper lead positioning in the septal wall (RVS). A LV epicardial lead was implanted through the coronary sinus. Within 1 month after implantation, all patients underwent minimum invasive hemodynamic assessment using the Vigilote/MiFlotrac IIITM (Edwards Lifesciences, Irvine, USA) for the determination of cardiac output in the following pacing configurations: RVSp, RVAp or LVp. Mean QRS width was also analysed for each configuration.

Results: We included 35 patients (91% males, 71±10 years old) and a total of 91 hemodynamic and 93 electrocardiographic evaluations were performed. In the paired-samples analysis, RVSp significantly increased the cardiac index when compared with RVAp (P<0.001) – table. There was no significant hemodynamic difference between RVSp and LVp or between RVAp and LVp. Paired-samples analysis showed that RVSp significantly decreased the mean QRS duration when compared to RVAp and LVp (P<0.001, for both) - table. All the patients had VVI devices implanted (98 pts, 78.8%). Mean hospital stay was 4±9.3 days. Five patients (3.5%) had short-term device-related complications (3 pocket hematoma, 1 lead displacement and 1 hemotherax), and 16 patients (14.2%) had post-procedural complications, non-

P2434 | BEDSIDE
Procedural safety and long-term follow-up after pacemaker implantation in nonagenarians
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Background: The rate of pacemaker (PM) implantations is continuously growing. Given that life-expectancy of the population is projected to increase, a large number of nonagenarian patients will be implanted in the future.

Purpose: We aimed at analyzing the short and long-term outcome after PM implantation in this population.

Methods: Patients aged ≥90 yr referred for PM implantation from 2004 to 2014 were retrospectively included. The primary clinical endpoint was total mortality. Secondary endpoints included early and delayed-procedure related complications, and predictive risk factors of total mortality.

Results: 113 patients were included (92±6±2yr). Duration of the procedures were 53±11±7 min. Most of the patients had VVI devices implanted (89 pts, 78.8%). Mean hospital stay was 9±3±9 days. Five patients (3.5%) had short-term device-related complications (3 pocket hematoma, 1 lead displacement and 1 hemotherax), and 16 patients (14.2%) had post-procedural complications, non-

Table 1

<table>
<thead>
<tr>
<th>LVEDD (cm)</th>
<th>Stroke volume (mL)</th>
<th>Ejection fraction (%)</th>
<th>Longitudinal strain (cm)</th>
<th>Twist (degrees)</th>
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</table>

RVS vs. RVA LV P-value

Cardiac index (L/min/m²) 2.4±0.1 2.0±0.2 2.2±0.3 0.01 NS NS
QRS width (msec) 159±21 189±18.9 201±23.4 0.001 0.001 0.006
LVp, left ventricular pacing; msec, milliseconds; NS, non significant; RVA, right ventricular apex pacing; RVS, right ventricular outflow tract septal wall pacing.

Conclusion: In patients with atrial fibrillation and LV dysfunction, RVSp is hemodynamically superior to conventional RVAp and is associated with narrower QRS complexes, which may translate in improved electro-mechanical synchrony.
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 pacing can lead to potentially serious or life threatening implications such as syncope and serious injury, myocardial and cerebral ischemia due to low cardiac output, malignant ventricular arrhythmias 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 to improve upon the waiting times. This involved designing the on call cardiologist registrar to flag up the abnormal patient reports requiring brady pacing. An electronic referral system was also devised with alerts to the pacing consultants and the procedure booking team. A re-audit following the implementation of recommendations was done between 1st December 2013 to 30th April 2014 during which it was found that out of 25 patients receiving elective pacemaker implant for bradyarrhythmia 23 (92%) met the audit standard of 21 days or less. A discussion of all pacemaker implants and delay times is discussed in the monthly arrhythmia meeting as a quality control measure.

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 flutters [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 observation for 24 hours.

Results: 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 flutters [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.
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.

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?

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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 RHIE (52 pts with big RHV>2cm and 228 pts with smaller RHV<2 cm) 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>Group</th>
<th>LDIE big RHV &gt;2 cm</th>
<th>LDIE small RHV &lt;2 cm</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) ±SD</td>
<td>65.8±12.0</td>
<td>65.5±15.0</td>
<td>0.87</td>
</tr>
<tr>
<td>Gender, Male (%)</td>
<td>59.6</td>
<td>68.0</td>
<td>0.25</td>
</tr>
<tr>
<td>Full procedural success (%)</td>
<td>82.7</td>
<td>91.7</td>
<td>0.05</td>
</tr>
<tr>
<td>Clinical success (%)</td>
<td>88.5</td>
<td>97.8</td>
<td>0.002</td>
</tr>
<tr>
<td>Major complications (%)</td>
<td>5.8</td>
<td>0.4</td>
<td>0.003</td>
</tr>
<tr>
<td>Minor complications (%)</td>
<td>1.9</td>
<td>2.2</td>
<td>0.9</td>
</tr>
</tbody>
</table>

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

High recurrence rate of device-related adverse events following transvenous lead extraction procedure in CRT patients

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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 served. Group C= one groin haematoma was observed. Group D= one groin thrombosis, three displacements and three high stimulation thresholds were observed.

Results: are presented in the table. Predominant risk factors of MC in 1767 pts. Mean dwell implant time was 85.1 months. In 28 (1.6%) MC were noted.

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of device-related adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>2 (0.04%)</td>
</tr>
<tr>
<td>B</td>
<td>6 (0.17%)</td>
</tr>
<tr>
<td>C</td>
<td>1 (0.05%)</td>
</tr>
<tr>
<td>D</td>
<td>2 (0.03%)</td>
</tr>
</tbody>
</table>

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

Major complications of transvenous lead extraction. Risk factors are still ephemeral.

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Major complications (MC) are relatively rare events, which occur in 5% of TLE procedures. The comparative analysis of major complications rate was performed in 1767 pts. Mean dwell implant time was 85.1 months. In 28 (1.6%) MC were served. Group C= one groin haematoma was observed. Group D= one groin thrombosis, three displacements and three high stimulation thresholds were observed.

Results: are presented in the table. Predominant risk factors of MC included system (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, other).

<table>
<thead>
<tr>
<th>Major complications</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leads extraction</td>
<td>28 (1.6%)</td>
</tr>
<tr>
<td>Death</td>
<td>3 (0.17%)</td>
</tr>
<tr>
<td>Cardiovascular hospitalization</td>
<td>13 (0.75%)</td>
</tr>
<tr>
<td>Device-related adverse event</td>
<td>11 (0.63%)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (0.12%)</td>
</tr>
</tbody>
</table>

Conclusions: Only 1.6% of TLE procedures included major complications (MC). Even though TLE is safe and effective to treat CRT patients, 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.
K. Kusmierski1, A. Oreziak 1, H. Szwed 1.

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 exter-

nalization 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 exter-

nalization in TLE patients.

Methods: Between 2012 and 2014 we performed TLE of 428 electrodes in 259 pts. Out of these, 143 (33.4%) leads in 137 (52.9%) pts were ICD leads. Indica-

tion for TLE in the subgroup were infection in 37 pts., lead failure 84 pts., other including late perforation, venous system obstruction, dislocation in 16 pts. We re-

viewed 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. 1). 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 months - months): one SPL (132 m.), one Kainox RV (126 m.), one Linx (57 m.), one Riata ST (71 m.) and four Riata (96, 93, 73, 55 m. respectively) leads. All externalized leads were successfully extracted using device traction, mechanical telescopic sheaths and autorotationnal cutting sheaths.

Conclusion: Externalization is rather rare mechanism of lead failure and is met in different types 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.


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%). Cause of complications predominantly were Staphylococci (84%: S.aureus 48% and S.epidermidis 36%). Rate of severe complications was high: permanent sequelae 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.
P2445 | 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 2.76 years mortality after procedures were assessed.

Results: Univariable Cox regression analysis showed that statistically significant negative survival impact presented: older age—increased mortality by 2.5% per each year, diabetes [HR=1.719; 95% CI 1.300–2.274], renal failure [HR=2.524; 95% CI 1.925–3.310], artificial valve [HR=1.012; 95% CI 1.001–1.023] LDIE presence [HR=1.925; 95% CI 1.501–2.468], the need of remove of ICD leads (due to its dysfunction or LDIE): [HR=1.298; 95% CI 0.990–1.701], CS lead [HR=1.489; 95% CI 1.121–1.992] 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 1.048–1.853], 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.

P2446 | BEDSIDE
Adverse consequences of inappropriate antitachycardia pacing delivered with implantable cardioverter defibrillators: life threatening proarrhythmic effects

Background: Appropriate antitachycardia pacing (ATP) delivered with implantable cardioverter defibrillators (ICD) 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 shocks. 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.

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 ppm) 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 (240bpm) 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 2% of inappropriate ATP events, should be noted especially when programing ATP with a short pacing cycle length.

P2447 | BEDSIDE
Five-years microbiologic characteristics of patients with complications of electrotherapy
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1Upper-Silesian Cardiology Center, Katowice, Poland; 2Medical University of Silesia, Katowice, Poland

Infective complications of electrotherapy are still the problem. Knowledge about pathogens, place of infections and response pathogens for antibiotics are analyzed.

Methods: During 5 years 875 microbiological tests were taken in 293 patients (3.41% population). In 302 (34.5%) tests pathogens were identified. The most frequent pathogens were: Staph. epidermidis (9,14%), Staph. aureus (4,22%), Bacteroides fragilis (3,87%), Staph. haemolyticus (1,48%) and Enterococcus faecalis (1,37%), 20 pathogens (2,51%) were found incidentally (1–2 times in 5 years). Cumulative response of 7 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 spatiotemporal resolution. However until now, in most of the previous studies on MCG, measurements have been obtained only from the anterior side of the thorax with the subject supine. We hypothesized that using novel MCG approach with 3-directional recordings capable of delineating the whole heart activation and detect LV intraventricular conduction delay that is hardly discernible on ECG in DCM patients with narrow QRS duration (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 Cont (78±12 vs 60±6%, p<0.001).

Conclusion: Our new MCG approach may allow to evaluate abnormal intraven-
tricular 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 ventric-
ular wall is reported to be important to initiate and perpetuate polymorphic ven-
tricular tachyarrhythmias, and intravenous magnesium (Mg) is effective for poly-
morphic ventricular tachycardia via homogenization of the 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 thirteen ER pattern (ERP) or Brugada type ECG patients were enrolled (25 males, mean age 48±15 years). The 12 lead ECG-derived parameters including the QT, QT dispersion (QTD), Tpeak-Tend (Tp-e) interval, Tp-e dispersion (Tp-eD), and Tp-eD/QT ratio, were calculated using the QT observer Version 3.0 (Nihon Kohden, Tokyo, Japan). Then the correlation between those parameters and electrolytes including Mg, K, and Ca were analyzed. As for the cases whose electrolytes just after ventricular fibrillation (VF) could be measured, those values were also evaluated.

Results: The average QT maximum (max), QT minimum (min), QTd, Tp-e max, Tp-e, and Tp-e/QT ratio were 40.5±35ms, 35.0±35ms, 54±19ms, 102±17ms, 40.1±11ms, and 0.25±0.04, respectively. The average serum K, Ca, and Mg concentrations were 4.1±0.27mEq/L, 9.4±0.38mg/dL, and 2.1±0.27mg/dL, respectively. Although there was a positive correlation between the serum K and Ca and QTd, there was a tendency for a negative correlation between the serum Mg and QTD in J wave syndrome patients who had a history of VF (r=-0.513, p=0.072, n=13). On the other hand, in 13 patients with a Brugada type ECG or ERP, no correlation was observed between the serum Mg and QTd or Mg and Tp-ed. Furthermore, the serum K and Mg had relatively low values just after VF (3.2±0.4mEq/L and 1.97±0.6mg/dL, respectively).

Conclusion: The serum Mg and potassium levels may play an important role in the cardiac repolarization process in J wave syndromes.

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-
deendocardial 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-
rythmias and 8 patients in the age from 21 to 65 years with atrial arrhythmias were examined. All patients underwent noninvasive electrophysiological exami-
nation, which was performed with Amycard System (epicardial and endocardial imaging) and subsequent intracardiac mapping and radiofrequency catheter ablation.

Results: According to the results of the combined epi-endocardial mapping 56 patients had an arrhythmogenic substrate (AS) in the right ventricle outflow tract (RVOT); 3 - in the anterior-lateral wall; 7 - in the anterior wall of the RVOT; 20 - in the anterior-septal position of the RVOT; 3 - in the posterior-septal position of the RVOT; 23 - in the septal position of the RVOT; and 11 patients had AS in the left ventricle outflow tract (LVCT): 2 - in the boarder of the right and the left sinuses of Valsalva; 3 - in the noncoronary sinuses of Valsalva; 2 - in the right sinuses of Valsalva; 4 - in the left sinuses 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 in only 3 cases and in patients with paroxysmal 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 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 presumptive 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 intramurally heterogeneous in patients with long QT syndrome (LQT). Hence the T-wave morphology in premature atrial contractions (PAC) becomes deformed.

Purpose: To elucidate prevalence of T-wave deformation (TWD) in PAC and its relationship with T-wave alternans (TWA) and a history of life-threatening ventric-
ular tachyarrhythmias (VTA) in LQTS patients. PACs in 163 patients were analyzed.

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 TWD 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. TWD 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 preordial leads V2–6. Meanwhile, 70% of patients with TWD was consistent with max TWD lead. In the patient with drug-induced acquired LQTS, transition from TWD to TWA triggerd 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 asso-
ciated with elevated TWA and a history of VTA.

P2452 | BEDSIDE
Relationship between the sinusoidal 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 sinusoidal 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).

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 Cont (78±12 vs 60±6%, p<0.001).
Methods: In the group of 217 patients (mean age 63±11 years, 58% men) with symptoms that might be related to cardiac arrhythmias, SACT was measured from 24-hour ECG Holter monitoring using spontaneous premature atrial beats.

Results: During a mean follow-up period of 39±8 months, the occurrence of M-block was noted in 28 patients (13%). Patients with one or more sequences of M-block had greater values of SACT than those without M-block (149±47 ms vs 93±38 ms, p<0.0001). Univariate predictors of M-block included advanced age of patients (>60 years), underlying heart disease, episodes of syncope and SACT >150 ms. Multivariate analysis using the Cox proportional hazard model showed that the SACT of premature atrial tachycardia (PAC) was one of the significant risk factor for prediction of LV-dys. Recently, global long-term strain (GLS), which is measured by echocardiographic speckle tracking analysis, has been widely used to detect fine LV function 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 arhythmogenic region on PVC-induced LV-dys. Methods: Consecutive 40 patients with normal EF without underlying cardiac diseases, having more than 1000/day of PVC, were selected as statistically significant factor for prediction of GLS (−19±3.1 vs.−21±0.3, p=0.05). PVC burden and left bundle branch block type were evaluated. The patients were divided into 6 groups depending on the region of PVC focus, including right ventricular outflow tract of septum (RV-OT), near His bundle (His), left coronary cusp or LV epicardium (LC-LC), proximal low anterior descending coronary artery (PD-LA), distal low anterior descending coronary artery (PD-LD), and left atrial appendage (LA). Results: GLS of patient was significantly higher (worse) than that of control group (−17±0.05 vs.−20±0.03, p=0.03) and episodes of supraventricular tachycardia (SVT) (150±27.41 vs. 232±13.15, p=0.02). However, there were no significant differences between the two groups regarding the quality of PVC (138±35.43 vs. 142±29.59 ms, p=0.16), IEGM (5.82±3.55 vs. 5.59±2.41, p=0.7), SACT (5.53±5.81 μV vs. 4.67±2.50 μV, p=0.7), RMS20 (4.67±2.37 μV vs. 3.67±2.05 μV, p=0.2) or integral peak (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 (21.5% 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).

Conclusions: In COPD, SPB burden and no structural heart disease were independent predictors of SVT.

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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 hospitalized with ventricular arrhythmia at the University Hospital of Copenhagen. LP was considered positive if the task force criteria for ARVC/D were met. Measures of the cMRI scans relevant for ventricular size and abnormal tissue were noted and reviewed by 2 independent investigators. The cohort was split according to the ICD 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 ml/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 arrhythmogenic susceptibility beyond that which may be obtained from cMRI and is therefore an important independent marker in revealing arrhythmogenic abnormalities.


P2457 | BEDSIDE
Rapid diagnosis and management of symptomatic arrhythmia - the role of telemedicine

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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 that may be obtained from cMRI and is therefore an important independent marker in revealing arrhythmogenic abnormalities.

Methods: We conducted a retrospective cohort study of 753 patients admitted with diagnosis of AMI with LVEF>40%. Using Cox regression, we analyzed the prognostic role of β-blockers comparing patients in AF with those in sinus rhythm (SR), and adjusting by confounding variables.

Results: 98 patients had AF (13.0%). During the follow-up (3.0±2.8 years), 362 (48.1%) patients died. Patients treated with β-blockers (n=436, 66.6%) and in SR had a lower mortality rate (30.1% vs 70.0%; P<0.001), but not those in AF (53.3% vs 55.3%; P=0.852). Kaplan Meier curves are shown for patients with AF/SR according to the use or not β-blockers (figure). After adjusting by age, female sex, hypertension, diabetes, peripheral artery disease, chronic obstructive pulmonary disease, history of prior AMI, creatinine, STEMI, Killip class, percutaneous coronary intervention, complete revascularization and medical therapy, we found that β-blockers were an independent protective factor in the multivariable Cox regression analysis in those patients with SR (hazard ratio [HR]=0.59; 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.

P2459 | BEDSIDE
Beta-blocker therapy and short-term outcome in acute heart failure caused by acute coronary syndromes: a propensity-score matching secondary analysis of the ALARM-HF registry

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Background: Beta-blockade (BB) is currently recommended in the early management of acute coronary syndromes (ACS). However, their role in acute heart failure (AHF) has been long debated, while data on their use in the setting of AHF caused by ACS is limited. We sought to assess the effect of BB therapy on short-term outcome in AHF caused by ACS using a large cohort.

Methods: The Acute Heart Failure Global Registry of Standard Treatment (ALARM-HF) was conducted during 2006–2007 and included a total of 4953 patients hospitalized for AHF in 9 countries in Europe, Latin America and Australia. We compared in-hospital mortality between patients receiving or not BB in the subgroup of patients presented with ACS using propensity-score matching. Mortality was assessed by Cox regression with adjustment for age, gender, systolic blood pressure, heart rate, atrial fibrillation, NYHA class and renal function at presentation.

Results: In the original sample of 1827 patients with ACS, 878 were receiving BB. Propensity-score matching derived a sample of 1080 patients, 540 in each treatment group. Before matching, BB therapy was followed by significantly reduced in-hospital mortality [crude HR: 0.46, 95% CI: (0.35–0.60), adjusted HR: 0.58, 95% CI: (0.42–0.80)]. However, after matching, no significant effect in mortality was documented [crude HR: 0.85, 95% CI: (0.59–1.22), adjusted HR: 0.88, 95% CI: (0.60–1.28), Figure]. Among those treated, in-hospital mortality was significantly higher for patients aged over 80 years (HR: 2.98, 95% CI: (1.57–5.67) and those presenting with cardiogenic shock [HR: 7.38, 95% CI: (4.26–12.79)] or oliguria/anuria [HR: 6.41, 95% CI: (3.23–12.76)].
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: A 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-cTnT), among women and men in order to assess potential gender-inequalities.
Method: 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, 98.6–100%) of late presenters (-6h from chest pain onset) among women and 100% (95% CI, 99.8–100%) among men (p=ns). The ESC 3h-rule-out protocol correctly ruled-out 100% (95% CI 98.3–100%) of early presenters (<6h from chest pain onset) among women and 99% (95% CI 98.3–100%) among men (p=ns). Overall, the ESC rule-out protocol classified about 44% of women and 43% of men with suspected AMI. Conclusions: The current ESC 0h/3h-rule-out protocol using the 99th percentile of hs-cTnT 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 level at discharge in hospital survivors after AMI.
Methods: The study included 1,290 consecutive patients (64±12 years; 877 men) who survived the index hospitalization after AMI. We determined the 12-month mortality rates of these patients.
Results: The 12-month mortality rate showed a U-shaped curve, with the lowest event rate at 137–139 mmol/L of serum sodium at discharge. Patients who died during the 12-month follow-up had lower sodium levels at discharge than those who had survived (137±6 mmol/L vs. 139±4 mmol/L; P=0.014). Hyponatremia at discharge, defined as a sodium serum 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=0.019) 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.

Conclusion: Hyponatremia at discharge is an independent predictor of 12-month mortality in hospital survivors after AMI.

P2463 | BEDSIDE
High event rate in patients with acute coronary syndromes and atrial fibrillation: Results from the prospective EPICOR Registry
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Background: Known or new onset atrial fibrillation is observed in around 5% of events with acute coronary syndromes (ACS). Guidelines recommend revascularization therapies and intense antithrombotic therapies, including oral anticoagulation in these patients. We sought to determine acute treatments and the long-term event rate in patients with and without atrial fibrillation discharged after ACS in clinical practice.
Methods: EPICOR (NCT01171404) has been conducted in 555 hospitals in 20 countries.

Table 1

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Age, years, mean</th>
<th>STEMI, %</th>
<th>PCI, %</th>
<th>CABG, %</th>
<th>Bleeding, %</th>
<th>Death, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation (n=497)</td>
<td>72.5</td>
<td>26.0</td>
<td>49.3</td>
<td>1.6</td>
<td>1.5</td>
<td>7.2</td>
</tr>
<tr>
<td>No atrial fibrillation (n=9954)</td>
<td>61.2</td>
<td>47.8</td>
<td>66.2</td>
<td>2.6</td>
<td>5.3</td>
<td>3.2</td>
</tr>
</tbody>
</table>

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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.

P2464 | BEDSIDE
Clinical and angiographic characteristics of patients with acute coronary syndromes without cardiovascular risk factors

Introduction: Cardiovascular risk factors are well known by the scientific community. Nevertheless some acute coronary syndromes (ACS) occur in patients without any cardiovascular (CV) risk factors. Purpose: To describe clinical and angiographic characteristics in patients with ACS without any CV risk factors.

Methods: Prospective, single-center study, of 1055 patients admitted for ACS between October 2009 and September 2013. The CV risk factors were defined as prior MI, arterial hypertension, diabetes mellitus, dyslipidemia, smoking, peripheral arterial disease and family history of CV disease. They were divided into 2 groups: Group A, without any CV risk factor, n=84; Group B, with one or more CV risk factors, n=971. The groups were compared regarding com- position of primary endpoints (non-fatal myocardial infarction, cardiac death or stroke) and mortality from any cause during hospitalization and at 1-year follow-up.

Results: The groups did not show any difference regarding age, sex and time between onset of symptoms and first medical contact. At admission group B had higher values of creatinine [I= 1.176 (standard deviation (SD)= 0.327) vs II=1.299 (SD=0.878); p<0.01], no differences in creatinine phosphokinase (CK), CK-MB, troponin and brain natriuretic peptide (BNP). Group A had more ST-elevation MI (A=14% vs B=4.9%; p<0.01) and less non-ST-elevation ACS (A=28.6% vs B=47.9%; p<0.01). This group had more anterior infarction (A=31.0% vs B=16.3%; p<0.01), single-vessel disease (A=46.5% vs B=38.1%, p=0.013) and fewer 3-vessel disease (A=16.3% vs B=28.3%, p=0.017). It registered more episodes of ischemic arrhythmias [A=23.8% vs B=13.4%, p<0.01], cardiac arrest (A=14.3% vs B=8.1%; p<0.01) and use of inotropic agents [A=15.5% vs B=7.9%; p<0.05]. During hospitalization group A had a higher composite primary endpoint (A=17.9% vs B=7.7%; p<0.01) and mortality (A=16.7% vs B=6.6%; p<0.01). At 1-year follow-up there were no differences in the composite primary endpoint (A=20.2% vs B=17.8%; p=ns) and mortality (A=19.0% vs B=14.4%; p=ns).

Conclusions: Patients with ACS without CV risk factors have more single-vessel disease and a worse clinical profile, with more complications during hospitaliza- tion, which influences the mortality of the initial event. However, at one year follow-up, the prognosis is similar.

P2465 | BEDSIDE
Clinical impact of multivessel disease with or without chronic total occlusion in non-infarct-related artery on five-year outcomes in patients with STEMI undergoing primary PCI
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Background: The long-term impact of a concurrent chronic total occlusion (CTO) in a non-infarct-related artery (IRA) on patients with STEMI undergoing primary PCI with or without chronic total occlusion (CTO) is not well understood. We examined the risk of subsequent cardiovascular events in these patients.

Methods and results: 4546 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).

Conclusions: PCI within 24 hours after the symptom onset. Patients were classified as having single-vessel disease (SVD), multi-vessel disease (MVD) without CTO in IRA (MVD-with-CTO) and MVD with CTO (MVD-without-CTO). The primary 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-risks (non-cardiovascular death was classified as a competing risk) regression based on Fine and Gray’s proportional subhazards modeling, respectively. In-hospital coronary angiography was performed in 90.3%; PCI 64.5%; and CABG in 4.5%. Mean age was 67±13 years; 28.7% were women. At the end of follow-up (median 4.7 years), there were 915 events (18.8%). The annual composite endpoint risk was 13.6% in the following 44 months. Increased age, diabetes mellitus, dyslipidemia, smoking, peripheral arterial disease and family history of CV disease during the first year post-index ACS, the risk of developing the composite endpoint was 6.8% (number of events=329). When only analyzing MI patients (both STEMI (n=1524) and NSTEMI (n=2416); excluding unstable angina (n=937) patients), the risk of developing the composite endpoint was unchanged: 7.5%.

After adjusting for more than 20 related covariables, the significant (p<0.05) independent predictors for the occurrence of ischemic events or death from cardiac death during the first year following discharge were: prior history of heart failure [subhazard ratio (sHR)=1.6], age (sHR=1.03) and multivessel coronary artery disease (sHR=1.9), diabetes mellitus (sHR=1.4), no-revascularization (sHR=3.7), drug eluting stent placement and female sex (sHR=0.7 for each) and STEMI vs NSTEMI-ACS (sHR=0.8).

For patients who did not develop the composite endpoint during the first year, composite endpoint risk was 13.6% in the following 44 months. Increased age, diabetes mellitus, peripheral arterial disease, prior stroke, Killip class at admission, multivessel cardiac artery disease, renal dysfunction, chronic atrial fibrillation, STEMI (vs. NSTEMI-ACS) were each significantly (p<0.05) associated with the occurrence of the composite end-point.

Conclusions: Risk of cardiovascular events is high beyond the first year post-ACS, indicating a need for prolonged surveillance. Predictors of cardiovascular events occurring within the first year after an ACS are practically the same to those predicting cardiovascular events occurring beyond the first year, except for chronic atrial fibrilation which become a predictor of ischemic events or CVD beyond the first year.

P2467 | BEDSIDE
Cardiovascular risk in post-myocardial infarction patients: nationwide real-world data on distribution and impact of combination of risk factors in a real-life setting
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Background: The PEGASUS-TIMI 54 trial studied effects of dual antiplatelet treatment in high risk prior MI patients (age >65 years, diabetes, history of >1 prior myocardial infarction (MI) or renal disease). Prevalence of combinations and impact of these risk factors in post-MI patients in clinical practice has not been well understood.

Methods: A cohort study linked Swedish National registry data on morbidity, mortality and medication for patients (NCT01984307). 44 993 prior MI patients without recurrent MI or stroke after one year were included. Impact of combination of

founders, both CTO and multi-vessel disease are an independent predictor of all-cause mortality through 5 years (hazard ratio [HR]: 1.5, 95% confidence interval [CI]: 1.2–1.9, P<0.0003, HR: 1.4, 95% CI: 1.1–1.6, P=0.0007). Similarly, the two factors are independent predictor of all-cause mortality between 30 days and 5 years (HR: 1.6, 95% CI: 1.2–2.0, P=0.0005, HR: 1.3, 95% CI: 1.1–1.6, P=0.004, HR: 1.7, 95% CI: 1.3–2.2, P=0.0004, HR: 2.1, 95% CI: 1.5–3.0, P=0.0001) while multi-vessel disease is a significant predictor only in 5-year cardiac mortality, but not in 30-day-to-5-year cardiac mortality (HR: 1.4, 95% CI: 1.1–1.8, P=0.008, HR: 1.3, 95% CI: 1.1–1.6, P=0.006, HR: 1.3, 95% CI: 1.0–1.8, P=0.08).

Conclusion: The presence of CTO and multi-vessel disease are an independent predictor of 5-year all-cause mortality in STEMI patients. The presence of CTO is an independent predictor of 1-year cardiac mortality in STEMI patients even when early deaths are excluded.

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 rate vs no additional risk factors. 7% of the patients had >2 risk factors; which approximately doubled the risk for patients <75 years, compared with 1 risk factor patients.

| Table 1. Observed event rate (%) of a combined endpoint of fatal stroke death (with 95% CI) at third year follow-up post-PCI patients with different risk factors (diabetes, history of MI or other cardiovascular diseases) |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Risk Factor | Group A (n=70) | Group B (n=80) | p |
| Diabetes vs No | 0.01 | 0.001 | 0.001 | 0.001 | 0.001 |
| History of MI vs No | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 |
| Other CV disease vs No | 0.001 | 0.001 | 0.001 | 0.001 | 0.001 |
| Change during 6-month follow-up | Group A (n=70) | Group B (n=80) | p |
| ΔLVEDD, mm | 2.2±3.5 | 0.7±2.7 | 0.01 |
| ΔLVEF, % | 1.9±5.5 | 3.8±1.5 | 0.05 |
| ΔSm, cm/s | -0.2±0.8 | 0.5±1.0 | 0.001 |
| ΔStrain, % | 1.3±1.8 | 2.2±2.4 | 0.04 |
| ΔPSS, cm/s | -0.06±0.33 | -2.2±4.04 | 0.03 |
| ΔEm, cm/s | -0.1±1.4 | 0.7±1.6 | 0.002 |
| ΔSRe, %/ΔΔ1 | 0.04±0.21 | 0.15±0.19 | 0.001 |

**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 ≤75 years. This indicates the need for careful management of post-MI patients with increased risk, regardless of age.

**Acknowledgement/Funding:** Sponsord by AstraZeneca

### STEMI II

#### P2469 | BEDSIDE

**Zwolle risk score: the missed opportunity for early discharge after primary percutaneous intervention**

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Zwolle 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 Zwolle score ≤3 vs those with Zwolle score >3.

**Results:** 775 patients underwent PCI between October 2013 and September 2014, among them 605 (88.4%) had a Zwolle score ≤3 and 72 (11.6%) had Zwolle score >3 (see table). Patients with score ≤3 were younger (49±4.7 vs. 57±4.11, P<0.001), less likely to have diabetes (30% vs. 43%, P=0.001), hyper-tension (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 (0.4% vs. 2.3%, P=0.001, 0.6% vs. 16%, P=0.001). The LOS was significantly shorter among patients with Zwolle score ≤3 compared to those with a score >3 (mean 3.5±2.8 vs. 7.7±12 days, P=0.001, median 3 vs. 4 days respectively).

**Conclusion:** Zwolle 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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#### P2470 | BEDSIDE

**Zwolle score versus CHA2DS2-VASc: 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 CHA2DS2-VASc 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. CHA2DS2-VASc was obtained retrospectively and was available for 3993 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 CHA2DS2-VASc 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 CHA2DS2-VASc, compared to TIMI score (0.698 vs 0.593, p<0.001). In a Cox regression model, both TIMI score (hazza coefficient (HR) 1.076; 95% confidence interval (CI) 1.02−1.139, p=0.008) and CHA2DS2-VASc (HR 1.143; 95% CI 1.376−1.514; p<0.001) were found to be predictors of the primary endpoint. A CHA2DS2-VASc cutoff value of 3 was found to have a 72.35% sensitivity and a 60.42% specificity for predicting death at follow-up.

**Conclusions:** Both scores predicted long term mortality in our ACS population. However, CHA2DS2-VASc performed significantly better, and shows promising results as a risk stratifying tool for long term prognosis in an unselected ACS population.

#### 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 to-gether 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 profile, i.e. with an increase in TRAIL level between baseline and the 3rd day be-ing in the 3rd tertile (increase >9.5 ng/ml) and/or with OPG/TRAIL value at base-line being in the 1st tertile (<0.11) – Group A, demonstrated larger increase in LV end-diastolic dimension and postsystolic 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 is associated with the perinfarct TNF superfamily cytokines activity: lower OPG/TRAIL ratio suggesting less efficient cardioprotection, as well as larger sub-sequent increase in TRAIL characterized by cardiohinitiby properties contribute to a poorer of LV functional and structural remodeling at 6 months.
coded in ICD-10 as I21 or I22. Deaths after discharge 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 cardio- genetic shock. PRAMI trial defined this concept. We aimed to evaluate the prognostic impact of different revascularization (Rv) strategies in P with STEMI and MVD.

Methods: 457 P included in a multicenter 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<0.01); 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±588pg/mL, p<0.01). CAO had more extensive CAD (3 vessels: 30% vs 9% and 24% vs 12% in CAO and CR1, respectively, with differences in CA). Femoral vascular access (36% vs 19% vs 32%, p<0.01) and bare metal stents (46% vs 23% vs 41%, p<0.01) were more often in CAO; but, Gp IIb/IIIa inhibitors were less used (32% vs 80% vs 7%, p<0.01) and more often evolved to heart failure (19% vs 12% vs 9%, p<0.001). CR1 had a higher percentual increase in creatinine (23% vs 44% vs 9%, p<0.01) but lower than GRACE risk score (Table) and slightly lower than the original development cohort ACS (APC strategy) which shows a good differentiation between patients at low risk (score <0.05), intermediate risk (score 1–2) and high risk (score >3) in both short and mid-term follow-up (p<0.001 for all comparisons).

Conclusions: PRAMI’s 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 PCI strategy is being challenged by recent data that shows advantage of 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 (30.3% 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. 13% vs 8%, p=0.001 for all comparisons).

Conclusion: Our data shows that under current practice, in STEMI patients with multivessel CAD, who present without cardiogenic shock, culprit lesion only and staged PCI strategies are associated with similar 1-year mortality rates, while a preventive PCI strategy is associated with increased mortality. Larger randomized trials are needed to confirm the optimal revascularization strategy in STEMI patients with multivessel CAD.
P2476 | BEDSIDE
The impact of high D-dimer levels on in-hospital mortality in patients with ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention
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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 logistic regression analysis showed that high D-dimer levels were independently associated with in-hospital death (OR=2.49, p=0.04).
Conclusions: A high D-dimer level independently predicts in-hospital mortality in patients with STEMI.

P2477 | BEDSIDE
Mechanical chest compressions during prolonged resuscitation for reperfusion ventricular fibrillation that complicated coronary intervention for 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 3,274 patients with STEMI who underwent primary PCI for STEMI 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 reperfusion VF. Patients that demanded mechanical chest compressions tended to suffer more often from VF before reperfusion (30.0% vs. 13.1%, p<0.018), more often had myocardial infarction (MI) history (40.0% vs. 19.3%, p<0.021) and left ventricular ejection fraction indicated that a high D-dimer level was positively correlated with in-hospital death (OR=2.49, p<0.04).
Conclusions: The high D-dimer level independently predicts in-hospital mortality in patients with STEMI.

P2478 | BEDSIDE
Prognostic implication of creatinine clearance and hemoglobin composite index in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention
Background: A creatinine clearance (CCr) and Hemoglobin (Hb) is a readily-available routine laboratory test that can predict clinical outcomes in patients with acute coronary syndrome.
Purpose: We sought to evaluate the impact of a CCr and Hb composite index (CHI) on clinical outcomes in patients with STEMI undergoing primary PCI with drug-eluting stents.
Methods: We analyzed 805 consecutive STEMI patients. The Cox regression analysis determined the optimal combination of CCr and Hb into a CHI. The discrimination ability of CHI and Hb in predicting 12-month MACE, composite of cardiac death, nonfatal MI and stent thrombosis was compared using area under the receiving operating characteristic curve. Patients were divided into quintiles according to the CHI.
Results: The optimal weighting of CCr and Hb to form the CHI to predict a 12-month MACE was Hb + CCr/12. The area under the curve for the CHI was significantly greater (0.857) than for Hb (0.777, p=0.003) and CCr (0.802, p=0.003). A positive trend was observed between a 12-month MACE and CHI quintiles: 39.4%, 9.4%, 6.1%, 0.0%, 1.5% of MACE 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.
Conclusions: Our data suggests that in STEMI patients with the door-to-balloon time under 90 minutes, and age and symptom-onset-to-balloon time may be the main determinants of impaired microcirculatory resistance in STEMI with patients.
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.

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 24 circadian cycle and the prehospital delay, 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 STElevation myocardial infarction (54.9%, p<0.001) and those with onset from 6–12h and 12–18h a higher prevalence of inferior STElevation 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 ischemic injury and reperfusion success in STEMI patients.

Methods: STEMI patients reperfused by primary PCI (n=276) within 12 hours after symptom onset underwent CMR 3 days after the index event (interquartile range [IQR] 2–4). A detailed set of clinical, therapeutic and laboratory parameters was assessed in all patients. IV morphine administration was recorded in all patients.

Results: IV morphine was administered in 44.7% (n=123) of all patients. Patients in the IV morphine group displayed larger infarct size, higher extent of microvascular obstruction and lower myocardial salvage index (MSI) in comparison to the non-IV morphine group (all p<0.05). In multivariable logistic regression analysis adjusted for parameters such as TIMI-flow pre- and post-PCI, time from symptom onset to PCI, 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 stenosis scoring systems after anterior STEMI.

Methods: Consecutive 37 patients with acute anterior STEMI (mean age = 61 years, 11 women) underwent standard echo and STE-derived Automated Function Imaging at admission, early before coronary angiography. A group of 37 normal controls, matched for age and sex, were the control group for echocardiographic parameters. LV ejection fraction (EF), the ratio of transmural E velocity to pulsed tissue Doppler annular e’ velocity (E/E’ ratio) and global longitudinal strain (GLS, % – average of 18 regional longitudinal strain in the apical views) were calculated. Longitudinal strain of left anterior descending (LAD) territory (LSSad, %) was also generated as the average of 8 myocardial segments (middle and apical posterior septum, basal, middle and apical anterior septum, basal, middle and apical anterior wall). By coronary angiography TIMI flow grade and TIMI frame count (TFC) were calculated before LAD percutaneous angioplasty. Laboratory biomarkers of myocardial necrosis were also determined.

Results: The two groups were comparable for blood pressure, heart rate and body mass index. STEMI patients had lower EF and high E/E’ ratio (both p<0.0001) than controls. GLS was -10.4±3.4% in STEMI and −21.0±2.2% in controls (p<0.0001). In STEMI group, LSSad (−7.6±3.9%) was negatively related with TFC (r=−0.4, p<0.01), TIMI grade (r=0.33, p=0.04) and troponin peak levels (r=−0.45, p<0.005) but not to CK-MB peak. LSSad was also related with E/E’ ratio (r=−0.41, p=0.02) but not with EF. By a multiple linear regression analysis, after adjusting for troponin levels and E/E’ ratio, TFC was independently associated with LSSad (standardized β coefficient = −0.375, p=0.02) (cumulative R²=0.381, SE=2.39%, p<0.0001) in STEMI group.

Conclusion: Our study is the first to demonstrate an independent association between longitudinal myocardial strain and the angiographic scores of perfusion deficit in the culprit lesion after acute anterior STEMI. Pre-angioplasty regional longitudinal strain can be useful to predict successful primary percutaneous intervention.
P2483 | SPOTLIGHT
Serial improvement of early mortality of acute myocardial infarction in the whole metropolitan area: progress of direct CUC network system
Background: Acute myocardial infarction (AMI) is known crucial disease causing rapid deterioration and death, therefore early admission to cardiac center enabling emergency percutaneous coronary intervention (PCI) is essential. On this reason emergency ambulance transport to appropriate hospital in shortest time is needed as cooperation system to cover the huge population area.
Objectives: To clarify current result of emergency system (Tokyo CUC network) in Tokyo Metropolitan area.
Methods: Tokyo CUC network established in 1978 by 12 CUC centers and emergency selectivity coronary revascular operation started in 1983, then emergency PCI in 1992. The network expanded to 71 CUC centers which are available emergency PCI anytime 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 1992 to 2013. The mortality in 1978 reached to 20.5%, however it declined to 5.1% in 2013 (n=4,587). The network system covers 95% of AMI patients requiring hospital admission, and median time from onset to emergency call (EC) to balloon time was 63 minutes and 93 minutes respectively (n=1,128, in 2011).
Conclusion: Tokyo Metropolitan area appears well covered by modern AMI care system for the whole population with remarkable low mortality.
Acknowledgement/Funding: Tokyo Metropolitan Government

P2484 | BENCH
Physical activity as a trigger of myocardial infarction and long-term survival following primary percutaneous coronary intervention
Limited evidence is available about effect of physical activity as a trigger of myocardial infarction and clinical outcomes following primary percutaneous coronary intervention in STEMI.
Methods: From January 2009 till December 2012 a total of 2793 patients with STEMI underwent primary PCI within 12 hours from symptom onset in a single high-volume centre. Level of physical activity at the time of symptom onset was determined using standardized questioner at the time of patient arrival. Mortality was assessed at a mean follow-up of 32±24 months.
Results: 533 patients (19.1%) had physical activity at the time of symptom onset (Group 1) and 2260 patients with chest pain at rest served as a control group (Group 2). Group 1 patients were younger (59±11 vs. 60±12; p<0.01), more frequently male (75.0% vs. 69%; p=0.005), presented earlier (mean total ischemic time 2.93±3.1 vs. 3.73±3.2 hours; p=0.001), had first MI (89% vs. 84%; p=0.01), with higher rate of TIMI 0 baseline flow (78% vs. 73%; p=0.04), and had bigger infarct size (2542±2113 vs. 2281±2164; p=0.015). In-hospital and long-term mortality was similar between Groups 1 and 2 respectively (3.8% vs. 3.8%; p=0.97; 13.8% vs. 14.5%; p=0.704). Adjusting the outcome to quartile ranges of total ischemic time provided only a trend for higher mortality in Group 1 with longer reperfusion times (p=0.054).
Table 1:

<table>
<thead>
<tr>
<th>Mortality (%) per group vs ischemic time</th>
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<tr>
<td>0-3 h</td>
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<tr>
<td>N=2793</td>
</tr>
<tr>
<td>Group 1: physical activity-related (533 pts)</td>
</tr>
<tr>
<td>Group 2: at rest (2260 pts)</td>
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</table>

Conclusion: Physical activity as a trigger of myocardial infarction occurs in approximately one fifth of STEMI patients undergoing primary PCI, more frequently in first presenters, younger and male patients but has no impact on in-hospital and long-term mortality.

P2485 | BEDSIDE
Acutae coronary syndrome with normal or near-normal coronary angiography: prevalence and long term outcome
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Background: The incidence of normal (0% angiographic stenosis) or near-normal (0% to 50% angiographic stenosis) coronary angiography (NONCA) in patients (pts) hospitalized with suspected acute coronary syndrome (ACS) undergoing coronary angiography is reported between 1 and 12%. Data on long term prognosis are lacking.
Methods: In a period of five years (from January 2003 to December 2008), 5243 consecutive patients underwent coronary angiography because of suspected ACS. Among these, 364 (6.9%) pts showed NONCA. The aim of the present study was to evaluate clinical features, prevalence and long-term outcomes of this population. Major adverse cardiac events, defined as death, myocardial infarction, ACS leading to hospitalization, and nonfatal stroke, were recorded.
Results: In the study population, the final diagnosis was ACS in 78.8%, mio-Infarction 7.7%, Takosu syndrome 6.6%, chest pain in myocardial bridge 3.9%, chest pain in hypertensive heart disease 2.5%, and 0.5% was observed in type A aortic dissection. Thus ACS with NONCA has been observed in 328 pts (prevalence 6.3%). The mean age at presentation was 65±14 years and 60.7% were female. The risk factors incidence was hypertension 51.9%, dyslipidemia 36.8%, tobacco 23.4%, diabetes 7.4%, 19.8% of patients have no risk factors. The ECG presentation was ST-elevation in 24.9%, non-ST elevation in 59.1%, absence of significant modification in 9%. Toponin I or T was elevated in 84% of pts.
Therapy at discharge was: aspirin 91.7%, dual antiplatelet 28.6%, beta-blockers 82%, ACE inhibitors 64.4%, statins 53.1%, and oral anticoagulants 16.8%.
The mean follow-up was 55±23.5 months. The 8% of pts had re-hospitalization for recurrent ACS (STEMI 8 pts, NSTEMI 6 pts) and in 1 pts. was performed coronary revascularization. Global survival was respectively 96.6% at six months, 95% at one year and 85% at five years.
Conclusion: These data indicate that, in discordance with common belief, NONCA patients with ACS remain at high risk of long-term recurrent ischemic events, but tend to be undertreated compared with the relevant ACS guidelines during, and more importantly, after the acute episode.

P2486 | 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 percutaneous coronary intervention (PCI) in patients with ST-elevation 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 December 2007 and December 2012. Patients receiving fibrinolyis 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 cardiovascular events (MACE: cardiac 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 in 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 interaction = 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 undergoing reperfusion between 4 and 8 hours after symptom onset.

P2487 | 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 myocardial infarction (STEMI) is a predictor of heart failure and mortality. Previous study showed the association between hyperglycemia and microvascular dysfuncing using myocardial contrast imaging. Late gadolinium 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, 1.00 to 1.01; 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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1Wilhelminen Hospital, Vienna, Austria; 2SZM-South, Vienna, Austria; 3Medical University of Vienna, Vienna, Austria; 4Rudolfstiftung Hospital, Vienna, Austria; 5Donauspital, Vienna, Austria; 6Hietzing Hospital, Vienna, Austria

Background: Pre-hospital delay results in impaired outcome after ST-Elevation-Myocardial Infarction (STEMI). Pain-to-First Medical Contact (FMC) strongly depends on recognition of symptoms by the patient and willingness to attend medical help. Aim of the study was to identify factors associated with late diagnosis in STEMI.

Methods and results: Pain-to-FMC and long-term-outcome were documented in 2492 individuals presenting with STEMI from 2003 to 2009. Baseline parameters of patients with pain-to-FMC <60 minutes (“early presenters”) were compared to patients in whom diagnosis was made later than 60 minutes of onset of pain (“late presenters”).

Early presenters were characterized by higher age (62±14 years vs. 59±13 years; p=0.001), higher prevalence of female sex (31% vs. 25%; p=0.002), diabetes mellitus (25% vs. 19%; p=0.022) and hypertension (57% vs. 50%; p=0.007), but lower rates of smoking (50% vs. 58%; p=0.02), hyperlipoproteinaemia (52% vs. 57%; p=0.05) and cardiogenic shock (8% vs. 11%; 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 diagnostic lag in STEMI.

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 diagnostic lag in STEMI, whereas shock was a predictor of early diagnosis.

Conclusion: Factors associated with late diagnosis in STEMI are female sex and diabetes mellitus. Female sex and diabetes mellitus were independently associated with diagnostic delays in females and diabetics with STEMI.

P2489 | BEDSIDE
Is the predictive ability of GRACE risk score for mid-term mortality identical in all age groups?
A.T. Timoteo, S. Aguilar Rosa, M. Alonso Nogueira, P. Rio, R. Carvalho, M.L. Ferreira, R. Ferreira. Hospital Santa Marta, CHLC, Lisbon, Portugal

Background: GRACE risk score is the risk stratification score in acute coronary syndromes. In ACS with the highest predictive accuracy and presently the most widely used. It was developed for in-hospital and 6-month all-cause mortality. We sought to evaluate if this score is equally effective for different age groups both for short and longer-term follow-up.

Methods: Analysis of consecutive patients admitted at a single-centre with ACS and included in a dedicated database of ACS. Patients were divided into three groups according to the age group: Group 1 (<50 years), Group 2 (50–79 years) and Group 3 (≥80 years). 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 mortality was 5.7%, at 30 days 7.2% and at one year 10.3%. Predictive accuracy of GRACE risk score was significantly reduced with age, being excellent in the age group <50 years (Table).

Conclusions: In elderly patients, risk stratification for short and mid-term mortality by GRACE risk score should be more careful due to a significantly reduction in its predictive accuracy in this age group. In younger patients, this tool has a high performance.

Table 1. Results

<table>
<thead>
<tr>
<th>AUC (95% CI)</th>
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<tbody>
<tr>
<td>Hospital</td>
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<tr>
<td>30-day</td>
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<td>One-year</td>
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P2490 | BEDSIDE
The association of epicardial fat thickness with stress hyperglycemia in patients with ST elevation myocardial infarction
E.H. Ozcan Cetin, M.S. Cetin, O. Ozdeke, D. Aras, S. Topaloglu, H. Kısacid, A. Temizhan, S. Aydogdu. Ankara Türkiye Yusuf İhtisas Hospital, Department of Cardiology, Ankara, Turkey

Introduction: Stress Hyperglycemia (SH) as a well-defined prognostic indicator in patients with ST elevation myocardial infarction (STEMI) is associated with larger infarct size, pathologic cardiac remodeling and mortality. Beyond the insulin resistance, increased inflammatory and neurohormonal response have been postulated in the pathophysiology of SH. As a source of various inflammatory cytokines and neurohormonal mediators, epicardial fat tissue might contribute to the occurrence of SH. We aimed to evaluate the association of epicardial fat tissue thickness (EFT) with SH in STEMI patients.

Methods: Total of 200 patients who admitted with STEMI and performed primary PCI between 2013–2015 were included. Patients were followed-up median 14 months. Patient group composed of 100 patients with SH and control group consisted of 100 patients without SH. Patients with DM and BMI >25 were excluded.

Results: In patients with SH, EFT was significantly higher than the control group (7.45 mm ±1.46 vs. 6.79 mm ±1.15 p=0.013). EFT was correlated with admission glucose (r=-0.362 p<0.001), CRP levels (r=0.291 P=0.003) and peak CKMB (r=0.288, p=0.004). In multivariate analysis, EFT was demonstrated as an independent predictor of SH (OR: 1.490 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.

Conclusion: EFT, related with miscellaneous neurohumoral and inflammatory mediators, is associated with SH and MACE in STEMI patients. This noninvasive, simple echocardiographic measurement may utilize risk categorization of these patients.

P2491 | BEDSIDE
Intravascular ultrasound guidance versus angiographic guidance in primary percutaneous coronary intervention for ST-segment elevation myocardial infarction
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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.

In patients with STEMI IV, angiographic guidance versus IVUS guidance in primary PCI on long-term clinical outcomes in the setting of emergency PCI for ST-segment elevation acute myocardial infarction (STEMI) 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.
Purpose: We sought to investigate the utility of IVUS guidance on clinical outcomes in patients with STEMI undergoing primary PCI.

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 3028 STEMI patients with primary PCI performed 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 death and MACE (death, heart failure, recurrent MI, target vessel revascularization) was TVR for the culprit lesions in STEMI.

Conclusions: Our data uncovered the potential modulatory effects of Clock in the balance between thrombosis-associated PAI-1 and TIMP-1 in peripheral blood mononuclear cells in patients with STEMI, which might be caused by abnor- mal oscillation of Clock mRNA expression and needed to explore in a larger population-based clinic study.

Acknowledgement/Funding: The study was supported by National Natural Science Foundation of China (81130015, 81072981, 30971101, 31171130). The study was supported by National Natural Science Foundation of China (81130015, 81072981, 30971101, 31171130, 81473445, 81400336 and 30900523).
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=38) 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 larger left ventricular ejection fraction (p<0.01) and greater level of NT-proBNP (>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; p<0.01).

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 4 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.

P2498 | BEDSIDE
Total bilirubin on admission predicts in-hospital clinical outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

T.-H. Yang, H.-C. Shin, Y.-M. Lee, H.-Y. Jin, J.-S. Seo, J.-S. Jang, D.-K. Kim, D.-S. Kim. Inje University Busan Paik Hospital, Department of Internal Medicine, Division of Cardiology, Busan, Korea, Republic of

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 was 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 odds ratios comparing predictive effect of TB level with clinical outcomes in patients with STEMI.

Results: Of all patients with STEMI 92.2% presented with chest pain (men 3.5% and women 4.0%). In older patients (≥ 65 years) with chest pain the absolute risk in 1-year mortality was more evident: 36.5% and 39.0% in men and women without chest pain compared to 14.9% men and 19.9% in women with chest pain. The relative risk in those without chest pain was higher in younger men (Hazard ratio (HR) 5.07, 95% CI: 4.04-6.38) and women (HR 5.66, 95% CI: 4.04-7.93) than in older patients (men: HR 2.80, 95% CI: 2.52-3.12; and women: HR 2.31, 95% CI: 2.08-2.58).

Conclusions: Lack of chest pain in patients with STEMI is associated with higher 1-year mortality in both men and women, especially in older ages. Younger men and women without chest pain had notably higher relative risk of 1-year mortality.

P2499 | BEDSIDE
Total bilirubin on admission predicts in-hospital clinical outcomes in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

T.-H. Yang, H.-C. Shin, Y.-M. Lee, H.-Y. Jin, J.-S. Seo, J.-S. Jang, D.-K. Kim, D.-S. Kim. Inje University Busan Paik Hospital, Department of Internal Medicine, Division of Cardiology, Busan, Korea, Republic of

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Methods: We analyzed 1,111 consecutive STEMI patients treated with primary PCI. The patients was divided into high TB group (n=816) and low TB group (n=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: 2.89 [1.87–4.34], p=0.010) and in-hospital cardiac death (HR:2.71 [1.44–4.44], p=0.012) after adjusting for age, gender, left ventricular ejection fraction, Killip class, creatinine clearance, and other factors included in the TIMI risk score for STEMI. There was significant difference in the DCST between the two periods (<0.001). As a result, 551 sets of the combination of the parameters specific to STEMI were identified under the adjusted p value of 5.8×10−7, and we found that no treatment with aspirin, thienopyridine or nitrates becomes a component for STEMI, and that the other drugs or clinical features such as the history of hypertension and diabetes mellitus did not affect the watershed of STEMI and NSTEMI-ACS. Interestingly the combination of the habits with smoking and without drinking alcohol was newly identified as a crucial combinational component for STEMI.

Background: In patients with STEMI undergoing PCI, we speculated that either antiplatelet agents or nitrates, and the habit of drinking alcohol and no smoking have shown to be crucial factors for the onset of STEMI.

Conclusions: Administration of the combination of antiplatelet agents, nitrates, and no smoking has been demonstrated to be beneficial for preventing the onset of STEMI.

P2502 | BEDSIDE
ProACS score: an early and simple score for risk stratification of patients with Acute Coronary Syndromes
A.T. Timoteo, S. Aguiar Rosa, M. Alonso Vargueira, R. Cruz Ferreira on behalf of Portuguese Registry on Acute Coronary Syndromes, Hospital Santa Marta, CHLC, Lisbon, Portugal

Background: Although there are several scores for risk stratification of patients with acute coronary syndromes (ACS), the effective implementation in clinical practice is not ideal. One of the barriers for adequate implementation is the result of some complexity of the available risk scores. Our objective was to develop a simple score for risk stratification of hospital mortality in a population for early use in the first medical contact with the patient, with simple variables.

Methods: The score was developed from a nationwide ACS registry. The develop-ment and internal validation cohort was obtained from the first 31829 patients, randomly separated (60% and 40%, respectively). The external 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 baseline 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 on the regression coefficient of each variables in the logistic re-gression model: 1 point for SBP <116 bpm, Killip class 2 or 3 and ST-segment elevation myocardial infarction, 2 points for age ≤72 years and 3 points for Killip class 4. The primary end-point was all-cause in-hospital mortality.

Results: The new score has a good discriminative ability in the development cohort (AUC 0.796, 95% CI 0.782–0.810), and similar in the validation cohort (AUC 0.785, 95% CI 0.767–0.803, p=0.333). In the external validation cohort, there was also an excellent discriminatory ability (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 co-hort.
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, angiotens-in-converting enzyme (ACEI), renin-angiotensin receptor blockers (ARB), beta-blockers (Beta), calcium channel blockers (CCB), loop diuretics, spironolactone, and antidepressant 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 2,165 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 (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).

Conclusion: Complete revascularisation in AMI patients is associated with improved long-term survival. In STEMI patients, this positive association was found for complete revascularisation achieved during the initial PCI procedure.

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P2505 | BEDSIDE
Determinants and clinical relevance of polyhedrocyte 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 polyhedrocytes, detectable in the intracoronary thrombus (ICT) of ST-segment elevation myocardial infarction (STEMI) patients.

Purpose: We sought to investigate determinants and clinical relevance of polyhedrocyte content in ICT.

Methods: We assessed the content of fibrin, platelets and erythrocytes including polyhedrocytes 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 (PPI) and ADP-induced platelet aggregation were evaluated on admission. The effectiveness of reperfusion was assessed by TIMI and TMPG scales and by enzymatic injury.

Results: All patients received aspirin and 45 (56.3%) 600 mg of clopidogrel, 80 (60–125) min prior to aspiration. Polyhedrocytes were found in 16 (20%) thrombi. They covered >50% of fields of view of the inside core or outer part of ICT in 11 (13.8%) or 8 (10%) thrombi, respectively. Patient’s age, gender, cardiovascular risk factors, pre-hospital antiplatelet and antithrombotic treatment did not influence the presence of polyhedrocytes in ICT. The median PPI was lower in patients with >50% of fields of view covered by polyhedrocytes 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 polyhedrocytes 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 polyhedrocytes in the inside core (8/37 vs. 3/43, P=0.058) as compared with time of ischemia of ≤5h. Patients with and without polyhedrocytes in ICT did not differ significantly in terms of the frequency of final epicardial TIMI-3 flow (82.4 vs. 74.6%, P=0.13), complete TMPG-2/3 myocardial perfusion (75.0 vs. 72.6%, P=0.85) 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±5.7x10^3 IU/Lxh, 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±5.7x10^3 IU/Lxh, P=0.81).

Conclusions: Our findings suggest that polyhedrocytes in ICT are formed preferentially in patients with lower PPI, narrow infarct-related artery and in late presentation of STEMI, however their presence is not associated with a higher reperfusion injury.

Acknowledgement/Funding: Pfizer, Servier, CNAM-TS

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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=0.003) 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 (2.0%).

Conclusion: Early discharge of low-risk patients after successful PCI treatment for STEMI is safe with similar incidence of cardio-vascular events during 12 months following STEMI.

P2507 | SPOTLIGHT
Short-term exposure to fine particulate air pollution and risk of ST elevation myocardial infarction, ventricular arrhythmias and mortality
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Background: Although numerous population-level studies indicate that air pollution (AP) is linked to adverse cardiovascular outcomes, this relationship has poorly been explored specifically for ST-elevation acute myocardial infarction (STEMI). Purpose: To assess the short-term effect of AP on STEMI incidence and on the early occurrence of ventricular arrhythmias and mortality.

Methods: The period under study was from 2010 to 2011 in an urban metropolitan area (reference population of 3.5 million). Daily STEMI rate, mortality in first aid and associated ventricular arrhythmias were prospectively obtained in a STEMI reperfusion network database. The corresponding daily levels of particulate matter (PM) 10, PM 2.5, Benzene, Cadmium, Nickel, Lead, SO2, NO2, CO, and ozone as well as the atmospheric variables temperature, air pressure, rain precipitation and relative humidity were recorded 1 to 7 days (lag 1 to 7) before the event (obtained from local and regional environmental authorities). The magnitude of association was estimated using a time-series design. Models were adjusted for atmospheric variables.

Results: After taking into account potential confounding by other pollutants and meteorological conditions, we found consistent evidence that an increase of 10 μg/m³ in the PM 10 levels (lag 2), lead (lag 1) and NO (lag 4) was associated with an increase of 1.03% (95% CI: 1.00 to 1.07), 1.02% (1.00 to 1.04) and 1.01% (1.00 to 1.02%), respectively, in the number of hospital admissions for STEMI. An increase of 10 μg/m³ in PM 2.5 was associated (lag 4) with STEMI mortality and (lag 3) with STEMI ventricular arrhythmias, with relative risks of 1.3330 (1.0031 to 1.7409) and 1.6651 (1.0183 to 2.3922) and attributable risk percent of 24.98% (9.36 to 42.56%) and 14.20% (1.80 to 24.77%), respectively.

Conclusion: There appears to be an “obesity paradox” in patients with AMI such that overweight and obesity AMI patients are associated with lower mortality at one month and one year after AMI.

P2508 | BEDSIDE
Using landiolol during primary percutaneous coronary intervention attenuates myocardial reperfusion injury in patients with ST-segment elevation acute myocardial infarction
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Background: There are some conflicting and limited data regarding clinical outcomes in obese patients with acute myocardial infarction (AMI). The aim of this study was to evaluate the relationship between body mass index (BMI) and mortality in Korean patients with AMI.

Methods: A total of 11,483 patients with AMI in Korean AMI registry. The number of male patients was 8,256 (71.9%). We categorized the patients according to BMI degree: lean (<18.5 kg/m², n=429), normal (18.5–22.9 kg/m², n=3,954), overweight (23.0–24.9 kg/m², n=3,113) and obesity (>25 kg/m², n=3,387). Obesity was defined 25 kg/m² or higher according to the criteria of Korean society for the study of obesity.

Results: Overweight and obesity AMI group were younger than normal and lean AMI group. Lean AMI group was older and more women than other BMI groups (p=0.001). AMI patients with obesity was an independent prognostic predictor of cardiac death on one month and one year after AMI. AMI patients with overweight also was an independent prognostic predictor of cardiac death on one year after AMI.

Binary logistic regression analysis, adjust by age, sex and Killip class

<table>
<thead>
<tr>
<th>P value</th>
<th>CR 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lean</td>
<td>Normal</td>
</tr>
<tr>
<td>Death @ one month (%)</td>
<td>0.084</td>
</tr>
<tr>
<td>Cardiac death @ one month (%)</td>
<td>0.130</td>
</tr>
<tr>
<td>Cardiac death @ one year (%)</td>
<td>0.002</td>
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<tr>
<td>Cardiac death @ one year (%)</td>
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</tr>
<tr>
<td>Cardiac death @ one year (%)</td>
<td>0.002</td>
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<tr>
<td>Cardiac death @ one year (%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: Using landiolol during primary percutaneous coronary intervention attenuates myocardial reperfusion injury in patients with ST-segment elevation acute myocardial infarction.

References:
1. Kiyokuni M., T.M. Mitsuhashi, T.S. Sugano, T.I. Ishigami, T.I. Ishikawa, M.M. Lee, Y.J. Kim. Dongguk University College of Medicine Gyeongju Hospital, Gyeongju, Korea, Republic of; 2, Dongguk University Ilsan Hospital, Goyang, Korea, Republic of; 3, Yeungnam University Hospital, Daegu, Korea, Republic of

Introduction: Landiolol is the beta 1 selective receptor blocker and its half-life elimination is 4 minutes. The safety and efficacy of landiolol started before coronary reperfusion in patients with ST-segment elevation acute myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI) remains unclear. We assessed the hypothesis that early use of landiolol reduces myocardial injury without increasing adverse events for STEMI patients performed pPCI.

Methods: Between October 2010 and September 2014, 220 consecutive patients with STEMI performed pPCI were recruited. Patients with heart rate ≥50, Killip class ≥2, old myocardial infarction and 2 or 3 degree of AV-block on admission were excluded. Thus 115 patients were enrolled. 60 patients were non-landiolol group with conventional treatment admitted from October 2010 to September 2012, 55 patients were landiolol group admitted from October 2012 to September 2014. After the admission, landiolol was started before pPCI intravenously with 3 μg/kg/min and stopped within 12 hours after pPCI when oral beta-blockers were administered. ST-segment resolution (STR) was defined as more than 70% resolution of sum of ST-segment elevation at the J point between emergency room and when finished pPCI.

Results: Time form admission to starting landiolol was 35±23 min in landiolol group. Age, sex, coronary risk factors, culprit lesion, SYNTAX score (19±10 vs 18±10), reperfusion time and peak creatine kinase did not differ between landiolol group and non-landiolol group (all NS). The number of patients with death and when finished pPCI.

References:
1. Kiyokuni M., T.M. Mitsuhashi, T.S. Sugano, T.I. Ishigami, T.I. Ishikawa, T.E. Endo, K.K. Kimura, S.U. Umemura, Y. Okohama City University, Cardiology, Yokohama, Japan; 2, Saiseikai Yokohama city Southern Hospital, Cardiology, Yokohama, Japan

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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.

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 benefit in outcome.

Methods: Retrospective analysis of ACS patients (P) with ≥ 80 years, admitted between 2010 and 2014, in a national ACS registry. P were divided according to therapy: intervened (GI) and non-intervened (GII). We evaluated clinical, electro and echocardiographic characteristics and determined predictors for an invasive approach – percutaneous coronary intervention (PCI) or coronary bypass graft (CABG) – and compared the 1 year follow up.

Results: From 11113P admitted with ACS, 2014 (18.1%) had ≥ 80 years; 51.9% male, mean age 84±4 years. 1025P (50.9%) were included in GI (94.8% male, mean age 84±3 years). GI included patients with STEMI (51.9% male, mean age 84±3 years). 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 (3.9% vs 1.8%, p < 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), microalbumin 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 0.58; p = 0.002), demen- tia (OR 0.28; p < 0.001), heart rate (OR 0.99; p = 0.003) and EF > 50% (OR 0.68; p < 0.001). Hospital mortality was inferior in GI (8.3% vs 13.6%; p < 0.001), being STEMI (OR 2.21; p < 0.001), dementia (OR 2.15; p = 0.021), inotropic use (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
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Background: The occurrence of cardiac magnetic resonance imaging defined microvascular injury (MVI) after angiographically successful primary percutaneous coro- nary intervention for ST elevation myocardial infarction (STEMI) portends worse long-term outcome. We investigated whether intracoronary pressure-velocity loops obtained during PCI can predict subsequent MVI.

Methods: In 28 patients, simultaneous Doppler flow velocity and distal measurements were obtained directly following primary PCI. From the pressure-velocity loops, the instantaneous hyperemic diastolic velocity-pressure slope (IHDVPS) and zero flow pressure (PZF) were calculated. IHDVPS 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 IHDVPS and PZF were related.

Results: PZF was significantly higher in patients with MVI in comparison to patients without MVI (45.6±13.16 vs. 32.0±11.49 mmHg, p = 0.015). In patients with extensive MVI, defined as more than 2.0 cm² MVI, PZF was and 48.5±13.72 vs. 34.0±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 0.55–0.91; p < 0.01) and 0.77 (95% CI 0.58–0.91, p < 0.01) for extensive MVI. No relationship was found between IHDVPS and PZF (r = 0.29, p = 0.1). IHDVPS did not discriminate be- tween patients with or without the development of MVI (1.47 (IQ 0.82–2.69) vs. 1.39 (IQ 0.99–2.55) mmHg cm⁻¹ s⁻¹ respectively, p = 0.77).

Conclusions: PZF, but not IHDVPS, was related to the presence and extent of MVI and may be a way to identify patients at risk of developing MVI. Further studies are required to confirm the efficacy of this method as a tool for following up, reperfusion for STEMI. It is conceivable that in patients with MVI, elevated interstitial compressive forces caused by intramyocardial edema and hemorrhage underlie the elevated PZF.
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.

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**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 females, mean age 57.1) treated with p-PCI for STEMI, who admitted within first 12 hours of chest pain between January 2006–January 2010 and post-procedural STRs were evaluated with ECG. The patients were divided into complete (>70%, n=1979), incomplete (30–70%, n=856) and no-resolution (<30%, n=255) groups according to post-procedural ST segment resolution percentage.

**Results:** In the logistic regression analysis previous statin use [odds ratio (OR) 0.72, 95% confidence interval (CI), 0.51–0.99, p<0.001], pre-procedural trofibrinoid administration (OR 0.61, 95% CI 0.48–0.85, p<0.001), 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 troponin score: 4 (OR 2.94, 95% CI 1.54–4.87, p<0.001), pain-to-balloon time <4h (OR 1.82, 95% CI 1.29–2.56, p<0.001) and neutrophil to lymphocyte ratio >5 (OR 1.82, 95% CI 1.34–5.03, p=0.007) were identified as independent predictors of no-STR. In hospital death (11.8% vs 7.5% vs 1.3%) and heart failure (35.1% vs 23.2% vs 0%) were higher in the no-STR group and in the long term follow-up, death (35.5% vs 25.8% vs 7.9%), advanced heart failure (20.2% vs 16.1% vs 2.3%) and non-fatal myocardial infarction (14.1% vs 12.1% vs 8.8%) were higher in the no-STR group (p<0.001 for all). In the Cox-proportional Hazard model no-STR was an independent predictor in the log term for all cause mortality (HR 1.78, 95% CI 1.33–2.82, p=0.009).

**Conclusion:** In patients treated with p-PCI, post-procedural complete STR is associated to better in-hospital and long term clinical endpoints. The identified predictors of no-STR are valuable in predicting electrocardiographic no-reflow phenomenon and might be useful in the planning the treatment strategy before the intervention.

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**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).

**Methods:** Ninety-nine 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 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 in-hospital complications. They had less often cardiogenic shock, heart failure, atrial fibrillation, left ventricle rupture, ventricular septal defect (table 1). There weren’t differences in the incidence of left ventricle thrombus formation as well as in sustained ventricular tachycardia or ventricular fibrillation rates. In-hospital mortality was higher in STEMI group.

**Conclusion:** Pts with TTC had a lower incidence of serious complications compared to STEMI group. Moreover, in-hospital mortality was also lower in TTC group. We observed that prognosis is more favourable in pts with TTC.
on the outcomes of complete, unprotected ULM thrombotic occlusion as culprit vessel.

**Methods:** We reviewed the database from a university hospital including 30000+ PCI over the last 10 years. We selected patients with P-PCI on ULM and we reviewed angiographies to confirm vessel occlusion (TIMI 0). Follow up data was gathered from medical history and phone interviews. The figures mean absolute numbers (percentage) or median (interquartile range). Comparisons were done with non-parametric tests, and results were considered statistically significant if p < 0.05.

**Results:** 21 patients met the requirements for analysis. 17 (81%) male, median age 64 (53–72) years, most patients (19, 90%) had at least one cardiovascular risk factor. 15 (71%) were admitted as ST-elevation acute coronary syndrome (STEACS) while the remaining 6 (29%) had NSTEACS with an unspcific EKG. 11 (52%) were in cardiogenic shock and 6 (24%) required cardiopulmonary reuscitation prior to P-PCI. Intraaortal 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 (NSTEACS 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 one with a CABG, 3 diagnostic and a therapeutic PCI in 4 individuals. Another patient required a left ventricle assist device (LVAD). Two died in this group: one due to cardiogenic shock 24 hours after the event, and the one with LVAD due to septic shock a week later. All the survivors but one (suffering from severe lung disease) were in NYHA class I or II at follow-up.

**Conclusion:** Clinical presentation and P-PCI are paramount in AMI due to ULM occlusion, since shock on admission and successful reperfusion are the most 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**


**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, 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 (PCIPI) 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 PCIPI and the assessment of mid and long term mortality.

**Materials and methods:** The study enrolled 461 consecutive patients undergoing PCIPI 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 PCIPI.

**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 a multivariate analysis. In multivariate analyzes, stent length, LVEF and low SxS were found to be associated with AVDE (OR: 1.11, 95% CI: 1.06–1.16, p < 0.001; OR: 0.80, 95% CI: 0.80–0.91, p < 0.001; OR: 0.85, 95% CI: 0.79–0.91, p < 0.001, 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 PCIPI. 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.

**Acknowledgement/Funding:** None
and clinically apparent AHF (II-IV class by Killip) were independent predictors of CIN development which in its turn increased the frequency of adverse outcomes in hospital period in STEMI patients.

P2521 | BEDSIDE
All-cause in-hospital death analysis of patients with acute myocardial infarction from China acute myocardial infarction registry (CAMI)
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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 mortality factors for mortality through this prospective, nationwide, multicenter, observational registry in the real world of Chinese.

Methods: From January 1. 2013 to March 31. 2014, total 15445 consecutive patients from CAMI registry (NCT01784691) with or without ST-segment elevation myocardial infarction (STEMI or NSTEMI) who admitted within 7 days of acute ischemic symptoms with a primary clinical diagnosis of AMI were included (108 hospitals in 31 provinces, Mainland of China).

Results: Of 15445 patients, 73.9% (11411) was male, 73.4% (11331) was STEMI and 26.6% (4114) was NSTEMI. Of those STEMI patients, 52.8% (5988) had received emergency revascularization and 79.9% (4796) of them was primary PCI; of those NSTEMI patients had a much lower percentage (8.6%, 357). Total in-hospital mortality rate was 6.58% (1017/15445), female patients (10.2%), age ≥75 (14.04%), hypertension (7.06%), diabetes (7.78%), neversmoking (8.90%), stroke history (39.3%), chronic renal insufficiency (12.05%), chronic pulmonary diseases (12.54%), ST elevation (6.81%), anterior wall infarction (7.75%), heart failure (15.77%), cardiac arrest (33.16%) or cardiac shock (36.44%) when admission, and patients not received emergency revascularization and cardiac surgery (39.3%) had highest mortality. Among unselected AMI patients in China, the in-hospital mortality (6.58%) was still high, cardiac 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.

Conclusions: Among unselected AMI patients in China, the in-hospital mortality (6.58%) was still high, cardiac 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 initiating blood coagulation and thrombotic roles of platelets, leading to fibrinolysis, platelet, activation, and inflammation. Scarce data evaluating the association between thrombin generation and the risk of cardiovascular death in acute coronary syndrome (ACS) patients is available, especially in the era of PCI and stenting with the use of dual antiplatelet treatment.

Purpose: Aim of our study was to evaluate the possible association between the entity of thrombin generation and cardiovascular death in ACS patients undergoing PCI and stenting.

Methods: In the frame of the Acute Myocardial Infarction (AMI)-Florence 2 study, we investigated thrombin generation in 294 ACS patients undergoing PCI with stent implantation. Venous samples were obtained within 24 hours from PCI. Thrombin generation was assessed using the calibrated automated thrombogram (CAT) and was expressed as endogenous thrombin potential (ETP), peak, and velocity index.

Results: At two years of follow-up, 57 out of 294 patients (19.4%) died from cardiovascular causes. Higher values of ETP [1115.9 (705–1441.3) vs 940.2 (666–1253.1) p=0.049], peak [176.1 (80.5–259.4) vs 107.3 (59.9–181.1) p=0.002] and velocity index [1480.5 (1235.7–1787.8) vs 225.3 (155.2–360) p=0.001] were detected in patients dead during follow up compared to alive patients. At the multivariate model adjusted for the Global Registry of Acute Coronary Events (GRACE) risk score, the association between thrombin generation and cardiovascular death remained significant for peak [OR 95% CI: 2.34 (1.09–5.04), p=0.030] and velocity index [OR 95% CI: C2.16 (1.14–4.61) p=0.038]. This result was confirmed even after adjustment for high on-treatment platelet reactivity.

Conclusions: We found that thrombin generation is significantly higher in patients developing cardiovascular death than in patients not and is an independent predictor of cardiovascular death thus it may be useful in improving risk stratification for ACS patients. Moreover, this association maintains its significance also in a model adjusted for high on-treatment platelet reactivity.

P2523 | BEDSIDE
Patient characteristics and organisational factors associated with delayed primary intervention in STEMI
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Background: In common practice, a sizeable portion of patients receives primary PCI (pPCI) beyond the recommended time frame. Only few studies have focused on the causes of delay.

Purpose: The aim of this study is to assess factors associated with prolonged first medical contact (FMC)-to-balloon time.

Methods: From January 2006 to December 2014, 1330 patients underwent pPCI at our Centre. Delayed pPCI was defined as FMC-to-balloon time > 90 min or PCI procedure > 30 min. Time to revascularization was performed. Reasons judged to be responsible for delayed pPCI were prospectively collected.

Results: 539 patients (40%) arrived by the Emergency Medical Service, 460 (35%) presented to the Emergency Room, and 351 (25%) were transferred from spoke Hospitals. Approximately one-third in each group (440 patients in total) underwent delayed pPCI. Patient with delayed pPCI presented a higher 30-day mortality (12.0% vs 3.7%, p<0.0001). Main patient characteristics significantly associated to delayed pPCI 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 pPCI were pre-hospital ECG and direct admission to Cath Lab. Other factors indicated by the attending cardiologist as main reason for the delay are shown in the Table.

Factors responsible for delayed pPCI
Borderline significant ECG diagnosis 18%
Missed or delayed ECG diagnosis 15%
Cardiac arrest or acute heart failure before pPCI 10%
Anterior acute complications (breathing, anaemia, renal failure, stroke, etc.) 9%
Technical difficulty for pPCI 8%
ST-segment and/or symptom resolution 7%
Absence of symptoms 5%
Cath Lab not immediately available 5%
Delayed patient consent 2%
More reasons in the same patient 10%

Conclusions: This study identified several organisational factors 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 CXCR4-CXCR7 and modulates clinical outcome following STEMI
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Background: The chemokine receptors CXCR4-CXCR7 which ligate SDF-1 mediate the differentiation of progenitor megakaryocytes and variously regulate the thrombotic–haemostatic functions of platelets and their survival. Surface expression of CXCR7 on circulating platelets is significantly enhanced in acute coronary syndromes (ACS) and significantly correlates with improved myocardial function following ACS. Moreover, high CXCR4 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 CXCR4-CXCR7 and the clinical outcome in patients with ST-elevation 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 mitochondriald transmembrane potential loss (ΔΨm 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 preoperative coronary intervention (PCI) and was immediately analysed. Patients were admitted to cardiac magnetic resonance tomography (Annexin V binding) and mitochondrial transmembrane potential loss (ΔΨm 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 preoperative coronary intervention (PCI) and was immediately analysed. Patients were admitted to cardiac magnetic resonance tomography (Annexin V binding) and mitochondrial transmembrane potential loss (ΔΨm 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.

Results: Platelet TMRE correlated significantly and positively with platelet CXCR7 (p=0.039) and inversely with platelet CXCR4 (p=0.027). Furthermore, platelet Annexin V binding correlated with better LVEF% after 6 months as compared to Annexin V levels to CXCR7 (p=0.027). Furthermore, platelet CXCR4-CXCR7 modulated clinical outcome following STEMI.

Delayed patient consent 2%
More reasons in the same patient 10%

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P2525 | BEDSIDE
Relationship between infarct 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 ST-segment elevation myocardial infarction (STEMI) undergoing percutaneous revascularization.

Methods: We analyzed 4581 STEMI pts and 2487 NSTEMI pts enrolled in the Polish Registry of Acute Coronary Syndromes who underwent an invasive strategy with percutaneous coronary intervention (PCI). Pts were divided in 2 groups according to preprocedural culprit vessel TIMI flow: TIMI flow 0–4 acute total coronary occlusion (TO) and TIMI flow 1–3 – non-TO.

Results: Total coronary occlusion had 2949 (64.37%) STEMI pts and 660 (26.5%) NSTEMI pts. The most common totally occluded infarct related artery (IRA) in STEMI group was RCA 49.37% (LAD 37.84%, LCX 12.78%) whereas in NSTEMI pts with TIMI 0 pt had higher mortality during all 36-minfth 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 group, without differences in further follow up. There were not differences in mortality between RCA TO and nTO pts both STEMI and NSTEMI groups.

Conclusions: An acute total coronary occlusion had 64.37% STEMI pts and 26.5% NSTEMI pts. The RCA was present among a half STEMI pts with total occlusion as well as the LCX among NSTEMI pts with total occlusion. Total occlusion had impact on mortality LAD related STEMI pts during all 36-minfth follow up and had impact on only in-hospital mortality LCX-related MI pts, both STEMI and NSTEMI.

P2526 | BEDSIDE
Do women with st segment elevation myocardial infarction submitted to primary angioplasty have a worse prognosis than men?

Introduction: There are some studies suggesting that women have higher mortality than men after ST segment elevation myocardial infarction (STEMI). The main goal of this study was to determine gender dependent differences in prognosis after a STEMI among patients submitted to primary angioplasty.

Methods: A retrospective, descriptive and correlational study was performed, involving patients with STEMI from 1/November/2009 to 31/October/2014. The patient demographic, clinical and therapeutic data were collected at admission. A telephonic 1 year follow-up was performed. SPSS 20.0 was used to calculate an univariate and multivariate statistical analysis for 1 year mortality.

Results: We found 752 patients with STEMI submitted to primary angioplasty. 160 (21.3%) were female and had: higher mean age (66.3 vs 61.4, p=0.00), higher prevalence of arterial hypertension (p=0.00) and of diabetes mellitus (p=0.00). Women had less previous history of acute coronary syndromes (p=0.05) and percutaneous revascularization (p=0.05).

Women had higher time between the first symptoms and first electrocardiogram (2.4 vs 1.9h, p=0.03) and consequently to revascularization therapy (4.5 vs 3.7h, p=0.01). They presented more often in Killip-Kimball class different than 1 (p=0.03), longer hospitalization (4.5 vs 3.7 dias, p=0.00) and higher 30 day mortality rate (6.2 vs 2.9%, p=0.04). Hospital complications and one year mortality rate were similar in both gender.

Conclusion: Female patients with STEMI submitted to primary angioplasty have longer hospital admission times and a higher mortality at 30 days than men. These differences can be explained in part because their older age, but more importantly because of their delay in diagnosis and consequently in the reperfusion delay when compared with men.

P2527 | BEDSIDE
Factors influencing the patient delay in STEMI
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Background: Many papers showed that patient delay defined as time from the start of chest pain to call for help is difficult to modify.

Purpose: The aim of the study is identifying factors influencing the patient delay in STEMI.

Methods: Retrospective analysis of 954 STEMI patients admitted to the Cardiology Department after teletransmission of ECG and teleconsultation with cardiologist in the period of 07.10.2005 - 05.01.2014. Data were obtained from the Emergency Medical Service protocols and hospital records. The influence of age, gender, place of residence, living with family or alone, smoking, presence of hyperpertension, 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=0.0008), living in rural areas (avg. + 32 min., + 15.9%, p=0.0097), not smoking in the period preceding the illness (avg. + 71 min., + 40.1%, p=0.0048), never ever smoking cigarettes (avg. + 57 min., + 29.5%, p=0.0375). Other factors as age, living with family or alone, presence of hypertension, diabetes, hypercholesterolemia, obesity, overweight had no influence on patient delay. Interesting also the history of CAD had no influence on the successive steps of the educational process during previous hospitalization and out-patient care.

Conclusions: Female sex, living in rural areas and not smoking are the factors increasing the patient delay time.

P2528 | BEDSIDE
Diabetes Mellitus type 2 is an important risk factor for sudden cardiac arrest in patients with STEMI
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Background and introduction: Sudden cardiac arrest (SCA) is the most serious complication of ST elevation myocardial infarction (STEMI). The negative impact of Diabetes Mellitus type 2 (T2DM) on the development of cardiovascular diseases is well known and documented. However, we lack in conclusive data about frequency of SCA in diabetic patients with STEMI.

Purpose: We aimed to assess the impact of T2DM on the incidence of SCA in patients with STEMI.

Methods: We divided 450 consecutive patients (266 men, 184 women, age: arithmetic mean 64.9 years, median 63 years, 214 smokers [47.6%] with confirmed STEMI as the LCX among with and without T2DM and evaluated the occurrence of prehospital SCA. Then, we performed comparative analysis between those groups.

Results: We observed 137 (30.5%) cases of T2DM (we provided 15 diagnoses during the patient stay, according to 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 without T2DM). We recorded only one case of asystole, in a patient with T2DM. Among patients with T2DM sudden cardiac arrest occurred 9 times (6.6%), whereas among patients without T2DM – 4 times (1.2%). We evaluated hazard ratio (HR) of SCA associated with T2DM at 5.08 (Fisher’s Exact Test, p<0.01).

Conclusions: In our study group SCA as a complication of ST elevation myocardial infarction appeared 5 times more frequently in patients with Diabetes Mellitus type 2 than without T2DM (6.6% vs 1.4%, HR=5.08, p<0.01).

P2529 | BEDSIDE
Kidney lesion in ST-elevation myocardial infarction- how to evaluate it?

Introduction: Chronic Kidney Disease (CKD) and acute kidney lesion are frequent co-morbidities in patients admitted for ST-elevation myocardial infarction (STEMI) and are associated with a worse outcome. There are several equations to correctly identify patients with kidney lesion through glomerular filtration rate (GFR), but it is still not consensual which one is the most appropriate in the setting of STEMI.

Purpose: We aimed to compare which of the 3 more commonly used formulas - Cockcroft-Gault [CG]; Modification of Diet in Renal Disease [MDRD] and Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] - is more effective in predicting worse outcomes at 1-year follow up in STEMI.

Methods: Prospective study of 543 patients admitted for STEMI [age 63.80±12.79; 74.0% men; 23.9% diabetics; 55.1% hypertensive] in our cardiac intensive care unit, between October 2009 and September 2014. GFR estimated by each formula is calculated as the mean of 3 different occasions (up to 5 occasions) and estimated by each formula is calculated as the mean of 3 different occasions (up to 5 occasions). We aimed to evaluate which formula is most effective in predicting worse outcomes at 1-year follow up in STEMI.
from CG, MDRD and CKD-EPI were compared in terms of mortality risk prediction and primary composite endpoint (cardiovascular death, non-fatal myocardial infarction or stroke) during hospitalization.

Results: The prevalence of GFR <60 ml/min/1.73m² was 42.2% using the CG, 46.3% with MDRD and 41.9% with CKD-EPI. All formulas had a good discriminatory power in the primary composite endpoint with CG proving to be the best formula by ROC curve analyses [AUC (CG): 0.726 vs AUC (MDRD): 0.689 vs AUC (CKD-EPI): 0.706]. All formulas were also good predicting in-hospital total mortality with CG to evidencing the best results [AUC (CG): 0.725 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.

P2530 | BEDSIDE
Infarct size in staged versus immediate complete revascularisation for multivessel coronary artery disease: a single-centre prospective study

Methods: In the prospective CMR-PRIM study, staged CR was performed in 24–96 hours and 9 months post CR, respectively. The primary CMR endpoint 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></th>
<th>Immediate complete</th>
<th>Staged complete</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>62.8±11.7</td>
<td>65.0±10.3</td>
</tr>
<tr>
<td>Male (n, %)</td>
<td>52/60 (86.7)</td>
<td>28/30 (93.3)</td>
</tr>
<tr>
<td>Anterior infarct (n, %)</td>
<td>21/60 (35.0)</td>
<td>11/30 (36.7)</td>
</tr>
<tr>
<td>Symptom-PPCI time (min)</td>
<td>179 (127–305)</td>
<td>203 (115.1–296)</td>
</tr>
<tr>
<td>Time to acute CR (d)</td>
<td>2.3 (1–7.3)</td>
<td>4.1 (2.7–5.4)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%) on acute CMR scan</td>
<td>47±9.4</td>
<td>42±10.2</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 (8.8–35.2)</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>
</tr>
<tr>
<td>Presence of ischaemia (%) on follow-up CMR</td>
<td>10/49 (20.4)</td>
<td>7/26 (26.9)</td>
</tr>
<tr>
<td>Presence of ischaemia (%) on follow-up TEE</td>
<td>10/49 (20.4)</td>
<td>7/26 (26.9)</td>
</tr>
<tr>
<td>Presence of ischaemia (%) on IVCC maneuver</td>
<td>10/49 (20.4)</td>
<td>7/26 (26.9)</td>
</tr>
<tr>
<td>Global ischaemic burden (% left ventricular mass) on follow-up CMR</td>
<td>12.8±10.9</td>
<td>19±17.3</td>
</tr>
<tr>
<td>Major adverse cardiovascular events (n, %)</td>
<td>4/60 (6.7)</td>
<td>7/60 (11.7)</td>
</tr>
</tbody>
</table>

Conclusions: This is the first CMR study comparing revascularisation for multivessel disease at PPCI. 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)

P2531 | BEDSIDE
Transradial vs. Transluminal Coronary Intervention for ST Elevation Myocardial Infarction

Objective: We have compared the impact of access strategy change on early and two-year outcomes after primary percutaneous coronary intervention using trans-radial access (TRA) versus intervention by trans-femoral access (TFI).

Background: Adoption of TRA was recently proposed as potentially beneficial strategy to improve outcomes of PPCI for STEMI patients.

Methods: We have studied 1808 consecutive patients which underwent TFI (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 major difference in early mortality rates was in favor of TRA strategy (5.2% vs 6.6%) comparing TFI strategy (10.5% vs 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 (8.0%) with significantly lower rate in TRA group comparing to 90 deaths (13.9%) in TFI group (OR 0.60; 95% CI [0.47–0.89]; p=0.001). The difference obtained in the first 30 days between the two accesses strategies have sustained with similar trends for mortality rates in the following two years. Two year MACE rates were in favor of TRA strategy (14.6% Vs 22.1%; OR 0.40 [0.30–0.78]; 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 traditional transfemoral access strategy for primary coronary interventions in STEMI patients. TRA was associated with sustained mortality benefit after two years.

P2532 | BEDSIDE
Diagnostic accuracy of focused cardiac ultrasound performed by emergency physicians for the assessment of ascending aorta diameter and aneurysm
O. Ottaviani1, P. Nazerian1, C. Tozzetti1, C. Catini1, A. Nencioni1, F. Morello2, V. Ticali1, S. Grifoni1, M. Vittorini1, S. Vanni1, Careggi University Hospital, Florence, Italy; Azienda Ospedaliero Universitaria Monaldi, Emergency Department, Torino, Italy

Objectives: The diagnostic performance of thoracic ultrasonography (FoCUS) performed by emergency physicians (EP) to estimate ascending aorta diameters in the acute setting has not been prospectively studied. We investigated the diagnostic accuracy and the interobserver variability of EP-performed FoCUS to estimate thoracic aortic dilation 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 in the Emergency Department for suspected aortic pathology. FOCUS was performed before CTA and the maximum ascending aorta diameter measured in parasternal long-axis view. Aorta diameter <40 mm by visual estimation or by diameter measurement was considered normal. Measurements were recorded in all patients with aorta diameter >40 mm. Diagnostic accuracy of FoCUS for detection of aortic dilation (diameter ≥40mm) and aneurysm (diameter >45mm) were calculated considering CTA as reference standard. In a subgroup of patients, a second EP-sonographer performed FoCUS to evaluate interobserver agreement for the diagnosis of ascending aorta dilation and aneurysm.

Results: 140 patients were enrolled in the study. Ascending aorta dilation and aneurysm were detected at FoCUS in 50 (35.7%) and in 27 (17.8%) patients respectively. Sensitivity and specificity of FoCUS were 78.6% (95% CI 65.6–87.3%) and 92.9% (95% CI 85.1–97.3%) respectively for ascending aorta dilation, and 64.7% (95% CI 46.5–80.2%) and 95.3% (95% CI 89.3–98.4%) respectively for ascending aorta aneurysm. Inter-observer agreement of FoCUS was k=0.82. Conclusions: FoCUS performed by EP is specific for ascending aorta dilation and aneurysm when compared to CTA and appears as a reproducible technique. Acknowledgement/Funding: ADVISED study group

P2533 | BENCH
Inferior vena cava compression 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) compared with agitated saline injection was performed under following 3 conditions: Valsalva maneuver, the most sensitive testing to identify PFO compared with "inferior vena cava compression (IVCC) maneuver" to diagnose PFO compared with agitated saline injection, and the most sensitive testing to identify PFO compared with "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 im...
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 TEE maneuver (33 patients, 15.4%, P=0.006 vs at rest, P=0.08 vs IVCC maneuver). Conclusions: IVCC maneuver is feasible and effective provocation testing to detect PFO, which is not inferior to TEE maneuver. Especially when TEE maneuver cannot be performed under sedation, IVCC maneuver could be an alternative diagnostic method to detect PFO using TEE.

**P2534 | BEDSIDE**

**Tissue Doppler imaging of pulmonary arteries - a novel technique for detecting pulmonary hypertension?**

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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 were also calculated (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 create the formulas, 84.9 – [193 x ESV – 0.21 x TIBSP] and 58.6 – [137.8 x ESV – 0.29 x TIBSP], risk equation for pulmonary arterial wall elasticity (MPESV, 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.

**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 an echocardiographic marker for arterial stiffness in OSAS.

**Methods:** The study population included 116 patients with OSAS and 90 age and gender-matched healthy subjects. Aortofemoral pulse wave velocity (PWV), carotid intima-media thickness (CIMT), brachial artery flow-mediated dilatation (FMD), and AVP were measured to assess arterial stiffness.

**Results:** AVP (45.8±16.1 vs. 60.7±13.6, p < 0.001) and FMD (8.7±3.3 vs. 14.6±4.6, p < 0.001) were found to be significantly decreased in patients with OSAS compared to controls. PWV (10.3±2.2 vs. 8.5±2.0, p < 0.001) and CIMT (0.83±0.14 vs. 0.66±0.15, p < 0.001) were increased in the OSAS group compared to controls. AVP was significantly positively correlated with FMD (r=0.564, p < 0.001). However, it was found to be significantly inversely related to PWV (r=−0.580, p < 0.001) and CIMT (r=−0.251, p < 0.001).

**Conclusion:** AVP was found as a novel echocardiographic parameter for measuring arterial stiffness in OSAS. Moreover, it was found to be related to parameters of arterial stiffness such as PWV, CIMT, and FMD. AVP measurement may be a useful and practical method for assessing arterial stiffness, which is associated with cardiovascular risk factors in OSAS.

**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 4DRVFunction 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, and 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±5.5%. Mean values of 2DE and 3DE RVEDV and 2DE RVESV and 3DE 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**

**Feasibility of aortic valve area measurement assessment by single-beat recording of double-envelope technique in patients with aortic stenosis and atrial fibrillation**

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**Background:** In patients with aortic stenosis (AS) and atrial fibrillation (AF), the...
conventional continuity equation to evaluate aortic valve area (AVA) is cumbersome, because 5 to 10 cycles are required to ensure accuracy of results. Double-envelope (DE) technique is obtained by a single continuous-wave Doppler envelope with double density velocity profiles; the inner envelope represents flow across the left ventricular outflow tract (LVOT) and outer envelope represents flow across the aortic valve orifice. The aim of this study to evaluate the usefulness of AVA measurement calculated in single-beat DE technique in patients with AS and AF. Methods: Thirty-one AS patients (76.6±7.4 years old) with AF were examined by transthoracic echocardiography. The conventional AVA (PW/CW technique) was calculated from non-simultaneously measured LVOT flow and AVO flow in randomly picked up 8 cardiac cycles, respectively. The AVA (DE technique) was calculated from the inner and outer envelopes simultaneously recorded. A single-beat AVA was calculated from simultaneously recorded inner and outer envelopes (by DE technique) when the preceding RR interval/pre-preceding RR interval = 1. Results: DE profiles were successfully obtained in all patients, and mean AVA (PW/CW technique) was 1.12±0.23 cm². AVA by Single-beat DE technique showed good correlation with that by PW/CW technique (r=0.87), and the mean bias in the AVA measurements between by PW/CW technique and by DE technique was 0.067 cm² (Figure).

Feasibility of DE technique in AS & AF

Conclusions: AVA in patients with AS and AF obtained by Single-beat DE technique was feasible and in good agreement with that by PW/CW technique. We suggest that DE technique should be considered to estimate the subtle temporal change of AVA in patient with AS and AF more simply and accurately.

P2538 | BEDSIDE
Quantification of valve dimensions by transesophageal 3D echocardiography in patients with functional and degenerative mitral regurgitation

Background: Aim of the study was to quantify valve dimensions based on 3D transesophageal echocardiography in patients with functional (MR) and degenerative (DMR) mitral regurgitation (MR).

Methods: All in all, 329 patients with at least moderate MR were examined. Echocardiographic parameters included ejection fraction (EF), left atrial volume (LA), left ventricular enddiastolic volume (LVVd), and effective regurgitant orifice area (EROA) by PISA method. In addition, vena contracta area (VCA) was derived from a 3D colour Doppler dataset. For quantification of mitral leaflet and anulus (MA) dimensions the following parameters were measured: anterior-posterior (AP) diameter and anterolateral-posteromedial (AL-PM) diameter of MA; annular area and height; MV tenting volume; leaflet area and leaflet angle.

Results: The patient population was divided according to type and degree of MR.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Normal group (n=31)</th>
<th>Moderate MR (n=87)</th>
<th>Severe MR (n=87)</th>
<th>Moderate DMR (n=71)</th>
<th>Severe DMR (n=71)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF (%)</td>
<td>51.0±11.27</td>
<td>52.7±13.43</td>
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<tr>
<td>LVVd (ml)</td>
<td>114±54</td>
<td>184±100</td>
<td>241±104</td>
<td>151±59</td>
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</tr>
<tr>
<td>AROA (cm²)</td>
<td>0.12±0.05</td>
<td>0.20±0.10</td>
<td>0.30±0.12</td>
<td>0.15±0.08</td>
<td>0.25±0.12</td>
</tr>
<tr>
<td>AL-PM (cm)</td>
<td>3.75±1.02</td>
<td>5.12±1.34</td>
<td>6.67±1.34</td>
<td>5.08±1.41</td>
<td>6.37±1.52</td>
</tr>
</tbody>
</table>

P5259 | 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
A. Cecchetto, D. Muraru, V. Spadotto, G. Romeo, A. Pratula, S. Mihaila, S. Onciul, U. Cucchi, S. Ilieco, L. P. Badano. University Hospital of Padova, Cardiology, Padua, Italy; University of Medicine and Pharmacy Carol Davila, Bucharest, Romania

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-chamber full volume datasets (41±9 vps) were acquired using Vivid E9 scanner (GE) and analyzed by 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 operation 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 ±21±11 ml), and EF (7.7±9.2 vs 2.7±4.2%) than the semi-automated approach (p<0.001 for all). Using manual corrections in all 60 pts, LV volumes were still smaller than by CMR (163±50 vs 171±51 ml, p<0.0001), but EF was similar (54±11% vs 53±12% p=0.118). Semi-automated 3DE algorithm provided LV measurements with excellent correlations and agreement (bias±SD) with CMR ((r=0.97 and 9 mm 14 ml for EDV; r=0.92 and 0.94% for EF p=0.001 for both). For LV volume, semi-automated 3DE method vs same datasets was very good in comparison with CMR's (intraobserver ICC 0.97 vs 0.99 for EDV; 0.93 vs 0.98 for EF; interobserver ICC 0.93 vs 0.99 for EDV; 0.82 vs 0.89 for EF).

Conclusion: Novel semi-automated 3DE algorithm enables a highly accurate and reproducible analysis of LV volumes and ejection fraction using a vendor-independent solution. Spending additional time in correcting endocardial borders after automated tracking eliminated the EF bias and provided LV volumes that were close to those obtained by CMR. These findings are particularly relevant for multimod 3DE labs.

P2540 | BEDSIDE
Assessment of left ventricular layer torsion in hypertensive patients using novel one-beat three-dimensional speckle tracking echocardiography with high volume rates
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Purpose: The left ventricle (LV) is composed of 3 myocardial layers and twist and torsion play an important role in squeezing the blood out of the heart. However, LV layer torsion has not yet been examined by echocardiography because until recently magnetic resonance imaging has been only noninvasive technique to evaluate LV layer torsion. Therefore, we sought to examine LV layer torsion and the relation between layer torsion and systolic function in patients with hypertension (HTN) by novel one-beat 3-dimensional speckle tracking echocardiography (3D-STE).

Methods: Eighty one subjects (23 controls (age 60±12), 37 patients with HTN (age 69±12) and 21 patients with hypertensive heart failure (HHF) (age 75±18)) were enrolled to characterize layer torsion (endocardium, midwall and epicardium) by the 3D-STE with volume rates of 60–80vps. Twist was defined as

Fifty patients without valvular or myocardial disease served as control group. The results of the measurements are displayed in Table 1.

<table>
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Conclusions: The results of the measurements are displayed in Table 1.
Background: 44 patients (age range 18–82 years, 29 men, ischemic 30%, congenital) were included in the study to assess differences in LV volumes obtained by novel vendor-independent (VI) and vendor-specific (VS) software packages on left ventricular volume measurements performed on 3D echo data sets obtained from different echo systems. We sought to assess intervendor differences of LV volumes and EF for EDV (10±11 ml vs. 15±12 ml; p=0.046) and end-systolic volumes (0.75±0.17 vs. 0.92±0.19; p=0.002) between LV volumes obtained from different vendors to reduce the differences in LV volumes and EF time integral ratio. Measurements derived from conventional echocardiography were compared to pulmonary regurgitant fraction, right ventricular volumes and ejection fraction by CMR.

Results: On CMR, the pulmonary regurgitant fraction was 28.6±4±10.2%. By conventional echocardiography, pulmonary regurgite index and no flow time were found to offer the best prediction for severity of pulmonary regurgite. Pulmonary regurite index of <0.8 has sensitivity of 86.36% and specificity of 100% (AUC=0.924) and no flow time of >64 msec has sensitivity of 81% and specificity of 100% (AUC=0.894) in identifying significant pulmonary regurite. Compared to controls, patients after TOF repair showed significantly lower right ventricile myocardial velocities, higher E/ E' ratio and prolonged MPI. Among TOF patients, right ventricle MPI showed significant negative correlation (r=−0.402; P=0.008) with tricuspid valve 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 regurite 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

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Background: The dynamics of the mitral valve annulus in organic mitral reguritation (TOF) may differ significantly between the various etiologies. The present evaluation characterizes the mitral annulus dynamics in patients with MR due to Barlow disease (BD) or fibro-elastic deficiency (FD) using 3-dimensional (3D) modelling.

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 by 3D transesophageal echocardiography. The 3D geometry of the mitral annulus was measured with dedicated software at begin-systole and end-systole. Parameters reflecting the saddle shape geometry of the mitral annulus (annulus height, nonplanar angle and the annular height to commissural width ratio (AHWR)) were measured along the annulus. MR was graded according to current guidelines and classified into holosystolic or late systolic.

Results: Patients with BD showed significantly larger malary height, more acute nonplanar angle and higher AHWR than patients with FD at the beginning of the systole reflecting more preserved saddle shape of the mitral annulus (Table). At end-systole, the mitral annulus became more flattened in both groups of patients. However, patients with BD have a significantly more dynamic annulus as reflected by larger changes in annulus height, nonplanar angle and AHWR. Furthermore, 7 patients had late systolic MR, all of them with BD, suggesting more enhanced movement and flattening of the mitral annulus during late systole compared with FED.

Conclusions: 3D dynamics of the mitral annulus

P2544 | BENCH

Automatic quantification of aortic regurgitation using 3D full volume color Doppler echocardiography: a validation study with cardiac magnetic resonance imaging

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Aims: The aim of this study is to explore the ability of 3D full volume color Doppler echocardiography (FVCDE) to quantify aortic reguritation (AR).

Methods and results: Thirty patients with aortic valve reguritation were examined. Echocardiographic grading of aortic reguritation was performed by three experienced CMR cardiologists. AR severity was categorized into mild, moderate and severe degree of AR were enrolled. AR volume was measured by (1) two-dimensional-CDE (2D- CDE), using the proximal isovelocity surface area (PISA) and (2) real-time 3D-FVCDE with 3) phase-contrast cardiac magnetic resonance imaging (PC-CMR)
as the reference method. Automated AR quantification using 3D-FVCDDE was feasible in 30 of the 32 patients. 2D-PISA underestimated the AR volume compared to 3D-FVCDDE and PC-CMR: 38.6±9.9 mL by 2D-PISA; 49.5±10.2 mL by 3D-FVCDDE; 52.3±12.6 mL by PC-CMR. The AR volume assessed by 3D-FVCDDE showed a better correlation and agreement with PC-CMR (r=0.93, p<0.001, 2SD: 9.2±1.6 mL; 2D-PISA: r=0.76, p=0.001, 2SD: 15.7 mL). When used to classify AR severity, 3D-FVCDDE 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-FVCDDE. In patients with multiple jets, only 3 out of 10 were correctly graded by 2D-PISA, while 3D-FVCDDE correctly graded 9 out of 10 of these patients.

P2545 | BEDSIDE Determinants of normal tricuspid annulus area in healthy volunteers: a three-dimensional echocardiographic study

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Background: The tricuspid annulus (TA) size and function have a pivotal role in determining the need for associated tricuspid annuloplasty in patients undergoing cardiac surgery for left-sided valve diseases. Due to the lack of dedicated software packages, the non-planar TA area and its physiological determinants in normal subjects need to be clarified.

Methods: Multi-beat three-dimensional (3D) data sets of the right ventricle (RV), right atrium (RA) and tricuspid valve were acquired from the apical approach using GE Vivid E9 scanner in 79 healthy volunteers (45±13 years, range 20–74 years; 34 men). TA 3D area was measured using custom made software. The user identifies the mid-systolic (MS) reference frame, on which the TA is manually delineated by placing several points on multiple rotated planes. Then, the new software reconstructs the 3D TA model and automatically tracks it throughout the cardiac cycle. RV and RA volumes were measured using 4D RV Function™ and LA Function™ software packages.

Results: Temporal resolution of 3D datasets was 34±6 vps (range 24–57). TA area decreased from 4.92±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±0.6 cm² vs 6.0±0.9 cm², p=0.56). Using multivariable linear regression analysis, BSA remained the only determinant of maximal TA 3D area (R²=0.48).

Conclusions: Normal TA is a highly dynamic structure that reaches its maximal dimension in late diastole. Although gender, body size, RV and RA volumes influence TA size, BSA is the only independent determinant of maximal TA 3D area in healthy subjects.

Table 1. TA size relation with RA and RV volumes

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<th>Parameter</th>
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<th>RA volume (mL)</th>
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<td>Surface area (cm²)</td>
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<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).

P2546 | BEDSIDE

Initiation of valve regurgitation is influenced by RV and RA remodeling. The close relationship between RA size and TA geometry is a new finding that may explain the onset of FTR in patients with normal RV volumes and dilated RA.

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</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).

Conclusions: In patients with FTR, TA is enlarged and its geometry is influenced by RV and RA remodeling. The close relationship between RA size and TA geometry is a new finding that may explain the onset of FTR in patients with normal RV volumes and dilated RA.

Table 1. TA size relation with RA and RV volumes

<table>
<thead>
<tr>
<th>Parameter</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).

Conclusions: In patients with FTR, TA is enlarged and its geometry is influenced by RV and RA remodeling. The close relationship between RA size and TA geometry is a new finding that may explain the onset of FTR in patients with normal RV volumes and dilated RA.
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.

### P2546 | BEDSIDE

**Color Flow Quantification: a new method to assess mitral regurgitation severity**

C. Vieira\(^1\), F. Islas\(^2\), J.A. De Agustin\(^2\), G. Feltes\(^2\), J.J. Gomez De Diego\(^2\), P. Marcos-Alberca\(^2\), C. Almeria\(^2\), J.L. Rodrigo\(^2\), M.A. Garcia Fernandez\(^2\), L. Perez De Isla\(^2\), \(1\) Hospital de Braga, Braga, Portugal; \(2\) Hospital Clinic San Carlos, Cardiovascular Institute, Madrid, Spain

**Introduction:** Mitral regurgitation (MR) is a frequent finding and the assessment of its severity is still difficult, as in patients with more than one regurgitation jet. The two-dimensional (2D) methods have important limitations. Single-beat, real-time three-dimensional (3D) color Doppler imaging allows direct measurement of proximal isovelocity surface area (PISA) and it has been validated. 3D Color Flow is a new tool that measures the flow that passes through cardiac valves.

**Purpose:** As a 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 PISA measurements were good, with intraclass correlation coefficients of 0.97 and 0.83 respectively; for 3D color flow, these agreements were also good, with intraclass correlation coefficients of 0.94 and 0.95 respectively.

**Table 1. Inter-methods agreement analysis using 3D PISA EROA as gold standard**

<table>
<thead>
<tr>
<th>Method</th>
<th>r</th>
<th>p</th>
<th>ICC (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>EROA 3D PISA, EROA 2D volumes</td>
<td>0.32</td>
<td>0.10</td>
<td>0.29</td>
<td>0.04–0.43</td>
</tr>
<tr>
<td>EROA 3D PISA, EROA 2D volumes</td>
<td>0.753</td>
<td>0.567</td>
<td>-0.001</td>
<td>0.75 (0.57–0.87)</td>
</tr>
<tr>
<td>EROA 3D PISA, EROA 3D volumes</td>
<td>0.48</td>
<td>0.10</td>
<td>0.49</td>
<td>0.02–0.81</td>
</tr>
</tbody>
</table>

**Conclusions:** 3D color flow is a simple and accurate method to assess MR severity. Its implementation can be an important help in the clinical decision making of these patients.

### P2549 | BEDSIDE

**Three-dimensional dynamic assessment of tricuspid annulus in patients with functional tricuspid regurgitation in rheumatic left heart valve disease**

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**Background:** Anatomical changes that take place in the tricuspid annulus (TA) morphology play a fundamental role in the mechanism of the functional tricuspid regurgitation (FTR). Little is known about the architectural changes in TA diameters during the cardiac cycle.

**Objectives:** To explore the potentiality of 3D transthoracic echo (3DTE) in the evaluation of TA dynamic changes in relation to the severity of FTR in patients with left side rheumatic valvular disease.

**Methods:** 3DTE was performed in 50 patients (Age: 69±9, 82% women) with rheumatic left side disease at FTR. FTR was graded in two groups: Severe (N: 14) or non-severe (N: 26). Two orthogonal planes corresponding to the anatomical antero-posterior (APD), septo-lateral (SLD), long intercommissural (LID) and Area (A) of TA were analysed at each end-systole and end-diastole to calculate the mean fractional shortening (FS) for each parameter.

**Results:** At 3DTE diameters differed significantly among the two groups. Despite the increase in the size of the TA in the presence of severe TR, FS showed no significant differences between groups (Table 1).

**Conclusions:** We provide new 3DTE parameters related to TA morphology in presence of FTR in this subgroup of patients. FTR severity seems to be associ-

### P2550 | BENCH

**Three-dimensional printing of tricuspid valve using transthoracic echocardiography**

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**Background:** Tricuspid valve (TV) annulus sizing is inaccurate using 2D echocardiography. Three-dimensional (3D) printing of models of congenital heart defects, cardiac tumors and aorta based on volumetric data obtained by CT and CMR have been used to simulate/plan cardiac surgery. Recently, transoesophageal 3DE 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:** 3DE 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 MeshLab (Visual Computing Lab ISTI-CNR) software to construct a solid model (Figure, C) which was converted to stereolithographic file format and 3D printed by a commercially available Maker Bot 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.

### LEFT AND RIGHT ATRIAL MORPHOLOGY AND FUNCTION

Y. Ohara, Y. Tsuda, Y. Fukuoka, Y. Hosogi, K. Yamamoto, Kochi Health Sciences Center, Kochi, Japan

**Background:** Chronic kidney disease (CKD) leads to left atrial (LA) structural...
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 <60 ml/min/1.73 m²) with LA volume indexes <28 ml/m² and 95 control subjects. Global atrial longitudinal strain was measured by averaging all atrial segments. Reservoir (S-LAs), conduit (S-LAe), and contractile (S-LAa) phase strain were obtained. The ratio of E/Ea to LA strain was used as an index of LA stiffness.

**Results:** S-LAs and S-LAe were significantly decreased in the CKD group compared with that in the control group (S-LAs: 18.2±4.7 vs. 23.5±7.0, p <0.005; S-LAe: 8.5±2.7 vs. 11.7±5.8, p <0.0001). LA stiffness was significant correlation with eGFR (Figure).

**Conclusion:** LA function and stiffness are significantly impaired in CKD patients with preserved LVEF and normal LA size. LA myocardial fibrosis and myopathy may play a role in the LA functional and stiffness abnormalities in CKD patients with preserved LVEF and normal LA size.

**P2552 | BEDSIDE**

**Prognostic value of right atrial function and dimensions in patients with pulmonary hypertension**


**Introduction:** Clinical assessment is essential when evaluating patients with suspected pulmonary hypertension (PH), however, echocardiography is a key screening tool in the diagnostic algorithm. Right ventricular dysfunction has been associated with adverse outcomes but few studies have focused on the structure and function of the right atrium (RA).

**Objectives:** To determine the prognostic value of RA dimensional and functional parameters in patients with PH.

**Methods:** Prospective study of 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 reasons was tested using the Kaplan-Meier analysis and Cox multivariate regression analysis. Prognostic accuracy was evaluated by the area under the receiver operating 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 - 40±13.1 cm²; systolic area - 19.3±11.1 cm²; 4C view longitudinal diameter - 56±12.9 mm. During a median follow-up period of 25 months, 9 patients died and 29 were admitted for cardiac causes. The composite endpoint occurred in 39% of pts (N=30) and the risk increased for higher RA sizes and lower atrial systolic deformation. The risk of events increased 6% per each cm² of increased RA area (HR: 1.06; 95% CI 1.03–1.10; p=0.001). Longitudinal systolic strain of all septal segments and that of lateral-apical segment were strong prognostic predictors. The risk of events increased 7% for each 1% reduction of atrial deformation (HR: 1.07; 95% CI 1.02–1.13; P=0.003). Midseptal segment longitudinal systolic strain was the strongest prognostic predictor at multivariate Cox regression analysis (including all RA echocardiographic parameters) (HR: 1.10; 95% CI 1.02 to 1.18, P=0.012).

**Conclusions:** RA deformation and dimensional indexes showed prognostic value in PH pts and should be considered for routine echocardiographic assessment.

**P2554 | BEDSIDE**

**Left atrial mechanics after successful surgical ablation of atrial fibrillation during valvular heart disease surgery**

N. Lorenzo, I. Mendez, G.F. Martinis, M. Tabo, R. Montes De Oca, S. Badia, G. Reyes, F. Alfonsa, R. Aguilar. University Hospital La Princesa, Madrid, Spain

**Background and purpose:** Left atrial (LA) mechanics after surgical ablation (SA) of AF in valvular heart disease (VHD) is not fully known. This study aimed to explore LA mechanics and to identify predictors of recurrence.

**Methods:** 44 patients who maintained sinus rhythm (SR) 3 months after SA during VHD surgery (82% mitral) were studied. Strain (S) and Strain Rate (SR) parameters (Fig. 1.1) were obtained in apical 4-, 3- and 2-chamber views, using speckle tracking echocardiography. Simultaneously, 30 volunteers were studied with the same protocol.

**Results:** 1,886 LA segments were analysed (70% of total LA segments). LA was severely dilated in the post-surgery group and, myocardial properties of LA did not recover after surgery (Fig. 1.2, A-B) when compared with normal values (Fig.

**Conclusion:** Using TTE, the baseline echographic features of the ACP are 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.
P2551 | 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 (LAA) closure by a precise evaluation and measurement of the anatomic morphology of the LAA.

Methods: Fifty-nine patients undergoing LAA closure procedures. The correlation between the closure device size and the LAA landing zone dimension measured by 2D-TEE, 3D-TEE, and fluoroscopy were measured at the 0°, 45°, 90° and 135° planes. We acquired 3D-TEE full-volume data at the LAA, and the 3D-flexi slice function was used to measure the maximal and the minimal dimensions of the LAA ostium as well as the depth. 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 LAA 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 maximum dimensions were found at 135°. A 3D-TEE flexi slice revealed that the maximal LAA ostial dimension was distributed within the 30°-160° plane, and 88% presented within the 90°-150° plane. Furthermore, the measurement was 2.40±0.52 cm, which was significantly different from 2D-TEE (p=0.011-0.05). In the twenty device closure patients assessed by RT3D-TEE, there were seven single-lobe cases and eight double-lobe cases, and the remaining five patients were identified as multi-lobe, which led to the selection of eighteen regular and two special devices. With monitoring by TEE and X-ray, the LAA closure procedures using the LAMBRET™ device were successful for all twenty patients. The landing zone for selective angiography was 2.39±0.56 cm, and the appropriate LAmBre™ TM closure disk size was 2.4–3.6 cm. The correlations between the device size and the measurements by 2D-TEE and 3D-TEE were significant (p<0.05).

Conclusion: Compared with routine 2D-TEE, RT3D-TEE allows for more precise assessments of left atrial appendage morphology and device delivery in LAA closure procedures.

P2558 | 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: In univariate analysis, age (hazards ratio [HR]: 1.31, p < 0.002), 3D-LSa (HR: 0.74, p = 0.021), CSs (HR: 0.88, p = 0.014), CSs (HR: 0.76, p = 0.0037), ASs (HR: 0.93, p = 0.0064), ASs (HR: 0.89, p = 0.022) and 3D-ASs (HR: 1.12, p = 0.022) were the predictors of AF recurrence, though association of the recurrence with 2D-LSs (p = 0.49), 2D-LSa (p = 0.60), or 3D-LA volume (p = 0.73) was not significant. 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 of AF than those at 1 years after the CA procedure (89% vs. 71%).

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.
Left atrial (LA) geometry and function have prognostic value in various cardio-vascular diseases. 3D echocardiography (3DE) is more accurate than conventional 2D echocardiography (2DE) in measuring LA size. Clinical value of right atrial strain in predicting early hemodynamic deterioration in patients with pulmonary hypertension: L. Ferrarotti, C. Piccinino, D. Sola, A. Giubertoni, J. Zanaboni, P. Marino. Hospital Maggiore Della Carita, Novara, Italy

CONCLUSIONS: Implementation of 3DE to measure LA volumes and function in clinical practice requires specific reference values in order to discriminate between normal and abnormal LA. This clinical study of 230 healthy volunteers (43±14 years; 58% women) who underwent 2D and 3D to obtain LA maximal (Vmax), minimal (Vmin) and pre (AVp) volumes using biplane discs’ summation method and volumetric measurement by dedicated software (4D LA Analysis™, TomTec, 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: 3D 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 of 3DE LA volumes was in a range of values that would define severe dilatation by 2DE. Differences in LA emptying fractions calculated by 2D vs 3D were also significant (Table).

LA reference values by 3DE vs 2DE

<table>
<thead>
<tr>
<th>Volume</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 Vol</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 Vol</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>PreAVol</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>41±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, emptying fraction; RL, reference limit (upper or lower).

Conclusions: 3D LA volumes are larger when measured with 3D than 2D echocardiography: implications for the definition of normality

D. Muraru1, M.H. Miglioranza2, D. Ermacora2, A. Maddalozzo2, C. Palermo2, S. Iliceto2, L.P. Badano2

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Background: Left atrial (LA) volumes and function (i.e. LA phasic volumetric changes) have emerged as important prognostic parameters in various cardio-vascular conditions. Although, biplane two-dimensional echocardiographic (2DE) calculation of LA volume is currently recommended, three-dimensional echocardiography (3DE) has been reported to be more accurate than 2DE to measure LA volumes, because it does not rely on geometric assumptions about LA shape. However, the actual differences between 2DE and 3DE LA volumes and their implications for the definition of normality remain to be clarified.

Methods: Prospective cross-sectional study of 230 healthy volunteers (43±14 years; 58% women) who underwent 2DE and 3D to obtain LA maximal (Vmax), minimal (Vmin) and pre (AVp) volumes using biplane discs’ summation method and volumetric measurement by dedicated software (4D LA Analysis™, TomTec, 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: 3D 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 of 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 3D were also significant (Table).

LA reference values by 3DE vs 2DE
P2562 | BEDSIDE
Cardiot plaque neovascularization is independently associated with asymptomatic 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 previously shown that there were 9 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 risk in this ethnic group.

Methods: Initial plaque neovascularization (IPN) was assessed in 192 patients with history of one of the following coronary events: cardiac death, non-fatal myocardial infarction, unstable angina in 11). On multivariate Cox proportional hazards analysis, plaque echolucency (lower IBS) was the independent predictor of coronary traditional risk factors, whereas maxIMT was not (HR: 0.44 and 0.96, 95% CI 0.24 – 0.82 and 0.76 – 1.23, p <0.01, respectively). The addition of plaque echolucency to traditional risk factors improved net reclassification improvement (NRI) and integrated discrimination improvement (IDI: 0.59; p <0.05; and IDI: 0.075; P <0.05), while addition of maxIMT did not (NRI: <0.03; p<0.63, and IDI: 0.01, p=0.57).

Conclusions: Plaque echolucent but not maxIMT was an independent predictor of recurrent coronary events. Moreover, the addition of IBS of the carotid artery to traditional risks had additive value for prediction of coronary events. Thus, measuring coronary plaque echolucency of the carotid artery was useful for assessment of residual coronary risk in patients with history of MI after LDL-C goal attainment on statin treatment.

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 analyse impact of systemic hypertension (HTN) on RV function by tissue doppler echocardiography.

Methods and patients: 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 stage II HTN) according to JNC 7. All patients underwent echocardiography with use of GE Medical Vivid 7. RV global systolic function was assessed as tricuspid annular plane systolic excursion (TAPSE). The RV global filling measurement was determined as E and A waves through the maximum velocity during early and atrial filling phases, respectively.

Results: The study included 90 patients (54 males, 60%) with a mean age of 48.57±6.82. TAPSE measurements did not show any significant differences between the 3 groups (control, stage I HTN and stage II HTN) patients. Doppler data obtained at the 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 annulus in the control, stage I HTN vs. Stage II HTN we found statistically significant differences for S (14.97±0.81 vs. 12.37±0.72, 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±1.17 cm/sec respectively; p=0.018). Similarly significant values were found in a subgroup analysis between the 3 groups with LSD test.

Conclusion: This study revealed that HTN, and severity of HTN as well, significantly affects the systolic and diastolic function of the right ventricle by pulsed wave and tissue doppler echocardiography. Tissue Doppler echocardiography is a useful tool in detecting right ventricular systolic dysfunction even with normal TAPSE measurements.

P2565 | BEDSIDE
3-year outcomes after test with measuring coronary artery flow velocity reserve at the peak of exercise

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

Background: 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 after coronary artery flow velocity analysis during exercise tests.

Methods: There is a single center prospective cohort study of 242 consecutive patients who underwent a bicycle exercise echocardiography with the analysis of coronary artery flow velocity in left anterior coronary artery (LAD) in November 2011–February 2012. Coronary flow velocities were measured before and at the peak of exercise at the medium segment of the LAD. In addition, the coronary flow velocity reserve (CFVR) and the differences between the peak and rest velocities (ΔV) were calculated. Two hundred and thirteen patients had well visualized coronary flow in LAD during exercise. One hundred and seventy-eight patients were accessible for follow-up analysis (55.4±9.9 years, 116 men). Cardiac events (MACE) during the period after stress test was 3.0±0.1 years.

Results: There were 46 patients with MACE. One cardiovascular death, 2 non-fatal myocardial infarctions, 1 cardiac arrest occurred, and 44 revascularizations were performed. The group with MACE vs. the rest patients had a lower velocity in LAD at the peak of exercise (59±27 vs. 70±26 cm/s, p<0.04), ΔV (18±22 vs. 37±26 cm/s, p<0.0002), and CFVR (1.5±0.7 vs. 2.1±0.7, p<0.00001). The group with the most severe MACE – death, myocardial infarction, and coronary artery bypass grafting also had a lower velocity in LAD at the peak of exercise (70±26 cm/s, p<0.02), ΔV (11±17 vs. 36±26 cm/s, p<0.0002) and CFVR (1.3±0.4 vs. 2.0±0.7, p<0.00005) to other patients. Among the group with CFVR >2.0, 0% had myocardial infarction, death or coronary artery bypass grafting, and 1.7% patients had coronary artery stenting in others non-LAD arteries.
Conclusion: The analysis of coronary flow in LAD during exercise can be used as a predictor of 3-year outcomes.

P2566 | BEDSIDE
Resting myocardial deformation by 2D speckle tracking echocardiography predicts left ventricular functional improvement 12 months after myocardial infarction
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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 predicting 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 before aortic valve closure, global peak longitudinal and transverse strain (PLS and PTS) – including possible 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 >8%.

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 dimension, LV mass index) and 2D speckle tracking (global SLS, SLS, PTS, PLS, STSR, STS) 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 0.0002–0.0014) 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 PTS and LV enddiastolic volume can be helpful in the prediction of LV remodeling 12 months after MI.

P2567 | BEDSIDE
Prognostic value of transthoracic coronary flow reserve in medically treated patients with remaining non-culprit stenosis of intermediate severity after primary percutaneous intervention

Background: Current guidelines recommend culprit lesion treatment with primary PCI in the setting of ST-elevation myocardial infarction (STEMI), while decision about revascularization of non-culprit lesions should be done later and guided by objective evidence of residual ischemia.

Objective: The aim of the current study was to examine the prognostic value of transthoracic coronary flow reserve (CFR) in medically treated patients with 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 32±15 months. CFR was defined as the ratio between maximal velocity of diastolic coronary blood flow during maximal hyperemia and in rest, induced by i.v. infusion of adenosine (140mcg/kg/min), with the cut-off value of 2 for detection of significant stenosis. Based on CFR value, which was done in the first week of the hospitalization, patients were divided into two groups: Group 1 - CFR ≥ 2 (n=163) and Group 2- CFR<2 (n=31). Primary end-point was MACE, defined as a composite of cardiac death, stroke, non-fatal ACS, PCI or CABG by severity of the examined vessel.

Results: There were 30 events related to the examined vessel. In Group 1: 5 patients had PCI of examined stenosis and 1 patient had AMI. In Group 2: 16 patients had PCI of examined stenosis, 5 patients had by-pass surgery, 1 patient had AMI, 1 patient had cardiac death and 1 patient had stroke. CFR in Group 1 was significantly higher than in Group 2 (2.44±0.37 vs. 1.90±0.34, p<0.001, respectively). By Kaplan-Meier method, Group 1 had significantly higher MACE free survival in follow-up time compared to the Group 2 (96.3% vs. 22.6%, p<0.001, respectively). Furthermore, patients with CFR≥2 had a 31.4-fold increase in cardiovascular risk compared to patients with CFR<2 (95% CI: 12.7–77, p<0.001). Negative predictive value of CFR≥2 was 96.3%.

Conclusion: In patients with non-culprit coronary artery stenosis of intermediate severity and CFR<2, deferral of revascularization and continuation of the medical therapy, might be reasonable option since it is associated with good long-term clinical outcome.

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.

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), left ventricle segmental strain (GCS), global area strain (GAS), and global radial strain (GRS) were quantified by 3D STE. Receiver operating characteristic curves (ROC) were computed to determine optimal strain cutoff values to predict severe multi-vessel coronary stenosis. Observer reliability of our study employing 3D STE was assessed by independent, blinded observers.

Results: Ninety-two patients were enrolled and divided into the following three groups according to the CAG: control group (without coronary stenosis, n=37), severe single-vessel coronary stenosis group (one vessels 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 coronary stenosis group were more dramatically decreased (GLS: 2.92±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: 29.08±10.92 vs 44.43±14.42, p<0.001). Similar changes were also observed for all four 3D STE parameters in the severe multi-vessel coronary stenosis group compared to the severe single-vessel coronary stenosis group, whereas only GLS and GRS had statistically significantly decreased (p<0.05). Receiver operating characteristic curve analysis demonstrated areas under the curve of 0.87 for 3D GLS, 0.75 for 3D GCS, 0.82 for 3D GAS, and 0.81 for 3D GRS. An optimal 3D GLS 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 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 CMR DCE. Furthermore, we aimed to determine the ability of 3DSTE to differentiate between patients with ischemic and patients with non-ischemic LV dysfuction. A total of 120 consecutive patients with ischemic (n=80) and non-ischemic (n=40) LV dysfunction underwent CMR DCE for myocardial scar identification and 3DSTE for left ventricular (LV) strain.

DCE analysis revealed 157 segments with transmural enhancement, 668 segments with non-transmural enhancement, and 730 segments without enhancement. The correlations between 3DSTE global strains and either the total or the percentages enhanced LV mass were modest and for 3DSTE regional strains were poor. All 3DSTE regional strain values except for radial strain were lower in segments with compared to segments without transmural hyperenhancement. However, the sensitivity and specificity for all strains were insufficient to differentiate between segments with different percentage of scar nor to differentiate between ischemic and non-ischemic patients.

Conclusions: Global strain by 3D STE is useful to detect severe multi-vessel coronary stenosis, wherein GLS and GAS are more valuable indicators.

Segmental 3DSTE strain & hyperenhancement

<table>
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<th>Variable</th>
<th>Non-enhanced (%) (A)</th>
<th>Transmural (%) (B)</th>
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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
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 compared their protein expression profile to hearts from neonatal and adult mice.

Using two-dimensional in-gel electrophoresis, we found a cerebral overlap between the proteome from adult mouse and adult zebrafish hearts. Similarly, there was a degree of mismatch between the protein expression in neonatal and adult mouse hearts. Gene enrichment analysis of the selected proteins revealed overexpression of DNA synthesis–related proteins in the cardiac proteome of the adult zebrafish heart similar to neonatal and adult mouse hearts, whereas in hearts of adult mice there was a mitochondria–related predominance in protein expression. Importantly, we noted pronounced differences in the myoflament composition: the zebrafish heart has just a single ventricle and lacks many of the myoflament 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 myf5) was expressed in interacting cardiomyocytes, highly expressed in adult mouse hearts, 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 myofilament 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 measurement in the general population.

Methods: A total of 2,500 individuals from the general population (mean age 55±11 years, age range 35–74 years, 49% women) in the Gutenberg Health Study were measured circulating L-arginine and the arginine derivatives, N-monomethyl-L-arginine (NMA) and symmetric dimethylarginine (SDMA) in relation to peripheral pulse amplitude (PPA), brachial artery diameter and flow-mediated dilation (FMD). ADMA derivatives were quantified by liquid chromatographic-tandem mass spectrometry. PAT was assessed by the Endo-PAT2000 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-Arginime 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 0.070.0.12 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 critical limb ischemia is associated with altered oxidative status
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Background: Effective 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 the popliteal artery of 30 patients with critical limb ischemia (T2D+CLI-MPs) (n=6 H-MPs) and 30 patients without critical limb ischemia (healthy controls, T2D−CLI-MPs) (n=6 H-MPs) were analyzed. Perivascular MPs were immunolabeled (MPs), endothelial cells, and myocytes.

Results: T2D+CLI-MPs expressed typical pericyte markers like the healthy counterparts, but showed impaired proliferation (0.16±0.06 vs. 1.98±0.46 Units, p<0.01). No effect of T2D was observed on migration or fusion into β-Mosion Heavy Chain (β2-MHC). Moreover, T2D+CLI-MPs generated less VEGF, VEGF-C and VEGF-D. Furthermore, T2D+CLI-MPs displayed a reduced expression of Myogenin and MyoD. In addition, T2D+CLI-MPs impaired network formation (number of intersection/field: 10.40±1.39 vs 13.73±0.64, p<0.05 vs. H-MPs). Simi-
lar result was obtained treating HUVECs with T2D+CLI-MP-conditioned medium (11.88±1.04 vs 16±1.4, p<0.05 vs. HUVECs alone). These altered functions of T2D+CLI-MPs were associated with an imbalance in the cellular redox state involving altered expression of SOD-1 (0.53±0.11 vs 1.03±0.11), catalase (0.41±0.1 vs 0.97±0.2), and p68Hsc (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-MP alterations by antioxidant treatment suggests possible therapeutic targets for attenuation of peripheral complications.

P2574 | BEDSIDE
Determinants of accelerated vascular aging: results from the Cardiovascular Risk factors Affecting Vascular age (GRAVE) study
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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±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
Female vasculopathy 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 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-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 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 (2.50–2.80) pg/ml vs. 2.10 (1.80–2.60) pg/ml, p=0.63] and in RANTES levels [12.25 (8.35–17.70) 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 (1.35–9.45) pg/ml vs. 20.25 (2.40–47.52) pg/ml, P>0.58], in TNFα levels [2.10 (1.70–5.89) pg/ml vs. 3.27 (2.40–4.32) pg/ml, P=0.17] and in RANTES levels [13.09 (10.43–30.42) pg/ml vs. 12.25 (5.90–29.88) pg/ml, P=0.69].

Conclusions: High dose folic acid administration in an atherosclerotic model of apoE deficient mice has only a modest anti-inflammatory effect and cannot reverse the additve atherosclerotic stimulus of a diet rich in cholesterol. These findings further elucidate the effects of folic acid administration in subjects with increased cardiovascular risk.

P2576 | BENCH
Mevinolin 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 diabetic mortality and morbidity in complications and mortality rates. Several recent studies have demonstrated beneficial effects of biguanide metformin and DPP4-inhibitor vildagliptin on certain processes associated with reduced renal function in diabetes. Indeed, in our previous study vildagliptin attenuated routine renal dysfunction markers in insulinopenic diabetic rats. However, mevinolin 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 mevinolin and vildagliptin.
Methods: 3 weeks after unilateral nephrectomy, adult male Wistar rats were randomly divided into diabetic group (fed high-fat diet for 5 weeks and then successively received nicotinamide (NA, 230 mg/kg) and streptozotocin (STZ,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 mevinolin (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±0.2%). 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 mevinolin did not attenuate routine kidney dysfunction markers such as creatinine, creatinine clearance and albuminuria (61±2.9 μmol/min/kg, 25±4.8 mg/24h and 18.18±1.98 mg/24h respectively) compared to P group (65±3.6; 2.30±0.21; 38.8±2.5; P<0.05 each), urinary levels of KIM-1 (589±93.3 ng/ml) and NGAL (1544.9±100.6 pg/ml in mevinolin-treated animals were significantly lower than those in diabetic rats without treatment (KIM-1 1918±118.1; 1919±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 did attenuate routine markers of kidney injury, mevinolin 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 15-04-01838].
protozoan metagenomic analysis using the RIdTM Next Generation Sequencing (NGS) analysis system, and specific protozoan multiplex PCR probes were used to assess the presence and composition of biofilm populations.

**Results:** Bacteria were not detected in peripheral blood; however, 4 of 12 filters and 2 of 5 atheroma debris samples had identified bacterial populations (2 patients had atheroma debris and filter evaluated). Evidence of protozoan populations was obtained in 4 of 15 peripheral blood samples, 11 of 12 filters and 4 of 5 atheroma debris samples. Microscopy illustrated a complex composition of biofilm communities in blood, devices, and atheroma debris samples. The identified bacterial and fungal atheroma debris suggest a diverse and novel population composition. Biofilm dwelling bacteria, while present in several atheroma or filter samples, were not detectable in peripheral blood and were not universally present in atheroma or filter. Taxonomic comparisons of sequenced protozoa are consistent with a diverse array of organisms similar to poorly characterized environmenmental protozoa.

**Conclusion:** Of 15 patients, 6 patients had evidence of bacteria and 13 had evidence of protozoa in debris and all exhibited evidence of complex biofilm communities. This data suggests that biofilm forming protozoa may play a key role in arteriolar vascular disease.

**P2578 | BENCH**

Microplate-induced thrombin formation predicts severity of coronary artery calcification in patients with severe aortic valve stenosis

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**Background:** Thrombin, the central pro tease of the coagulation cascade exerts proinflammatory effects potentially involved in the progression of atherosclerosis. Recently, thrombin generation was shown to be associated with coronary artery calcification itself suggesting the formation of microparticles (MPs) from endothelial cells and various blood cells, including platelets.

**Hypothesis:** Procoagulant activity of circulating MPs mediates CAC via enhanced thrombin formation.

**Methods:** In a cross-sectional study of 55 consecutive patients with severe aortic valve stenosis (AS) who were referred for transcatheter aortic valve implantation (TAVI), we assessed CAC and aortic valve calcification (AVC) by 128-row computed tomography. Patients with CAC Score above the median.

**Results:** Procoagulative activity of circulating MPs was assessed using a two-step amidolytic assay for thrombin formation. Patients with CAC Score above the median.

**Conclusion:** Procoagulative activity of circulating MPs mediates CAC via enhanced thrombin formation.

**P2580 | BENCH**

Evaluation of the immunomodulatory properties of cardiac adipose tissue progenitor cells: a step towards their use in cell-based cardiac regeneration

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**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-derived mesenchymal stem cells (UCMSCs) 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 (IL-6, TNFα and IFNγ) was also specifically modulated by the different numbers of cardiac ADTPCs co-cultured (Figure 1).

**Conclusions:** 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 intravascular coagulation (DIC) and vascular function in LPS-induced endotoxemia

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**Objective:** Sepsis causes disseminated intravascular coagulation (DIC) and severe hypotension, accompanied by high mortality in the setting of septic shock. Inhibition of dipeptidyl peptidase 4 (DPP4) and supplementation with glucagon-like peptide 1 analogues (GLP1a) are new therapeutic approaches in diabetes. There...
is a growing body of evidence for an immunomodulatory effect by DPP4i therapy and GLP1a supplementation. With the present study we investigated whether DPP4i and supplementation with GLP1a may improve sepsis associated vascular complications and disseminated intravascular coagulation.

**Methods:** C57BL/6, DPP4−/− and GLP-receptor−/− mice were used. DPP4i (linagliptin) and GLP-1a (ligandluide) were applied s.c. Sepsis was induced by lipopolysaccharide (LPS) injection. Fluorescence-based imaging technique was used to detect microvascular coagulation in lungs. Vascular function was tested by isometric tension recording. Aorta and heart tissue was used for Western blotting and RT-PCR. 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 reduced by DPP4i. This was confirmed by GLP1a and DPP4 inhibitory effects in platelet-rich plasma (PRP), cell count and quantification of oxidative stress were tested. Echocardiography (2DE) longitudinal strain in subjects with dilated AscAo (21mm/m²).

**Background:** Inflammation and inflammatory cells play a vital role in tissue repair process and in defence against infectious agents, yet an unresolved immunomodulatory effect by DPP4i therapy and GLP1a supplementation may be important in the development of hypertension. We assessed levels of aging-associated signalling molecules in arteries from stroke-prone spontaneously hypertensive rats (SHRSP) and Ach1 knockout mice infused with aldosterone (300μg/kg/day). Gene expression was evaluated by qPCR and protein levels by immunoblotting. Aldo levels were quantified by ELISA. In SHRSP rats, mRNA levels of Nox1 (4 fold), aging-associated inflammatory markers, such as RANTES (5 fold), MCP-1 (6 fold) and IL-6 (2 fold); as well as ald levels (6-fold), H2A.Z (marker of aging-associated DNA damage ~1.5-fold) and cell cycle inhibitors, P27 (2-fold) and P21 (4-fold), were increased compared with control rats (WKY), p < 0.05. In cultured vascular smooth muscle cells (VSMCs) from WKY and SHRSP rats, basal activation of P66Shc (pro-senescence) was increased in SHRSP (2.8-fold, p < 0.05). Aldo stimulation increased P66shc phosphorylation in WKY (3.1-fold) and SHRSP (2-fold); an effect that was blocked by ML171 (Nox1 inhibitor). In mice treated with ald, activation of JNK (pro-inflammatory ~69%) and p66Shc (92%) was increased in mesenteric arteries (p < 0.05); an effect blunted in vessels from Nox1 KO mice. In VSMCs from aged control mice, and adult Nox1 transgenic mice (VSMC specific overexpression) basal levels of p66Shc (39%) and OGG-1 (48%), markers of senescence, were increased compared to VSMCs from control adult mice. Aldo effects on p66Shc activation were enhanced in VSMCs from adult Nox1 transgenic mice. In conclusion, ald induces vascular damage through Nox1-p66Shc-dependent mechanisms and modulation of pro-aging responses, which may be important in the development of hypertension.

**VASCULAR REMODELLING**

**P2584 | BEDSIDE**

Effect of diltiazem ascending aorta on LV deformation mechanics. A 2D speckle tracking echocardiography study

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It has been recently shown that aneurysmal ascending aorta (Ascao) exhibit increased stiffness, but their effect on the left ventricle has not been studied yet. Diltiazem (3.8%) and propranolol (8%) were used in this study. The results showed that ventricular function was improved, but not sufficient to change the stiffness of the aortic valve.

**Background:** We have previously shown that diltiazem improves LV function in patients with diastolic dysfunction, and that the improvement is associated with reduced stiffness of the ascending aorta. We hypothesized that diltiazem may also improve LV systolic function, and that this effect is associated with reduced stiffness of the ascending aorta.

**Methods and results:** Patients with aortic stenosis (AS) were recruited from a tertiary referral center. All patients underwent echocardiography and cardiovascular MRI. The primary endpoint was the change in LV systolic function, as assessed by 2D speckle tracking echocardiography. The secondary endpoints were changes in LV geometry, stiffness, and fibrosis.

**Results:** The primary endpoint was met in all patients. The left ventricular ejection fraction increased from 48.6±2.6% to 52.3±2.8% (p<0.05). The left ventricular mass index decreased from 105.8±14.2 g/m² to 98.9±13.0 g/m² (p<0.05). The mean gradient across the aortic valve decreased from 40.3±12.7 mmHg to 32.5±10.8 mmHg (p<0.05). The stiffness index decreased from 3.9±1.2 kPa to 3.3±0.9 kPa (p<0.05). The fibrosis index decreased from 0.7±0.2 to 0.5±0.1 (p<0.05).

**Conclusion:** These results suggest that diltiazem improves LV systolic function and reduces stiffness of the ascending aorta in patients with aortic stenosis. This effect is associated with reduced fibrosis and improved LV geometry.

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**P2583 | BENCH**

Premature vascular aging in aldosterone-associated hypertension: role of Nox1

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Endothelial dysfunction, vascular remodelling and pro-inflammatory responses are hallmarks of vascular injury during hypertension and aging. Vascular alterations in young hypertensive patients resemble those in aged individuals, suggesting that in hypertension, vessels undergo premature aging. Elevated reactivity to angiotensin II (ANG) and elevated expression of angiotensin (ANG) in platelet-rich plasma (PRP), cell count and quantification of oxidative stress were tested. Echocardiography (2DE) longitudinal strain in subjects with dilated AscAo (21mm/m²).

**Methods and results:** Patients with aortic stenosis (AS) were recruited from a tertiary referral center. All patients underwent echocardiography and cardiovascular MRI. The primary endpoint was the change in LV systolic function, as assessed by 2D speckle tracking echocardiography. The secondary endpoints were changes in LV geometry, stiffness, and fibrosis.

**Results:** The primary endpoint was met in all patients. The left ventricular ejection fraction increased from 48.6±2.6% to 52.3±2.8% (p<0.05). The left ventricular mass index decreased from 105.8±14.2 g/m² to 98.9±13.0 g/m² (p<0.05). The mean gradient across the aortic valve decreased from 40.3±12.7 mmHg to 32.5±10.8 mmHg (p<0.05). The stiffness index decreased from 3.9±1.2 kPa to 3.3±0.9 kPa (p<0.05). The fibrosis index decreased from 0.7±0.2 to 0.5±0.1 (p<0.05).

**Conclusion:** These results suggest that diltiazem improves LV systolic function and reduces stiffness of the ascending aorta in patients with aortic stenosis. This effect is associated with reduced fibrosis and improved LV geometry.

**ACKNOWLEDGEMENT/FUNDING:** partly funded by HD Leducq.
LVGLS is supranormal in pts with dilated AscAo, despite normal LVEF and the absence of more than mild aortic regurgitation, possibly as a result of increased afterload which is due to the stiff, dilated aorta. Deformation mechanics of the LV gives us valuable insight into the pathophysiologic interaction of the left ventricle and the aorta.

P2585 | BEDSIDE
CMR assessment of arterial stiffness in patients with large vessel vasculitis
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Background: Large-vessel vasculitis (LVV) is often characterized by increased arterial 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 arterial 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 Wegener granulomatosis and 8 with other systemic associated disease 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 aortic valve surgery, and heart failure hospitalization. Mean aortic PWV was 10.3±4.3 m/s; PWV was highest in patients with polymyalgia rheumatica and lowest in those with Takayasu arteritis. After a mean follow-up time of 760 days (SD, 559 d), major cardiovascular events occurred in 50 patients (27.3%). In a multivariable Cox regression model, aortic PWV and diabetes mellitus were independent predictors of major cardiovascular events (odds ratio, 1.10 [95% CI, 1.01–1.18]; P=0.04; and odds ratio, 2.03 [95% CI, 1.04–3.97]; P=0.04, respectively). Patients with PWV >10 m/s had a higher incidence of cardiovascular events than those with PWV <10 m/s (log rank P=0.007).

Conclusion: CMR-derived aortic PWV is a powerful independent predictor of major cardiovascular events in patients with LVV.

P2586 | BENCH
Role of sildenafil in the recruitment of hematopoietic progenitor cells in hypoxia-induced pulmonary hypertension
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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, sustaining 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 hypoxia (CH) or normoxia (N, n=12). CH increased RVSP (46.2±6.3mmHg) and MWT (37.2±0.5%) compared to N (24.8±1.6mmHg and 24.6±0.9%, respectively), but sildenafil reduced these values to 34.5±1.4 mmHg and 30.4±1.6%, respectively. CH increased plasma SDF-1 and EPO by 1.4-fold and 2.4-fold compared to N (P<0.001) in pulmonary arteries adventitia by 5-fold (P<0.001) and 8% (P=0.001) and 8% (P=0.001) and 8% (P=0.001) and 8% (P=0.001) and 8% (P=0.001) and 8% (P=0.001) and 8% (P=0.001).

Results: Even in the absence of exogenous aldosterone, spironolactone, eplerenone and MR silencing ameliorated phosphate-induced osteogenic transformation of HAoSMCs. Sildenafil stimulated aldosterone synthase (CYP11B2) expression and MR activation in the absence of exogenous aldosterone in HAsMCs. Increased expression of CYP11B2 was observed in aortic tissue of hyperphosphematic k/kii mice. In right coronary artery tissue of patients with reduced and maintained renal function, CYP11B2 mRNA expression was correlated with CFBAI mRNA levels. In HAoSMCs, silencing of CYP11B2 ameliorated phosphate-induced osteogenic reprogramming and calcification. Phosphate treatment induced nuclear export of the transcriptional repressor APEX1. Silencing of APEX1 upregulated CYP11B2 expression and mimicked the effects of phosphate in HAoSMCs. Spironolactone treatment abrogated the effects of APEX1 silencing on osteoinductive transformation without modifying increased CYP11B2 expression in HAoSMCs. Conversely, APEX1 overexpression reduced phosphate-induced HAoSMCs transformation. Early stage aortic osteoinductive reprogramming of k/kii mice following discontinuation of dietary rescue was ameliorated by spironolactone treatment, but not by adrenalectomy. In the adrenalectomized k/kii 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 senescent-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 endothelial dysfunction and atherogenesis. But the molecular basis of which is not fully defined. We have recently 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 during passages. Briefly, PDLs was computed as Log2 (Ct/C0), where C0 was the number of viable cells at harvest and Ct was the number of cells seeded. PDL and 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 about 15 days. We also found that telomerase activity was dependent on APEX1 silencing of miR-216a level, which confirms a crucial role for miR-216a in regulating HUVEC senescence. To further analyze the effect of miR-216a on endothelial functions, we tested the cell proliferation, migration, adhesion, and tube-formation abilities. The results showed that miR-216a overexpression accelerated the decline of endothelial functions at about 15 days, which led to a significant inhibition of endothelial proliferation and migration by 15% (P<0.001) and 8% (P<0.001) and 8% (P<0.001) and 8% (P<0.001) and 8% (P<0.001) and 8% (P<0.001) and 8% (P<0.001) and 8% (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.
Deregulation of thioredoxin system contributes to monocyte dysfunction in diabetes mellitus: Implications for impaired arteriogenesis in type 2 diabetic patients


**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 (Trx1 and Trx2) and Trx-interacting protein (Trxip) were detected by using qPCR and WB. Activities of protein tyrosine phosphatase (PTP) and Trx were measured in the monocyte cytosol. 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 the mouse xenograft assay in a murine model. Hindlimb perfusion in db/db and WT mice with unilateral hindlimb ischemia (HILI) receiving TMP or placebo was determined.

**Results:** DM led to significant downregulation of Trx1/2 and an upregulation of Trxip in monocytes. Likewise, Trx 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 VEGF1 signal transduction defect. Blockade of Trx activity by pharmacological inhibitors in normoglycemic (non-diabetic patients and Wt mice) and hyperglycemic (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 Trx system contributes to altered signaling responses in activated vascular cells in vitro and in vivo. This study suggested that restoring Trx activity might improve monocyte function and help to reverse arteriogenesis defects seen in DM patients.

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Ctr. with 13±3 collagen/lmuscle (n=8, p<0.05). In addition, a significantly lower perivascular monocyte infiltration revealed to the arteriocytes 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 86±134 capillaries/mm² vs. Ctr 34±134 capillaries/mm² (n=6, P<0.01) in the lower limb. This results for an inadequate blood supply because of less collateraliization within the upper limb. In clinical score, the reduced revascularization confirmed after ligature in the aPC-high group. CTR. 1.3 vs. 3.7 aPC-high on day 7. Over the time clinical outcome between the groups was more substantial (day 14; CTR. 1.17±1 vs. 3.4±1 (P<0.01) and day 21 (0.17±3 vs. 3.7±1 aPC-high (P<0.05, n=6). In our experiments of activated protein C has an inhibitory effect on arteriosclerosis. This results for an inadequate blood supply because of less collagen 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

P259 | 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 underlying pathologies including Marfan syndrome (MS).

Methods: We searched our database from 2014 backwarks 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). Ascending aortic 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 matrix. 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 adjustment 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 MS and AS patients, without a statistically significant difference between the two pathologies (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.

P259 | 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 established risk factor for cardiovascular disease. Dietary ferric reducing antioxidant power (FRAP) has been suggested to reflect the overall antioxidant capacity of a diet, while uric acid (UA) and gamma glutamyltransferase (GGT) have been suggested to play a role in low-grade chronic inflammation.

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 frequency questionnaire. UA and GGT were assessed at baseline. High sensitivity C-reactive protein (hs-CRP) was assessed at baseline and 10 years later, whereas adiponectin, leptin, plasmogen 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), associations 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; 0.23) and PAI-1 (β=0.09, 95% CI: 0.03; 0.14) whereas no association was observed 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.

P259 | 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 clinical 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 total mass.

Purpose: Establish a novel index describing the quality of adipose tissue by quantifying the expression of femoral AT (FemAT), and linking it with vascular function and systemic oxidative stress.

Methods: FemAT thickness was measured by U/S in 185 pts undergoing coronary bypass surgery (CABG), and defined as the average AT thickness at the anterior 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 oxidative stress marker, was measured in plasma and FemAT culture supernatants. Brachial flow mediated dilation (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 information on AT and systemic inflammation, predicting vascular function in human atherosclerosis. This new marker of adiposity partly explains the “obesity paradox”, 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 receptor of the innate immune system recognizing RNA. How TLR3 is activated in response to 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 Toll-like receptors (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 used in a transfection assay. Furthermore, TLR3 activation was measured upon SWT of human umbilical vein endothelial cells and cardiovascular human atheroma.

Conclusions: Mixtures of LL37 and RNA were not able to activate TLR3 reporter cells. However, LL37/RNA complexes were able to activate TLR3 reporter cells. This effect could be blocked by the TLR3 inhibitor TAK-242. These results suggest that LL37/RNA complexes are able to activate TLR3, which might be relevant in the context of shock wave therapy.
were treated with RNAse and protease. 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 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=0.0001). Analysis of the supernatant revealed increased RNA levels (CTR 21±2.44 vs. SWT 37±1.5, p=0.0174). The effect could not be abolished by pre-treatment of the supernatant with RNAse but only by a sequential digestion with proteinase and RNAse hinting strongly towards the involvement of protein/RNA complexes. Indeed, LL37 expression was significantly increased after SWT. LL37/RNA complexes could be visualized after staining with anti-LL37. Cellular RNA uptake was significantly increased after SWT (CTR 31.67±28.17 vs. SWT 19757±1054, p=0.0001). Treated muscles of C57BL/6 mice showed significantly increased expression of LL37. Finally, SWT resulted in significantly higher numbers of capillaries (SWT 1262 vs. CTR 461, p=0.001) and arterioles (SWT 461 vs. CTR 160.5, p=0.001) and improved limb perfusion (SWT 0.74±0.01 vs. CTR 0.486±0.01, p=0.021) in treated muscles.

**Conclusion:** TLR3 activation upon SWT is mediated via the release of LL37. The antimicrobial peptide forms complexes with extracellular RNA and can thus stimulate innate immune processes. We have evaluated the mechanism behind the previous findings and analyzed cardiac lymphatic organization and cardiac function.

**Methods:** Mice expressing soluble sVEGFR3 were crossed with atherosclerotic mouse models increases circulating cholesterol levels, alters lymphatic vessel development and reduces the amount of lymphatic vessels in atherosclerotic lesions. Here we evaluate the mechanism behind the previous findings and analyzed cardiac lymphatic organization and cardiac function.

**Results:** In our previous study, we showed that the expression of soluble VEGF332 decoy receptor in an atherosclerotic mouse model increases circulating cholesterol levels, alters lymphatic vessel development and reduces the amount of lymphatic vessels in atherosclerotic lesions. Here we evaluated the mechanism behind the previous findings and analyzed cardiac lymphatic organization and cardiac function.

**Conclusion:** Our data indicated that inflammatory cytokines, IL-6 modulates angiogenesis through bone marrow cells activation, resulting in promoting neovascularization. The modulation of IL-6 might be a potential target for treatment for the patients diagnosed as arteriosclerosis obliterans.

**Objectives:** We have reported on right ventricular (RV) remodeling prior to the plethoriferm 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 cultured with HPAECs and incubated under hypoxic conditions (37°C, 1% O2, 9% CO2 for 72 h or without SU-5416 for 72 h). The mRNA expression of VEGF, VEGF receptor, ERK and BNP, and the cell viability were measured using real-time RT-PCR and WST-8. After echocardiography, heart was excised and fine structure was examined by electron microscopy and immunohistochemistry.

**Results:** mRNA expression of VEGF, VEGF receptor, ERK and BNP were significantly decreased in HPAECs cultured with SU-5416 compared with control and V+Hypo groups. In addition, male sVEGFR3 x LDLR−/−/ApoB100/100 mice had less liver steatosis and smaller adipocytes than control mice. The organization of cardiac lymphatic vessels was altered significantly in sVEGFR3 x LDLR−/−/ApoB100/100 mice when compared to controls. However, abnormal lymphatic vessels ceased only a slight increase in diastolic volume and cardiac mass in female sVEGFR3 x LDLR−/−/ApoB100/100 mice. In conclusion, even though the organization of cardiac lymphatic vessels is altered in these mice, it does not seem to affect the functionality of the heart.

**Conclusion:** Delayed overexpression of vascular endothelial growth factor in the right ventricular myoccardium accelerates irreversible cardiac remodeling in pulmonary arterial hypertension.

**Methods:** We have reported that expression of soluble VEGF332 decoy receptor alters lipid accumulation and changes cardiac lymphatic vessel organization in mice. We have evaluated the mechanism behind the previous findings and analyzed cardiac lymphatic organization and cardiac function.

**Results:** Expression of sVEGFR3 decoy receptor increases plasma cholesterol levels possibly by affecting lipid accumulation.

**Conclusion:** 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 differentiation to form new 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 increased in WT mice.

**Conclusion:** In addition to these investigations, we performed transplantation bone marrow cells collected from femur and tibia of WT mice to KO mice, as recipient. On the other hand, SWT is known to promote bone marrow cell migration to the sites of injury and to the ischemic limb. We used SWT and analysed bone marrow cell migration to the ischemic limb using the transgenic mice expressing enhanced green fluorescent protein (EGFP).
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 TF, αTF and miRNA126 under normal conditions. The treatment with TNFα for 2h and 6h reduced the expression of miRNA126 and induced mRNA expression of αTF and αTF (p<0.05). The αTF and αTF mRNA expression was increased 24h post stimulation with TNFα. The μTF isoform expression and the miRNA126 mimic for 24h significantly reduced the IF and αTF protein expression compared to the transfection with the co mimics and inhibitors. 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 TF isoform expression under normal and inflammatory conditions, thereby regulating endothelial thrombogenicity.

**P2601 | BENCH**

**CD14+CD16+ patrolling macrophages 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 inflammatory mediators. Macrophages 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 Wnt-signaling pathway.

**Purpose:** The aim of this study was to investigate whether macrophages observed in atherosclerotic lesions express LRP5 and whether expression is associated to a subset of monocyte/macrophages.

**Methods:** Magnetic cell sorting with CD16 monoclonal antibodies was used to separate macrophages from healthy individuals yielding highly purified populations of CD16- and CD16+ monocytes, corresponding to M1 and M2 macrophages, respectively. LRPS 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 LRPS expression is significantly increased in human M2 macrophages derived from patrolling CD14+CD16+ monocytes and not derived from classical CD14++CD16− monocytes. Circulating monocytes from WT mice also show increased expression of LRPS in CD11+GR1-low monocytes, the mice equivalent for human patrolling macrophones. M2-high-LRPS-expressing macrophages secrete anti-inflammatory cytokines as opposed to M1-low-LRPS-expressing macrophages that secrete large amounts of proinflammatory cytokines supporting an anti-inflammatory role for the M2/LRPS+ macrophage subset. LRPS 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. LRPS-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 LRPS suggesting that M2 macrophages in advanced atherosclerotic plaques trigger the anti-inflammatory, defective and repair response through LRPS signalling.

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**P2602 | BENCH**

**TGFβ1 signaling as modulator of endothelial-to-mesenchymal transition during chronic thromboembolic pulmonary hypertension**

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**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 thrombofibrotic pulmonary artery remodelling are largely unknown.

**Purpose:** To investigate the role of TGFβ2 released from activated platelets, during CTEPH and to determine whether it may promote pulmonary fibrosis via endothelial-to-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 are ex vivo 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 (SMA, 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 a few of the known TGFβ receptors (i.e. TGFβRII, ALK1, 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-SD2A2 and phospho-SMAD2 indicating active TGFβ signaling. qPCR and immunohistochemical expression analysis suggested that activation of TGFβ signaling occurs primarily through TGFβ1 or BMPs (BMP2 and BMP4), whereas TGFβ3 or the TGFβ antagonists BMP7 were not detected. To study the chronic remodelling response following thrombus and venous thrombosis and the role of TGFβ1 in disease, mice with platelet-specific TGFβ1 deletion (P4.Cre x TGFβ1fl/flR2Ox) 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 TGFβ1-induced signalling events in endothelial cells and myofibroblasts may enhance post-thrombotic fibrosis in CTEPH by promoting EndMT.

**P2603 | BENCH**

**Fish oils, eicosapentaenoic acid and docosahexaenoic acid, attenuate oxidative stress-induced DNA damage in vascular endothelial cells**

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**Background:** Accumulative evidence has suggested that omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are effective in the prevention of coronary artery disease (CAD). Some progeroid syndromes caused by genetic DNA repair deficiency present the early onset of atherosclerosis, which suggests that DNA damage plays a causative role in its pathogenesis. We have previously reported the presence of DNA damage in atherosclerotic lesions.

**Purpose:** To clarify the mechanisms whereby EPA and DHA prevent CVD, we investigated the effects of EPA and DHA on DNA damage in human endothelial cells.

**Methods and results:** We examined the effect of EPA and DHA on H2O2-induced DNA damage response in human aortal endothelial cells (HAECs). HAECs were treated with EPA or DHA for 4h prior to H2O2 (100μM) exposure for 15 min. DNA damage was detected by immunofluorescence staining as a cytologically visible “foci” using an antibody against the phosphorylated form of the histone H2AX (γH2AX). H2O2-induced γH2AX foci formation was significantly reduced in HAECs treated with EPA (30%; 30 min and 47%; 24 h incubation after the H2O2 exposure) and DHA (27% and 48%, respectively). H2O2-induced phosphorylation of ATM, a major player for the DNA damage response, was significantly reduced with EPA and DHA treatment (31% and 33%, respectively). These results suggested that EPA and DHA have protective effects on DNA damage rather than promoting DNA repair response. Thus we examined the effect of EPA and DHA on reactive oxygen species (ROS) production in HAECs. Chloromethyl-2′,7′-dichlorodihydrofluorescein 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 the effect of EPA and DHA on ROS production on reactive oxygen species (ROS) production in HAECs. Chloromethyl-2′,7′-dichlorodihydrofluorescein 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 the effect of EPA and DHA on ROS production on reactive oxygen species (ROS) production in HAECs.

**Conclusions:** 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 with no specific therapy available up to date.

**Purpose:** The present study investigates the role of the osteogenic transcription factor Runx2 as a potential mediator and therapeutic target of aortic fibrosis and aortic stiffening in diabetic monkeys.

**Methods and results:** Using a murine model of type 2 diabetes (db/db mice) we identify progressive structural aortic stiffening (by pressure myography; Figure 1) that precedes the onset of arterial hypertension. At the same time, Runx2 is aberrantly upregulated in the medial layer of db/db aortae as well as in thoracic aortic samples from type 2 diabetic patients. Vascular smooth muscle-specific overexpression of Runx2 in transgenic mice increases expression of its target genes, Col1a1 and Col1a2, leading to medial fibrosis and aortic stiffening. Interestingly, increased Runx2 expression per se is not sufficient to induce aortic calcification. Using in vivo and in vitro approaches, we further demonstrate that Runx2 expression in diabetes is regulated via a redox-sensitive pathway that involves a direct interaction of NF-E2 with the Runx2 promoter.

**Figure 1. Pressure-diameter curves; +/db ctr**

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**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 CaCl2-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 inflammatory independent of the increase in circulating glucagon-like peptide-1 level.

We investigated the incretin-independent effect of a DPP4 inhibitor, vildagliptin on monocyte inflammation and vascular remodeling in murine aorta induced by CaCl2.

**Methods:** The effects of vildagliptin were investigated in a monocyte cell line, U937 cells. The expression of DPP4 in U937 was knocked down by siRNA. As a model of inflammatory vascular remodeling, CaCl2-induced abdominal aortic dilation was used. After application of 0.5 M CaCl2 to the infrarenal aorta, then mice received oral vildagliptin (30mg/kg/day, n=10) or a vehicle (n=10) for six weeks.

**Results:** In vitro experiments, induction of interleukin-6 by lipopolysaccharide in U937 cells was suppressed by vildagliptin alone (20M-2μM). In addition, silencing of DPP4 in U937 cells by specific siRNA suppressed the production of interleukin-6 by lipopolysaccharide (62% reduction compared to scramble siRNA). The addition of vildagliptin to lipopolysaccharide-stimulated U937 cells was accompanied by suppression of MAPK phosphorylation both of ERK and p38. In vivo experiments, the expression of DPP4 in abdominal aorta was strikingly increased at 6 weeks after application of CaCl2. Then, vildagliptin significantly attenuated aortic dilation (external diameters; 1.1±1.06 mm [CaCl2] vs. 0.95±0.05 mm [CaCl2-vildagliptin] by 0.64±0.02 mm [Saline], p<0.05, respectively). Histological analysis showed that the recruitment of macrophages into media and adventitia in CaCl2 group was significantly greater than that in vildagliptin group (3.3±5.2 cell/μm² vs. 1.2±5.2 cell/μm², 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.

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**Conclusion:** Vildagliptin suppressed inflammatory response through suppressing MAP kinase pathways in monocyte and may ameliorated vascular remodeling, partly independent of incretins.

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**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 reaction (RT-PCR) reaction after 8 hour of VICs stimulation.

Calcification was measured using Alizarin Red S staining after 14 days of culture in osteoblastic medium containing lactic acidophosphate, 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 Ang I and 5.6-fold and 4.9-fold, respectively for Ang II (all p<0.01). Furthermore, calcification of cultured VICs was 5.8-fold and 8.3 fold higher after Ang II and AngI, respectively (p<0.01) stimulation. No changes in ACE and AT1R mRNA expression after Ang I 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 leaflets partially via AT1R.

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**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
planimetry on MDCT and combined with Doppler hemodynamics to obtain the fusion AVAi. The group of patients with normal flow had significantly larger AVAi and LVOT area index compared with the low flow group. Although the MDCT-derived LVOT area index was comparable between the 2 groups, the fusion AVAi was significantly larger in the normal flow group. By using the fusion AVAi, 52% (n=24) of patients with normal flow and 12% (n=5) of patients with low flow would have been reclassified into moderate AS due to low gradient and AVAi ≥ 0.6cm²/m². 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 remained severe with low gradient.

Conclusion: In patients with low gradient severe AS with echocardiographic AVAi <0.6cm²/m² and preserved LVEF, fusion AVAi evaluation permits reclassification to true moderate AS in 52% of the normal flow and 12% of the low flow patients.

P2609 | 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 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 this indication.

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 after failure of surgical ring annuloplasty. All patients were evaluated by a multidisciplinary heart team as high or extreme risk for redo-surgery and underwent MSCT and TEE evaluation prior to the procedure. Annuloplasty rings were semi-rigid in all 3 cases and valve sizing was based on MSCT measurements: 1) St. Jude Seguin 34mm, perimeter 86.1mm, 29mm DFM; 2) Edwards Physio 30mm, perimeter of 75.6mm, 27mm DFM; 3) Medtronic CG Future 26mm, perimeter 65.8mm, 25mmDFM. All cases were performed via the transapical approach with a 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 responsive and retrievable valve within a failed mitral annuloplasty ring with excellent acute hemodynamic outcomes.

P2610 | 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%) preoperatively treated with medically intravenous severe angina preoperatively.

Results: The MR degree was promptly reduced in 22 patients (43.1%) postoperatively, in association with a significantly less rate of in-hospital treatment for cardiac failure long-term, compared with the 29 patients that showed residual mild or more MR postoperatively (P=0.01). One or more of the preoperative factors 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 indicated to be a predictive factor in reversibility of functional MR after isolated CABG.

Conclusions: Sustained objective functional benefits at 12 months are obtainable in patients with severe symptomatic mitral regurgitation who undergo transcatheter edge-to-edge mitral valve repair.

P2611 | 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 mitral (MGM) or the systolic pulmonary artery pressure (SPAP) are increased up to 15mmHg and 60mmHg at peak stress, respectively. 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 I-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 table of stress echocardiography. In no dyspneic patients, the MGM was >15 mmHg and SPAP >60 mmHg in respectively 99.1% and 66.1% of the peak of the effort, reflecting the low specificity of the tests with these values. At the peak of the effort, the optimal thresholds are 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 highlight 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 33.5mmHg 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
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**Background:** Atrial fibrillation (AF) is common in patients with degenerative mitral regurgitation (DMR) due to mitral valve prolapse, associated with atrial remodeling and worse outcome. However, the impact of AF on mitral annular morphology and implication in repair strategy remain unclear.

**Purpose:** To test the hypothesis that mitral annulus of DMR patients with AF has significant morphological differences from that in patients with sinus rhythm (SR).

**Methods:** A total of 34 subjects including 24 patients with 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) transesophageal echocardiography. The 3D geometry of mitral valve was measured with custom software. Left atrial maximal volume was measured by 3D transesophageal 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; 67 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 atrial peak systolic strain (all P<0.05) (Table). There were no differences in regurgitant volume, left ventricular volumes and ejection fraction between DMR-SR and DMR-AF groups (P>0.05).

**Conclusions:** In patients with severe DMR, AF is associated with more severe left atrial remodeling and dysfunction, causing more severe atrial flattening and dilatation. These findings imply that restoration of annular saddle shape with annuloplasty may be more important in DMR patients complicated by AF.

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P2611 | BEDSIDE
Mitralclip 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. Cathereter-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±2 y, 72% males, LVEF 31±9%, NYHA III 91%, Euroscore II 19±14%) and 56 matched patients (Heartport; age 76±4 y, 57% males, LVEF 31±7%, NYHA III 91%, Euroscore II 13±12%) with severe systolic heart failure and significant FMR underwent implantation of Mitraclip or Heartport mitral valve annuloplasty. Median follow-up was 1.9 years (IQR 0.5–1.5 years).

**Results:** Incidence of life threatening peri-procedural 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: +2±9% vs +1±14%; 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 (>30%) have poor prognosis regardless of treatment strategy and these patients should not undergo mitral valve repair.
the two groups (NYHA > II: 48.9% vs. 49.9%, p=0.648). Patients with AF had more frequently a Wilkons score >8 (51.4% vs. 30.9%, p<0.001), a larger left atrium (41 cm² vs. 32 cm², p<0.001) and a lower transmirtal gradient (11.1 mmHg vs. 16.6 mm Hg, p<0.001).

BMV was equally successful in the two groups (90.6% vs. 94%, p=0.187) but resulted in a smaller post BMV area (2 cm² vs. 2.15 cm², p<0.012) with a lower mitral valve area gain (0.9 cm² vs. 1.0 cm², p=0.015). BMV was not associated with a higher risk of complications (4.3% vs. 4.7%, p=0.844).

After a mean follow-up of 74 months, patients with AF had the same rate of complications including death, restenosis, systemic embolism and mitral valve replacement were: 68.8%, p=0.047).

One hundred and forty patients (18.3%) had LVEF ≥ 40%, 66% had 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 between EF or MTG over 40 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 symptomatic limitted 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 or MTG x systolic pressure) and higher peak-rest transaortic mean gradient difference (AMG). At multivariate analysis, only AMG resulted independently associated with impaired functional capacity (p=0.048; CI 1.001–1.323).

Conclusions: AS patients can present functional impairment which is related to cardiac response to exercise rather than to stenosis severity. These results suggest the role of inotropic and contractile reserve supporting the routine evaluation of cardiac reserve as a determinant of symptoms development.

P2619
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
P2620 | BEDSIDE
Serial NT-pro-B-type natriuretic peptide measurements after transcatheter aortic valve replacement: diagnostic and prognostic value for mortality, cardiac decompensation and cardiac regression
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Background: The serum level of NT-pro-B-type natriuretic peptide (NT-proBNP) is related to the severity of both valvular aortic stenosis and chronic aortic regurgitation. In this context patients with elevated preoperative NT-proBNP levels show a higher postoperative morbidity (e.g. NYHA class, heart insufficiency) and mortality after aortic valve replacement and after transcatheter aortic valve replacement (TAVR).

Purpose: The aim of the present study is to examine the serial changes and the prognostic significance of NT-proBNP in a large cohort of patients undergoing TAVR within a long-term follow-up.

Methods: Consecutive patients (n=503) undergoing TAVR were included. NT-proBNP levels were measured prior to and directly after the procedure, 4, 24, 48, and 72 hours afterwards, and 6 days afterwards. Patients were followed for 1 year. Patients who died within 10 days after TAVR or for whom a blood sample at one of the time points was missing were excluded.

Results: All patients included (n=423) had elevated NT-proBNP levels at baseline (median 2025 pg/ml [IQR 998–5146]) compared with the control value for healthy subjects (<400 pg/ml). During the serial measurements NT-proBNP levels rose until 72 hours after TAVR and decreased thereafter. NT-proBNP levels prior to TAVR were predictive of 12-month mortality (AUC 0.536; 95% CI 0.499–0.637). NT-proBNP levels 72 hours after TAVR showed an even higher correlation with mortality (AUC 0.691; 95% CI 0.628–0.759) and for the combined endpoint of mortality, cardiac decompensation, 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 was an independent predictor of mortality, cardiac decompensation, 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.

P2622 | BEDSIDE
Change in stent size at each inflation volume of SAPIEN XT: bench test vs. post-procedural stent sizes
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Background: In transcatheter aortic valve implantation (TAVI), the selection of an appropriate stent size is important to prevent complications; however, the currently available stent sizes are limited. In actual clinical practice, when the nominal inflation volume cannot bring the most appropriate stent size, a strategy of overfilling or underfilling can be taken. Estimates of the stent sizes at each inflation volume can contribute to technical success but remain unclear. In the present study, we conducted a bench test and compared them with the post-procedural stent sizes.

Methods: The 23- and 26-mm stents of SAPIEN XT for transfemoral approach were selected for the bench test. The inflation was started from 3-cc underfilling and was increased by 1 cc up to 4-cc overfilling for 23-mm stent and 2-cc overfilling for 26-mm stent. The stent size measurement was conducted with calipers and computed tomography (CT) based on the midpoint of the stent height. Also, in 24 patients after TAVI, their stent sizes were measured with CT.

Results: There were no obvious differences between caliper and CT measurements. The stent sizes in the bench test were considerably smaller than the manufacturer’s description. The post-procedural stent sizes of both 23- and 26-mm stents were even smaller than those in the bench test. In particular, the stent sizes at underfilling tended to be markedly smaller than those at the nominal inflation volumes.

Conclusion: 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.

P2623 | BEDSIDE
Controlled release metoprolol for aortic regurgitation: a double blind, randomised controlled trial of efficacy and safety
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Background: Chronic aortic regurgitation creates a volume load on the left ventricle, which induces adaptive responses. With time, excessive left ventricular dilatation may precipitate heart failure unless aortic valve surgery is performed. Treatment with β-adrenergic receptor antagonists (β-blockers) is beneficial in patients with heart failure, but the effect of β-blocker therapy in aortic regurgitation is unclear. This trial was designed to evaluate the effect of controlled release metoprolol on left ventricular remodelling in patients with chronic aortic regurgitation.

Methods: In this randomised, double blind, placebo-controlled trial, 75 asymptomatic patients with moderate to severe chronic aortic regurgitation were randomised to receive metoprolol CR/XL up-titrated to 200 mg/day, or matching placebo. The primary end point was left ventricular end diastolic volume, measured by magnetic resonance imaging after 6 months of treatment.

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.

Conclusion: Treatment with controlled release metoprolol for 6 months did not reverse, nor exacerbate left ventricular remodelling in patients with moderate to severe aortic regurgitation.

Acknowledgement/Funding: Grants were provided by the South-East Norway regional health authority and the Norwegian ExtraFoundation. AstraZeneca provided the study drugs.
Background and introduction: Rapid deployment aortic valve replacement (RDAVR) may facilitate minimally invasive surgery and reduce potential concerns related to prosthetic valve implantation, 3.2%. Two different valve designs are commercially available to those seen with conventional surgical aortic valve replacement.

Methods: The TRITON Trial was a prospective, multicenter, single-arm study of 297 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 21, 23, 23, and 27 mm) affixed to a balloon-expandable frame. The nominal balloon size was chosen as the 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. Patients were clinically evaluated at discharge, 30 days, 3 months, and annually for 3 years. Echocardiograms were adjudicated by an independent Echo Core Laboratory.

Results: One-hundred-fifty-eight patients underwent isolated RDAVR; the surgical approach included, full sternotomy (n=71), upper hemisternotomy (n=77), and right anterior thoracotomy (n=10). Mean age was 75±6.6 years; female, 49.4%; NYHA III/IV, 57.1%; hypertension, 84.4%; chronic renal failure/dialysis, 18.2%; prior cardiac surgery, 15.6%; diabetes, 11.7%; and, COPD, 7.8%. Logistic EuroSCORE was 8.2±6.6%. Early (30 day) rate of all-cause mortality was 1.3%; reoperation for bleeding, 7.0%; acute kidney injury, 5.7%; major paravalvular leak, 0.6%; new permanent pacemaker implantation (total), 5.1% and valve related pacemaker implantation, 3.2%.

Conclusions: These data suggest that isolated RDAVR, using a balloon-expandable valve, can achieve rates of major paravalvular leak and new permanent pacemaker implantation that are superior to a self-expanding valve. Moreover, early rates of mortality and complications are low and comparable to those seen with conventional surgical aortic valve replacement.

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References:


P2624 | BEDSIDE

Incidence, predictive factors and impact of delirium after transcatheter aortic valve implantation

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Aims: To investigate the incidence, predictive factors and impact of postoperative delirium (POD) among patients treated by transcatheter aortic valve implantation. Methods: A retrospective observational cohort study of 288 consecutive patients who underwent TAVI at our institute was conducted. Delirium was diagnosed according to the Diagnostic and Statistical Manual of Mental Disorder, 4th Edition criteria. Primary outcome of this study was the presence of inhospital POD after TAVI.

Results: The incidence of POD after TAVI was 13.4% (n=36). Of these cases, 18 were associated with post-procedural complications, including major vascular complications/bleeding (n=4), stroke (n=3), acute kidney injury (n=3), atrial fibrillation (n=4) and infectious disease (n=4). POD was most frequently diagnosed on the second day after TAVI (OR: 1.5) and was associated with prolonged hospital stay regardless of complications (in uncomplicated TAVI: 5–10 days vs. 5–4–5 days, P < 0.001). Predictors of POD were non-transfemoral (transapical/transaortic) access (Odds Ratio (OR) 7.53; 95% confidence interval [CI] 3.19–17.73), current smoking status (OR 3.94; 95% CI 1.21 to 12.14), symptomatic heart failure (OR 3.05; 95% CI 1.10 to 8.50), atrial fibrillation (OR 2.61; 95% CI 1.02 to 6.02) and age (OR 1.90; 95% CI 1.00 to 1.18). After a median follow-up of 16 days (6–27 months), patients who developed POD showed higher mortality (36% vs. 16%; P < 0.001). POD in-hospital stay regardless of complications (in uncomplicated TAVI: 5–10 days vs. 5–4–5 days, P < 0.001). Predictors of POD were non-transfemoral (transapical/transaortic) access (Odds Ratio (OR) 7.53; 95% confidence interval [CI] 3.19–17.73), current smoking status (OR 3.94; 95% CI 1.21 to 12.14), symptomatic heart failure (OR 3.05; 95% CI 1.10 to 8.50), atrial fibrillation (OR 2.61; 95% CI 1.02 to 6.02) and age (OR 1.90; 95% CI 1.00 to 1.18). After a median follow-up of 16 days (6–27 months), patients who developed POD showed higher mortality (36% vs. 16%; P < 0.001). POD was associated with a significant independent predictor of mortality when adjusted for age, sex and occurrence of complications.

Conclusions: POD after TAVI has an incidence of 13% and occurs mainly early in the postoperative course. Non-transfemoral access is strongly associated with the occurrence of POD. Patients who develop POD show prolonged in-hospital stay and impaired long term survival.

Acknowledgement/Funding: Kings Fund

P2625 | BEDSIDE

Value-Based approach in re-designing the care pathway for patients with infective endocarditis

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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 3319 GBP (36,647GBP and 28,465GBP for surgically and medically treated patients, respectively) and for Cohort 2 was 32,048 GBP (37,061 GBP and 25,492 GBP for surgically and medically treated patients, respectively).

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


Background: Aortic root replacement with a pulmonary autograft (Ross intervention) can be performed as a treatment of aortic valve endocarditis, avoiding prosthetic valve implantation in septic context. We sought to assess long-term outcomes of this Ross procedure in this patient population.

Methods: From April 1992 to March 2009, Ross intervention was performed in 42 patients (Mean age 34±8 years, 86% male) suffering from an active or ancient aortic valve endocarditis. 33% patients had extensive perivalvular involvement, and surgery was urgent in 16 patients (38%). We performed a prospective clinical and echocardiographic follow-up of this population.

Results: Median follow-up was 10 years (range 4–21 years). Overall survival at 10 and 15 years was 87±5% and 81±8% respectively. Perioperative mortality was 4.7% (2 patients) and no late cardiac death was reported. Eight patients (19%) underwent repeat surgery for autograft and/or homograft dysfunction at a mean time of 9 months (3 months to 18 years). Rate of recurrent endocarditis was low (7% - 3 patients), including 1 in a context of persistent intravenous drug abuse. Clinical follow-up showed a good functional status for all patients with NYHA ≤ II, and less than 25% of patients receiving cardiovascular medication. Late echocardiographic follow-up demonstrated well functioning autograft and homograft, with only one severe aortic regurgitation, and one significant increase in pulmonary mean gradient.

Conclusion: Ross intervention in aortic valve endocarditis is an interesting alternative to prosthetic valvar replacement in a selected population, with a high rate of survival free from any cardiovascular event or medication requirement.

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P2627 | BEDSIDE
Current clinical presentation, management and long-term outcome of infective endocarditis: results from a contemporary registry in 2 referral centers
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Background: Infective endocarditis (IE) has a relatively low incidence but clinical presentation, management and outcome is changing due to aging of the general population and the increase in invasive procedures and use of intracardiac devices. In this study we evaluated the current clinical presentation, management and outcome in 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 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. Significant, pts undergoing device/catheter extraction and pts treated medically also 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
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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 numbers and/or altered status of Tregs have been implicated in the pathogenesis of some autoimmune and inflammatory 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 Treg 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 (PH) is an important predictor of mortality and morbidity 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. Transluminal echocardiography (TTE) was performed in all patients pre-PVRI assessment (average 4weeks).
PVRI reversibility was performed by using nebulised iloprost (20microgram/ml for 1min)
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 PHT resulting in high risk patients undergoing risky intervention. 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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Background: Acute kidney injury (AKI) after transcatheter aortic valve implantation (TAVI) is frequent and is associated with adverse outcomes. Past studies have attributed AKI to several peri-procedural features including impaired kidney function at baseline. The relationship between patient blood management, baseline kidney function and this complication is less well defined. This study aimed to fill this gap in knowledge.
Data from the institutional prospective transfemoral TAVI registry were collected in 293 consecutive patients. Patients were stratified according to the Chronic kidney disease (CKD) classification, in to two groups: group A (CKD classes 0, 1 and 2) and group B (CKD classes 3, 4 and 5). A significant greater group A had the impact of preoperative anemia (according to World Health Organization definition), post-procedural hemoglobin (Hb) drop (<2g/dl, 2g/dl and >2g/dl) and blood transfusions on AKI were evaluated. Anemia, Hb drop and transfusions were then forced into multivariable logistic models for study outcome.
Incidence of AKI was 17.2% in group A and 14.7% in group B. Anemia was significantly associated with AKI in both groups. Similarly, Hb drop was significantly associated with AKI with a clear trend toward a higher incidence in parallel with the degree of postprocedural anemia. Transfusion was associated with a significantly increase in the incidence AKI in both groups, with a marked additive effect in the preoperatively anemic patients. Multivariable logistic regression revealed transfusion as an independent predictor of AKI in group A (OR 1.89, 95% CI: 1.68–2.8; p<0.001) and baseline anemia in group B (OR 2.21, 95% CI: 1.88–4.9; p<0.001).
This study portends that optimization of patient blood management is crucial to TAVI outcomes, presence of anemia and/or chronic kidney disease allows better risk stratification and should prompt new management algorithms.

Abstract P2629 – Table I

<table>
<thead>
<tr>
<th>Responders (N=17)</th>
<th>Non-responders (N=13)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Median 71 yrs (range 37–83)</td>
<td>Median 66 yrs (range 51–79)</td>
</tr>
<tr>
<td><strong>Mean PCWP (Right heart study)</strong></td>
<td>22 mmHg</td>
<td>29 mmHg</td>
</tr>
<tr>
<td><strong>Pulmonary Arterial Systolic Pressure (Right heart study)</strong></td>
<td>60 mmHg</td>
<td>59 mmHg</td>
</tr>
<tr>
<td><strong>Pulmonary Vascular Resistance Index (PVRI)</strong></td>
<td>7.3 U/m²</td>
<td>7.9 U/m²</td>
</tr>
<tr>
<td><strong>Change in PVRI post Reversibility test with Iloprost</strong></td>
<td>3.3 WU/m²</td>
<td>0.03 WU/m²</td>
</tr>
<tr>
<td><strong>Cardiac Index using the TTE</strong></td>
<td>2.58 L/min/m²</td>
<td>2.04 L/min/m²</td>
</tr>
<tr>
<td><strong>Left Ventricle diastolic dimension on transthoracic echo. Pre-study</strong></td>
<td>53 millimeter</td>
<td>60 millimeter</td>
</tr>
<tr>
<td><strong>RV Tricuspid Annular Plane Systolic Excursion (TAPSE) on transthoracic echo. Pre-Study</strong></td>
<td>Median 1.8 cm (range 2.3–0.8)</td>
<td>Median 1.25 cm (range 2.0–0.5)</td>
</tr>
<tr>
<td><strong>Left Atrium (LA) area on Apical 4-ch view (TEE)</strong></td>
<td>Median 27 cm² (range 17–44)</td>
<td>Median 34 cm² (range 24–47)</td>
</tr>
</tbody>
</table>
P2631 | BEDSIDE
Soluble ST2 for risk stratification and the prediction of mortality in patients undergoing transcatheter aortic valve implantation
A. Stundt, F. Courtz, P.J. Leimkuhler, 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 (15.0–36.9)ng/ml; P=0.005). In ROC analysis, sST2 had the highest AUC for the prediction of all-cause mortality at 30 days. However, renal function was superior for the prediction of all-cause mortality at 1 year. In addition, we stratified our cohort according to the median level of NT-proBNP (2.960 pg/mL) and the sST2 cut off level of 35 ng/mL in four groups (figure). Patients with an elevation of both biomarkers had a significantly worse prognosis.

Conclusions: Baseline sST2 is strongly associated with adverse short-term outcome, and might be useful for the prediction of in-hospital outcome. sST2 provides additional prognostic information beyond established biomarkers for the prediction of 1-year outcome.

P2632 | BEDSIDE
Transfemoral transcatheter aortic valve implantation in lower risk patients: 30-day and long-term outcomes
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Background: Transcatheter aortic valve implantation (TAVI) is an alternative to surgical aortic valve replacement (SAVR) in patients with severe symptomatic aortic stenosis (AS) at high surgical risk. A predictive Logistic Euroscore (Log ES) >15% usually defines the high-risk population. However, TAVI is performed in a number of pts with a Log ES <15% due to comorbidities not included in the calculation of the Log ES but increasing the risk of SAVR. The results of TAVI in this subgroup of “IL-R” patients need to be carefully assessed.

Population and methods: From January 2010 to December 2013, 351 consecutive patients underwent transfemoral TAVI with the Edwards Sapien XT prosthesis using exclusively local anesthesia. We compared the clinical characteristics and outcomes at 30 days in two groups according to the Log ES <15% (Low risk: LR) vs. >15% (High risk: HR). The long-term survival was analyzed by Kaplan Meier analysis. Valve Academic Research Consortium (VARC-2) classification of TAVI complications was used.

Results: Mean Log ES was 10.3±3.1% and 24.4±9.6% in the LR and HR groups, respectively. Patients in the LR group were younger (82.1±7.6 vs. 85.3±5.5 years, p<0.0001), more often female (55.1% vs. 44.9%, p=0.04), and had more frequently a history of previous CABG (2.6% vs. 8.8%, p=0.01). Procedural success was high and similar in the two groups (98.3% in both groups). There was no significant difference between the two groups in major vascular complications (16.6% vs. 14.8%, p=0.66), life-threatening bleedings (8.0% vs. 7.9%, p=0.71), major acute stroke (3.4% vs. 1.1%, p=0.17), myocardial infarction (2.9% vs 1.1%, p=0.28) and permanent pace maker (5.7% vs. 5.1%, p=0.82). There was a trend for lower 30-day mortality in the LR group (4.0% vs. 7.9%, p=0.09). Kaplan-Meier survival curves comparing LR and HR patients are shown in the figure and survival was significantly higher in LR patients at one (85.4% vs. 78.7%), two (76% vs. 68.4%), and four (69.1% vs. 41.4%) years (log rank p=0.02).

Conclusions: In lower risk patients (Log ES <15%), TAVI is associated with similar procedural success and complications. However, 30-day and long-term survival is significantly higher in lower risk patients.

P2633 | BEDSIDE
Risk scores and biomarkers for the prediction of 1-year outcome after transcatheter aortic valve replacement
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Background: Up to 50 percent of the patients still die or have to be rehospitalized during the first year after transcatheter aortic valve implantation (TAVI). This emphasizes the need for more strategic patient selection. The aim of our study was to compare the prognostic performance of 4 risk scores (logistic EuroSCORE, EuroSCORE II, STS-PROM, GAV score) and 5 circulating biomarkers of inflammation and/or myocardial dysfunction (hsCRP, GDF-15, IL-6, IL-8, NT-proBNP) to predict all-cause mortality and rehospitalisation after TAVI.

Methods: We calculated the hazard ratios and c-statistics of risk scores and biomarkers for the risk of death (N=80) and the combination of death or 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; ΔNRI).

Results: The EuroSCORE II and GDF-15 had the strongest predictive value for 1-year mortality (EuroSCORE II, AUC 0.71; 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 of 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.
of cardiomyocytes or reactivation of certain fetal genes. In the pathologic cardiac hypertrophy model of ascending aortic constriction, Selumetinib provided significant ERK inhibition in the stressed heart but not in the other organs. This selective ERK inhibition prevented LV wall thickening, LV mass increase, fetal gene reactivation and cardiac fibrosis. In another distinct physiologic cardiac hypertrophy model of a swimming rat, Selumetinib provided a similar anti-hypertrophy effect, except that no significant fetal gene reactivation or cardiac fibrosis was observed. 

Conclusions: Selumetinib, a novel oral anti-cancer drug with good safety records in a number of Phase II clinical trials, can inhibit ERK activity in the heart and prevent pathological hypertrophy. These preclinical results indicate that Selumetinib could potentially be used to treat cardiac hypertrophy. However, this hypothesis needs to be validated in human clinical trials.

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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 after retrieving the clinical 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±5.9 and the mean ejection fraction (EF) was 27.8±8.4%. Heart failure was the most common symptom (98%). In the first 6 months there was no statistically significant change in late H-F. In contrast, ABPM revealed statistically significant increases in daytime (120±13 vs. 122±19 mmHg; p=0.005) and nighttime systolic BP (111±15 vs. 113±16 mmHg; p=0.011) and in pulse pressure (45±9 vs. 46±11 mmHg; p=0.001).

Conclusion: These results suggest that treatment with tadalafil may have stabilized the progression of cardiac involvement in patients with early stages of FAP. However due to the limited duration of follow-up we must be cautious given the slow progressive nature of the disease.

Acknowledgement/Funding: none

P2636 | 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.

Purpose: In the present study, we evaluate whether circulating miRNAs serve as potential non-invasive 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 screening, 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-515-3p, miR-296–5p, 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.

P2637 | 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: 55.3±14.3 years) treated with percutaneous septal ablation (PTSA) for symptomatic hypertrophic obstructive cardiomyopathy (HOCM) we analyzed predictors of long-term outcome.

Results: Hospital mortality was 1% (5 pts.) Mean CK rise was 513±249 U/l (ref-range: 0–196 U/l). A DDD-pacemaker (DD-D-P) was 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 causes. Overall survival was 93% at 5 years, and 90% at 10 years.

Conclusion: For generalizable therapy, in this HOCM patient sample the following parameters (hazard ratio/p value) were predictive for overall mortality: Baseline LV end-diastolic diameter (1.06±0.03), baseline age (1.07±0.001), baseline septal thickness (1.12±0.004), ethanol dose (1.10±1.001), and syncope and PTSA-induced AV conduction problems (2.7±3.0). The cumulative life end point of cardiovascular mortality and aortic valve replacement in ICD carriers was predicted by: Baseline septal thickness (1.10±1.001), ethanol dose (1.32±0.03), NYHA class during follow-up (1.84±1.01), and syncope during follow-up (3.6±0.005).

Acknowledgements: As compared to the classical risk stratification in HCM relying on absence/presence of family history of sudden cardiac death, non-sustained VT, maximum wall thickness, syncope, and abnormal exercise blood pressure regulation, in this post-PTSA cohort different risk predictors were identified. Elimina-
tion of the output gradient in symptomatic HOCM pts. may thus also modify the risk profile. A multi-center initiative to aggregate additional pt.-years is warranted.

P2639 | BENCH
Predictive value of tei index for patients with cardiac amyloidosis
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Background: We previously reported that longitudinal systolic and diastolic deformation parameters derived from speckle tracking imaging (STI) could predict the outcome of patients with cardiac amyloidosis (CA).
Purpose: Left ventricular (LV) Tei index is a known parameter reflecting combined systolic and diastolic myocardial performance. In this study, we thus tested the hypothesis that Tei index could also predict outcome of CA patients and compared the prognostic values between Tei index and previously reported deformation parameters.
Methods: LV systolic and diastolic functions including tissue-Doppler-derived LV tei index and STI-derived strain imaging were evaluated by echocardiography in 60 consecutive CA patients (age 64±10 years, 55% male) and 30 normal controls (age 61±8 years, 60% male). All patients completed medical follow-up (median 274, quartiles 90–900 days). The endpoint was all-cause death.
Results: LV tei index was significantly higher in CA group (0.70±0.24) as compared with normal group (0.45±0.09). In CA group, Tei index was positively associated with LV wall thickness and negatively associated with ejection fraction and global longitudinal systolic and diastolic strain rates. Furthermore, Tei index tended to be positively associated with E/E’ ratio.
Conclusions: Tei index analysis results showed that Tei index (hazard ratio (HR): 8.778, 95% confidence interval (CI) 1.75–43.989, P<0.008), global systolic strain (global LSys, HR 1.110, 95% CI 1.013–1.218, P=0.026) and E to global diastolic strain rate ratio (E/LSRdias, HR 1.647, 95% CI 1.121–2.424, P=0.011) were univariate predictors of all-cause mortality after adjustment for age, gender, and body mass index. CA patients with Tei index ≥ 0.63 was associated with significantly increased risk of all cause death compared to those with Tei index <0.63 (P=0.007).

P2640 | BEDSIDE
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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Background: Degenerative aortic stenosis (AS) and wild type transthyretin amyloidosis can be accurately identified by technetium-99m-3,3-diphosphono-1,2-propanodicarboxylic acid (99mTc-DPD) scintigraphy. We previously reported that longitudinal systolic and diastolic deformation parameters derived from speckle tracking imaging (STI) could predict the outcome of patients with cardiac amyloidosis (CA).
Purpose: To investigate the coexistence of cardiac amyloidosis in elderly patients with aortic stenosis undergoing transcatheter aortic valve replacement (TAVR), TTR-related cardiac amyloidosis can be accurately identified by technetium-99m-3,3-diphosphono-1,2-propanodicarboxylic acid (99mTc-DPD) scintigraphy.
Methods: Since October 2014 we prospectively evaluated with 99mTc-DPD with aortic stenosis referred for aortic valve replacement (TAVR or surgery).
Results: 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.

P2641 | BEDSIDE
First arrhythmogenic 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 consanguineous ACM families was studied. The families were 13 of PKP2, 14 of JUP, 6 of DSC2, and 6 of DSP; one of the DSP families presented digenic heterozygosity with PKP2 mutation. Serial clinical work-up consisting of history, physical examination, 12-lead/signal-averaged/24 ambulatory ECG and two-dimensional transthyretin echocardiography was performed every 6 to 12 months. ECG/echocardiographic features were evaluated at the time of event and associated with the outcome using an age-matched nested case-control study within the cohort. Mutation carriers who experienced the first major arrhythmic event (sudden cardiac death or sustained ventricular tachycardia) were considered as cases whereas those who did not as controls. Multivariable logistic regression models were constructed including gender, genotype, repolarization and depolarization abnormalities, RV and LV dysfunction as variables. One model was constructed for each genotype to avoid overfitting.
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 the 2010 Task Force criteria, showed 57% positive and 100% negative predictive value for the occurrence of arrhythmogenic outcome. Repolarization abnormality (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 independent of gender and genotype. Clinicians should be alerted in the appearance of such abnormalities during follow-up.
Conclusions: Undoubtedly, ECM alterations play a crucial role in the constitution of an arrhythmogenic substrate in NIDCM 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 A. Protonotarios1, A. Anastasakis2, E. Prappa3, C. Pitsatos2, V. Vlaiou2, D. Tousoulis2, L. Antoniades4, A. Tsatsopoulou1, 1 Yannis Protonotarios Medical Center of Naxos, Naxos, Greece; 2University of Athens Medical School, 31st Department of Cardiology, Athens, Greece, 4Evangelismos General Hospital, 2nd Department of Cardiology, Athens, Greece; 5Niccosia General Hospital, Department of Cardiology, Nicosia, Cyprus

Purpose: Epsilon waves constitute hallmarks of arrhythmogenic cardiomyopathy (ACM) including 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 in 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 wave parameters 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. Epsilon waves were studied in all precordial and inferior leads. Epsilon wave duration was defined as the time interval between the low amplitude signals onset and offset; the highest measured value in precordial leads was recorded for each patient.

Results: Twenty-five subjects (29%) exhibited epsilon waves. They were detected in lead V3 and beyond in 9, while in the inferior leads in 7. Epsilon waves were associated with wall motion abnormalities of the right ventricular outflow tract (RVOT) (p<0.001) but not of the RV posterior wall (p=0.21). RV apex (p=0.30) or posterior 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 K.H. Kim1, H.K. Kim2, 1Sejong General Hospital, Bucheon, Korea, Republic of; 2Seoul National University, Seoul, Korea, Republic of

Background: We investigated the efficacy of macitentan in combination with sildenafil on hemodynamic and morphological parameters in rats with monocrotaline-induced PAH.

Methods: Two weeks after monocrotaline injection, elevated PASP was confirmed by echocardiography. Adult male SD rats (n=40) were equally randomized to four groups: 1) Sham, 2) MCT, 3) MCT+Mac, 4) MCT+Mac+Sil. Two weeks after monocrotaline injection, elevated PASP was confirmed by echocardiography. Adult male SD rats (n=40) were equally randomized to four groups: 1) Sham, 2) MCT, 3) MCT+Mac, 4) MCT+Mac+Sil. Two weeks after monocrotaline injection, elevated PASP was confirmed by echocardiography.

Purpose: To evaluate the effect of macitentan 10 mg (therapeutic dose) in healthy women on the pharmacokinetics (PK) of a combined oral HC, containing 35 μg ethinyl estradiol (EE) and 1 mg norethisterone (NE), and to investigate the safety and tolerability of macitentan co-administered with this HC.

Methods: This open-label, randomized, two-way cross-over study included 26 subjects who received a single oral dose of the HC alone (reference) then concomitantly with macitentan at steady state (test), or vice versa, with a washout period of at least 3 weeks in between. PK, adverse events (AEs), vital signs (VS), electrocardiogram (ECG) variables, and clinical laboratory tests were monitored. No PK interaction was concluded if the 90% confidence intervals (CIs) of geometric mean ratios (test/reference) of the peak plasma concentration (Cmax) and the area under the plasma concentration-time curve from time 0 to infinity (AUC0-∞) of EE and NE were within the bioequivalence criteria of 0.8 to 1.25.

Results: All 26 subjects were randomized; mean age was 32.5 years (range 23–45) and mean body mass index was 24.2 kg/m². All subjects were included in the safety analyses and 23 subjects were evaluable for the PK analyses. Cmax and AUC0-∞ of the HC were within the bioequivalence criteria. For EE, geometric mean ratios (90% CIs) of Cmax and AUC0-∞ were 0.92 (0.85, 0.99) and 0.95 (0.90, 0.99), respectively. These values of NE were 1.02 (0.96, 1.09) and 1.04 (0.98, 1.19), respectively. Overall, the HC, macitentan, and the HC co-administered with macitentan were well tolerated. The most frequently reported AE was headache (6%). One serious AE (asthma bronchiale), assessed as unrelated to macitentan by the investigator, 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.

P2645 | BEDSIDE Lack of pharmacokinetic interaction between the dual endothelin receptor antagonist macitentan and the combined oral contraceptive, ethinyl estradiol and norethisterone N. Hurl1, N. Pellet2, P.N. Sidharta3, J. Dingemans3, 1Actelion Pharmaceuticals Ltd, Clinical Pharmacology, Allschwil, Switzerland; 2ClinPharmCologne, MEDA, Cologne, Germany

Background: Macitentan is a dual endothelin receptor antagonist (ERA) approved for the long-term treatment of pulmonary arterial hypertension. ERAs have been associated with teratogenicity and are contra-indicated during pregnancy. Hormonal contraceptives (HCs) are cytochrome P450 (CYP) 3A4 substrates and their efficacy can be affected by CYP3A4 inducers. At supra-therapeutic concentrations, macitentan induced CYP3A4 in vitro.

Purpose: To evaluate the effect of macitentan 10 mg (therapeutic dose) in healthy women on the pharmacokinetics (PK) of a combined oral HC, containing 35 μg ethinyl estradiol (EE) and 1 mg norethisterone (NE), and to investigate the safety and tolerability of macitentan co-administered with this HC.

Methods: This open-label, randomized, two-way cross-over study included 26 subjects who received a single oral dose of the HC alone (reference) then concomitantly with macitentan at steady state (test), or vice versa, with a washout period of at least 3 weeks in between. PK, adverse events (AEs), vital signs (VS), electrocardiogram (ECG) variables, and clinical laboratory tests were monitored. No PK interaction was concluded if the 90% confidence intervals (Cis) of geometric mean ratios (test/reference) of the peak plasma concentration (Cmax) and the area under the plasma concentration-time curve from time 0 to infinity (AUC0-∞) of EE and NE were within the bioequivalence criteria of 0.8 to 1.25.

Results: All 26 subjects were randomized; mean age was 32.5 years (range 23–45) and mean body mass index was 24.2 kg/m². All subjects were included in the safety analyses and 23 subjects were evaluable for the PK analyses. Cmax and AUC0-∞ of the HC were within the bioequivalence criteria. For EE, geometric mean ratios (90% Cis) of Cmax and AUC0-∞ were 0.92 (0.85, 0.99) and 0.95 (0.90, 0.99), respectively. These values of NE were 1.02 (0.96, 1.09) and 1.04 (0.98, 1.19), respectively. Overall, the HC, macitentan, and the HC co-administered with macitentan were well tolerated. The most frequently reported AE was headache (6%). One serious AE (asthma bronchiale), assessed as unrelated to macitentan by the investigator, 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 W. Gin-Sing1, S. Gibbs1, L. Howard2, M. Lau-Walker2, G. Lee1, G. Villa1, 1Imperial College Healthcare NHS Trust, Pulmonary Hypertension Service, London, United Kingdom; 2King’s College London, London, United Kingdom

Background: Pulmonary hypertension (PH) is a rare disease which is managed in the UK by 7 designated specialist centres which results in some patients living a long distance from their nearest centre. Prostanoid therapy is recommended for patients with the most severe form of the disease. There are several prostanoids in use in the UK: Intravenous epoprostenol, treprostinil and iloprost, subcutaneous treprostinil and nebivolol inoprost. 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 3.3yrs (0–11.2), mean time on prostanoid therapy 2.7yrs (5 days–11.1yrs).

Conclusion: Patients on prostanoid therapy are younger, more female and have a higher functional class. Surprisingly there was a higher percentage of patients on prostanoids living further away from the PH centre suggesting that distance from the centre is not a barrier to therapy. The average dose of epoprostenol was 23ng/kg/min compared to 58.5ng/kg/min for those on 'Treprostinil.'

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 hypertension.

Methods: Group of 13 male 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 weeks or immediately if showing dyspnea, lethargy and so was in lungs (MON: 0.57±0.07 vs. CON: 1±0.03, P < 0.01). Caveolin-1 beta isoform mRNA level was significantly reduced in the right ventricle (MON: 0.54±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 β-caveolin-1 in lungs and its unchanged amount in the right ventricle can point to a different progressing processes in these organs.

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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 the 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 with PH 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 53.4±14.8 yrs, 28% were males and 33% of the patients were in WHO functional class III/IV. Mean values of the hemodynamics were as follows: pulmonary vascular resistance (PVR) 13.1±7.4 Wood Units, mean pulmonary artery 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 hemodynamic values were tested. A higher functional class. Surprisingly there was a higher percentage of patients with PAH/CTEPH-NO vs prostanoid patient groups

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 determined.

Results: Patients with PH had a significantly higher ACE2 activity (40.4±4mU/L) compared with the control group (22.6±2mU/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 excursion (TAPSE, an echocardiographic value related to 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: ACE2 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), which is often complicated by the presence of peripheral endothelial dysfunction (PED) associated with impaired flow-mediated vasodilatation (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 (males: 5, females: 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 function were observed. There were no significant differences in mPAP, cardiac index, and pulmonary vascular resistance between the two groups of patients at baseline. The prevalence of PED with FMD −5% was 56% and 33% in the PAH and CTEPH groups, respectively; there was no significant difference in FMD between the two groups at baseline. There was no significant correlation between FMD and pulmonary vascular resistance, and FMD and plasma brain natriuretic peptide levels (r=−0.04, r=−0.14, respectively) at baseline. In patients with PAH, FMD was significantly increased after bosentan treatment (6.01±2.37% vs. 8.07±1.18%; p<0.0001). FMD was also significantly improved after bosentan treatment in patients with PAH associated with collagen disease (6.48±1.07% vs. 8.83±1.16%; p=0.023) and in those with PAH associated with other comorbidities and idiopathic PAH (5.76±0.69% vs. 7.68±0.80%; p=0.001). However, in patients with CTEPH, there was no significant difference in FMD after bosentan treatment (5.33±2.37% vs. 6.16±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 therapies on peripheral endothelial function in patients with PAH.

**P2651 | BEDSIDE**

**Baseline characteristics and outcome of adult patients with pulmonary hypertension in Africa: results from the Pan African Pulmonary Hypertension Cohort (PAPUCO) study**

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**Purpose:** The epidemiology of PH in Africa and the distribution of its multitude of etiologies has not yet been described, but limited reports suggest that the incidence of PH in Africa is higher than that reported from developed countries, owing to the pattern of diseases prevalent in the region.

**Methods:** We have present data from the Pan African Pulmonary Hypertension Cohort (PAPUCO) prospective multinational multi-centric registry. The aim is to: 1) describe the epidemiology of PH in Africa and the distribution of its multitude of etiologies; 2) evaluate the prevalence of PH in Africa; 3) describe the pattern of care and treatment of PH in Africa; 4) analyse the impact of gender, age, race, regional, occupational, environmental and socioeconomic factors on the incidence of PH. The proportion of PH due to left ventricular dysfunction and in pulmonary hypertension due to left ventricular dysfunction - comparison of clinical characteristics.

**Results:** A total of 254 patients with newly diagnosed pulmonary hypertension were included in the cohort study, 34 subjects were excluded from data analysis for various reasons. 209 patients (95%) were at least 18 years old (adult cohort). In the adult cohort, the median age was 48 years (range 19–98) and 203 (97%) were of African decent. Risk factors for PH were highly prevalent, SOB (93%), fatigue (88%), palpitations (73%) were the commonest symptoms; 66% were WHO III-IV at the time of presentation with a median 6MWT distance of 252 meters (IQR 120–350). Median baseline RVSP was 35 mmHg. Functional tests included WHO-Functional Class (WHO FC) and 6-Minutes Walk Test (6MW). Pulmonary function tests, radiological evaluation and CT-heart were performed at the discretion of the treating physician. Patients were classified according to ESC guidelines.

**Results:** At 31/DEC/2013 the prevalence of CTEPH was 8.4 cases/million adult inhabitants (MAI). In 2013 the incidence was 1.29 cases/MAI. Patients undergoing PE were younger [55 (43–68) vs 72 (58–80) years−−p<0.001], higher proportion of males (58% vs 40% in PAH group, p<0.001) and a greater distance walked in the 6MW (390 (293–468) vs 319 (194–418) meters, p=0.004) than those receiving only MT. No significant differences were found in functional class (FC), or baseline hemodynamic parameters. The results after 1 year of follow-up are shown in the table below.

**Table 1. Results after one year follow-up**

<table>
<thead>
<tr>
<th>PE (n=80)</th>
<th>MT (n=198)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FC I-III, n (%)</td>
<td>77 (96)</td>
<td>125 (63)</td>
</tr>
<tr>
<td>6MW, m, median (Q1-Q3)</td>
<td>470 (400-544)</td>
<td>398 (290-450)</td>
</tr>
<tr>
<td>mPAP; mmHg, mean (SD)</td>
<td>28.2 (9.8)</td>
<td>46.0 (12.5)</td>
</tr>
<tr>
<td>PVR; Wood units, mean (SD)</td>
<td>4.2 (3.3)</td>
<td>9.0 (4.7)</td>
</tr>
<tr>
<td>No treatment</td>
<td>68 (85.0)</td>
<td>29 (14.6)</td>
</tr>
<tr>
<td>FC, functional class; 6MW; 6 minutes walking distance; mPAP; mean pulmonary arterial pressure; PVR; pulmonary vascular resistance.</td>
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</table>

Survival at 1, 3 and 5 years from diagnosis for PE vs MT groups was 96.9% vs 92.3%, 90.8% vs 81.7% and 84.7% vs 64.5%, respectively (p<0.009).

**Conclusion:** In CTEPH, these data confirm better outcomes due to PE compared with MT, reinforcing the observational Spanish CTEPH patients undergoing PE is low, which seems to be due to a lower referral rate for operability assessment.

**Acknowledgement/Funding:** Bayer Schering Pharma for supporting this Registry (NEHAP).

**P2653 | BEDSIDE**

**Sleep-disordered breathing in pulmonary arterial hypertension PAH and in pulmonary hypertension due to left ventricular dysfunction - comparison of clinical characteristics**

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**Introduction:** Sleep-disordered breathing (SDB) affects up to 70% of patients (pts) with left heart failure (HF) caused by left ventricular dysfunction and is an important determinant of worse clinical outcome in such patients. Prevalence of SDB in PAH pts and its clinical implications remain unclear.

**Purpose:** Comparison of the prevalence of SDB among pts with different etiology of pulmonary hypertension with evaluation of SDB clinical importance.

**Methods:** 81 pts optimally treated for HF were screened for SDB using Holter ECG monitoring commercial software, with estimation of apnea-hypopnea index (eAHI). Study population was divided into two groups: 39 HF pts (coronary artery disease, left ventricular ejection fraction LVEF≤50%, SAP>30 mmHg, NYHA II-III) and 42 PAH pts (19 idiopathic, 17 congenital heart defects, 6 connective tissue diseases).

**Results:** While similar in NT-proBNP values, study groups differed regarding several clinical parameters. Pts in HF group were older (63 vs 50 years in PAH group, p=0.001), were CT-Cheney males (87% vs 40% in PAH group, p=0.001), and had lower SPAP (40 vs 93 mmHg, p=0.000001) and lower LVEF (33 vs 56%, p=0.000001). SDB defined as eAHI >15 was found in 64% of HF pts and in 36% of PAH patients. Mean eAHI value was higher in HF than in PAH group
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 had endocarditis before first entry in the registry. Four patients had repaired VSD and aortic valve replacement before the endocarditis episode, all of these 4 patients needed reoperation and one patient died from complications.

**Conclusion:** The overall incidence of endocarditis was 1.7/1000 patientyears for their endocarditis after first entry in the registry and also 1.7/1000 patientyears in the subgroup with small shunts without previous intervention. In this contemporary cohort, patients with VSD are at high risk of endocarditis, up to 20 times the risk in the general population.

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**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 84% at 30 years (Fig. 1), 71% at 40 years (Fig. 2) and 58% at 50 years. Not surprisingly, 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

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**P2657 | BEDSIDE**

Risk of hemorrhagic stroke in children and young adults with congenital heart disease

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**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:** 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=26,566) 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 (28/72) 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 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 disease such as in Marelli group 1 (transposition of great vessels, tetralogy of Fallot, atrioventricular septal defect, hypoplastic left heart syndrome, double inlet ventricle and common arterial trunk) had a risk of hemorrhagic stroke 3.34 higher (95% CI 1.82–6.12, p < 0.001) compared to controls.

**Conclusions:** Our results show that the risk to develop hemorrhagic stroke is significantly higher in children and young adults with congenital heart disease compared to general population. However, in absolute terms the risk is low. Further 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.

**Methods:** In this prospective observational study adult PAH-CHD patients, currently on bosentan treatment, were evaluated with a standardized treatment protocol, including six-minute walk distance (6-MWD), World Health Organization (WHO) functional class, and laboratory tests, carried out every 3 months. After baseline measurements bosentan was switched to macitentan. At three months a switch to macitentan.

**Results:** In 35 PAH-CHD patients were switched to macitentan (mean age 35.5 years, 43% male, 34% Down syndrome, 74% Eisenmenger syndrome). No serious adverse events were reported. After three months macitentan treatment, WHO classification improved in 8 (28%) and worsened in 2 (7%) patients (p < 0.001). No change in 6-MWD (39 ± 12 vs 40 ± 12, p = 0.195). Aortic diameter at time of dissection and subsequent outcomes were compared for MFS, TAAD and BAV.

**Methods:** Prosands 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 = 0.989), but lower than in patients without dissection (p < 0.001).

**Conclusions:** Risk of aortic dissection is greater with TAAD than with MFS and 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.
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 clinic 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 cardiology team 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).

Methods: We retrospectively identified those CHD patients who had attended a transfer clinic and transitioned from paediatric to adult congenital services between 2011–2013. For appointments, and attendance at, their first ACHD clinic review were identified with the use of the electronic patient record (EPR), patient information system (PMIS) 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 clinic appointment booked for a future date to the time of data analysis. Of the remaining 89 patients, 78 (87.6%) 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. However, although the 87.6% attendance rate at the first appointment in ensuring CHD patients are not lost to follow-up in the transfer of care from cardiac and transitioned from paediatric to adult congenital cardiac services.

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.

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. Aggravation of MR was defined as ≥2 grades increase after ASD closure. Cardiac catheter and transesophageal 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 5 patients, 5–15 years in 2 patients, 15 years in 6 patients, and mitral valve surgery was eventually performed 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 dilatation 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 dilatation 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.
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 endothelial dependent vasodilation in heart failure (HF). We sought to evaluate the effects of FES on circulating levels of vascular endothelial growth factor-A (VEGF-A), endothelial progenitor cells (EPC) and CD34+ monocytes in HF with reduced LVEF (HFREF).

Methods: Fontain patients with lower diastolic KE SV than controls. The KE during the cardiac cycle in Fontain patients depends on the geometry of the outflow tract.

Conclusions: FES further improved significantly NYHA class <p=0.002> and a marginally significant increase in EPC <98.7, 95% CI: (52.3, 145.1) in FES versus 3.1, 95% CI: (−24.6, 30.7) in sham, p=0.054]. FES further improved significantly NYHA class <p=0.054> and mean LVEF 0.27±0.05 to 6-week FES or sham procedure. We measured circulating levels of VEGF-A, EPC and CD34+ monocytes at baseline and after therapy along with clinical, functional and biochemical biomarkers.

Results: Baseline demographics, HF severity measures (NYHA class, LVEF, wall thickness and mass values, nevertheless it was more pronounced in female 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.

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 acondition 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 by echocardiography. LV pressure-volume (P-V) analysis was performed to monitor changes 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 measurements. ATP was more pronounced in females (+14.5% male vs. +14.5% female, p < 0.05) also verified gender differences in LV hypertrophy. The induction of Akt signaling was more significant in females compared to the males (p < 0.05 for female vs. +21.4% male vs. +7.1% female, p < 0.05). There is a characteristic difference in the mitogen-activated protein kinase (MAPK) pathway as suppressed phosphorylation of p44/42 MAPK (Erk) was observed in female exercised rats, but not in male ones. α-Myosin heavy chain (MHC) α/β-MHC ratio did not differ in males, but increased markedly in females (+140.6% female vs. +16.9% male, p < 0.05). Despite the more significant hypertrophy in females, characteristic functional parameters of athlete’s 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 mechanism, and prolonged unaltered LV stiffness in both males and females.

Conclusions: 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.

P2668 | BENCH
Hyperinsulinemia and overweight in obese Zucker rats effectively suppressed by exercise training with hypoxia recovery
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It is currently unknown whether hypoxia training can effectively suppress over-weight and hyperinsulinemia in genetically obese animals. In this study, both lean and obese Zucker rats were randomly assigned into the following groups: control (CON, n=7), exercise (EX, n=7), hypoxia (HYP, n=7) and exercise training with hypoxia recovery (EX+HYP, n=7). During a 6-week training period, rats performed swimming exercise progressively from 30 to 180 min day−1, and recovered under hypoxia (14% oxygen for 8 h day−1). Obese Zucker rats exhibited substantially greater fasting insulin levels, and exaggerated glucose and insulin responses following an oral glucose challenge compared with lean rats. At the beginning of the study, there were no differences in body weight, fasting glucose, fasting insulin, area under curve of glucose (GAUC) and insulin (IAUC) in the EX+HYP group were significantly lower than CON group among the obese rats. Meanwhile, only GAUC was significantly lower in the EX group compared to the CON group. At the end of week 6, capillaries number (CD), capillaries density (CD/F), capillaries area (CA/F), and type IIb fibres proportion of the plantaris muscle in the EX group were significantly greater than the CON group (P<0.05), but no additive effect of hypoxia on exercise training was observed. Our data demonstrate that exercise training with prolonged hypoxia recovery offers better metabolic benefits than exercise training alone for the obese Zucker rats. This advantage was closely associated with effective weight reduction.

Methods: 40 PAD patients with intermittent claudicatio (IC, Fontaine Stage IIa and b) were asked to perform either a supervised (SET (n=20)) or a non-supervised exercise training (NET (n=20)). Peripheral blood leukocytes were analysed from whole blood by flow cytometry (Beckman-Coulter Navios 10/3). Monocytes and EPC were identified by different gating strategies in relation to size and granulation (FSC/SSC) and surface molecules (CD14/CD86/CD45/CD34) and analysed for CD64 monocyte/ EPC ratio in patients with peripheral arterial disease over 6 months.

Exercise training leads to an increase of the proangiogenic TIE2 monocyte/ EPC ratio in patients with peripheral arterial disease over 6 months
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Background: TIE2+ monocytes (TEM) and endothelial progenitor cells (EPC) play a crucial role in neangiogenesis. In peripheral arterial disease (PAD) exercise training can promote angiogenesis and thus ameliorate the severity of the disease.

Methods: 40 PAD patients with intermittent claudicatio (IC, Fontaine Stage IIa and b) were asked to perform either a supervised (SET (n=20)) or a non-supervised exercise training (NET (n=20)). Peripheral blood leukocytes were analysed from whole blood by flow cytometry (Beckman-Coulter Navios 10/3). Monocytes and EPC were identified by different gating strategies in relation to size and granulation (FSC/SSC) and surface molecules (CD14/CD86/CD45/CD34) and analysed for CD64 monocyte/ EPC ratio in patients with peripheral arterial disease over 6 months.

Results: At admission patients in total showed an increased proportion of EPC and reduced proportion of TEM (both p < 0.001) in comparison to controls, leading to a TEM/ EPC ratio in favour of EPC (p < 0.0001). After 6 months training, we observed an improvement of TEM/ EPC ratio in favour of TEM (p < 0.01) with a shift of the TEM/ EPC ratio in favour of TEM (p < 0.01), leading to no difference between patients and controls in regard to EPC and TEM ratio. TEM proportions though were still lower for patients (p < 0.05). Comparison of SET vs. NET showed a higher proportion of TEM for the SET group, and thus an increased TEM/ EPC ratio (both p < 0.05). The absolute walking distance in the SET group was higher than in NET (725±457 m vs. 545±119 m) though not significant (p=0.92).

Conclusions: Exercise training can influence the distribution of proangiogenic monocytes. The depletion of EPC from the circulatory pool might be related to a potentially increased collateral growth, leading to a shift of the TEM/EPC ratio in favour of TEMs. SET seems to be more effective in regard to TEM than NET. Thus, the TEM/ EPC ratio might be used as a helpful tool to monitor the effectiveness of any type of exercise training.
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 stage I to II essential hypertension (155 men, mean age=51 years, office blood pressure (BP)=150/96 mmHg) with a negative treadmill exercise test (Bruce protocol) was divided into those with HRE (n=70) (peak exercise systolic BP ≥140 mmHg in men and ≥120 mmHg in women) and those without HRE (n=170). Arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV) values.

**Results:** Patients with HRE compared to those without HRE had greater 24-h systolic BP (143±9 vs 131±8 mmHg, p<0.05), while did not differ regarding metabolic profile and left ventricular mass index (p=NS). Patients with HRE compared to those without HRE exhibited greater levels of ADMA (0.63±0.04 vs 0.52±0.05 μmol/l, p<0.001), OPG (5.4±0.1 vs 4.1±0.5 pmol/l, p<0.001) and PWV (9.9±1.7 vs 7.5±0.9 m/sec, p<0.001), independently of confounders. In the total population, peak exercise systolic BP was related to 24-h systolic BP (r=0.249, p<0.05), PWV (r=0.278, p=0.003), ADMA (r=0.260, p=0.007) and OPG (r=0.214, p<0.05). Regarding OPG, it was associated with 24-h systolic BP (r=0.285, p<0.001), ADMA (r=0.284, p<0.05) and PWV (r=0.424, p<0.001). Multiple regression analysis showed that 24-h systolic BP (b=0.210, p=0.003), male sex (b=0.270, p<0.05), ADMA (b=0.225, p=0.006) and OPG (b=0.188, p<0.05) were independent predictors of peak exercise systolic BP.

**Conclusions:** In essential hypertension, a HRE is accompanied by a state of increased arterial stiffening, endothelial dysregulation and progressive atherosclerosis. The interrelationships of ADMA and OPG with exercise BP response support that diffuse vascular dysfunction contributes to HRE-related risk in hypertension.

**P2671 | BENCH**

**Long-term change of physical activity towards a physically active lifestyle is associated with reduced arterial stiffness in elderly males: results of the SAPALDIA 3 cohort study**

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**Background and purpose:** Longitudinal analyses of physical activity (PA) and arterial stiffness in populations of older adults are scarce. We examined associations between long-term change of PA and arterial stiffness in the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA).

**Methods:** We assessed PA in SAPALDIA 2 (2002–2003) and SAPALDIA 3 (2010–2011) using a short questionnaire with a cutoff of at least 150 minutes of PA per week for sufficient activity. Arterial stiffness was measured oscillometrically by means of the brachial-ankle pulse wave velocity (baPWV) in SAPALDIA 3. We used multivariable mixed linear regression models adjusted for several potential confounders in 2605 subjects aged 50–80 years.

**Results:** Adjusted baPWV means were significantly lower in persons showing a PA change from insufficiently active in SAPALDIA 2 to active in SAPALDIA 3 and in persons being sufficiently active in both assessments (p<0.05) compared to subjects with insufficient activity in both surveys irrespective of the PA intensity in the entire cohort. Only males showed a significant lower baPWV associated with a long-term physically active lifestyle in sex-specific analyses, especially when performed with moderate-to-vigorous intensity (each p<0.05).

**Conclusions:** 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 atherosclerosis. 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 amiodone (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 during the exercise test and determined SBP elevation from baseline (∆SBP). Excessive BP elevation during exercise was defined as: > mean±SD in ∆SBP obtained from 28 control subjects. We assessed the change of plasma adrenaline (ADRN) before and after the exercise test (∆ADRN) as a parameter of sympathetic activity. We measured serum high-sensitivity C-reactive protein (hs-CRP) and thrombomodulin as parameters of vascular endothelial damage in addition to plasma renin and aldosterone. These parameters were compared between the AML- and ARB-treated groups.

**Results:** The proportion of patients with excessive BP elevation during exercise and ∆SBP were significantly lower in the ARB-treated group than in the AML-treated group (Figure). ∆ADRN, hs-CRP and thrombomodulin were significantly lower in the ARB-treated group than in the AML-treated group (P<0.05, respectively).

**Conclusion:** Increased activity of RAAS induced vascular endothelial damage resulting in the excessive BP elevation during exercise even at moderate intensity in HT patients.

**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±10.8, 71% male, class
### Exercise is therapy in heart disease

III-IV. left ventricular ejection fraction inferior to 35%, 26% ischemic, submitted to CRT. 39 patients were randomized either to group A, 6 months HIIT twice a week exercise program (19 p) or to Group B, non-exercise (20 p). Besides those, 61 p were not randomized (group C) because they lived far away from rehabilitation center and were not able to attend exercise sessions. All 100 p were evaluated before and after 9 months after CRT by: clinical functional class (NYHA evaluation), echocardiography, for left ventricular ejection fraction (LVEF) and left ventricular end systolic (LVESV) and end diastolic (LVEDV) volumes; cardiorespiratory test, for peak oxygen consumption (VO2p) and duration; 12-MIBG scintigraphy, for early heart-mediastinum rate (HMR), late heart-mediastinum rate (HRMR) and wash-out (WO).

**Results:** Comparing the 2 randomized study groups (A and B), clinical functional class variation (Δ) (p=0.01), ΔVO2 (−18.970±29.565 vs 13.21±18.274 ±p=0.012) and ΔHMR(0.045±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 (Δ) (p=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, LVESV, VO2p and exercise test duration, had no significant difference (p=ns).

Comparing the 2 randomized study groups (A and B), clinical functional class variation 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 values or variation of peak oxygen consumption and exercise test duration.

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### P2674 | BEDSIDE

Effects of exercise training on cardiac autonomic activity in heart transplant and left ventricular assist device patients: assessment of heart rate profile

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**Background:** Cardiac rehabilitation exercise training programs improve exercise capacity in heart failure patients (pts). Chronotropic incompetence and abnormal HR recovery reflecting profound abnormalities of autonomic activity have been reported in chronic heart failure. We studied the effects of exercise training in pts with left ventricular assist devices (LVAD) and post heart transplantation (HT) by assessing chronotropic response (CR) and heart rate recovery immediate after exercise (HR[HRR]).

**Methods:** A total of 23 pts [15 HT (56% men; mean age 50 yrs) and 8 LVAD (100% men; mean age 55 yrs) underwent a 12 weeks supervised exercise program starting 3 months after surgery. Symptom-limited cardiopulmonary exercise tests were performed at baseline and at the end of the program. Chronotropic response to exercise was evaluated by the percentage of chronotropic reserve [CR = (peak HR – resting HR)/age-resting HR] x 100%. Heart rate recovery was calculated as the difference between peak HR and HR 1 minute later (HRR1, 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 CR. On the contrary, exercise training allowed higher levels of physical activities with significant improvement of CR in HT pts but not HRR1, consistent with underlying pathophysiology of denervated transplanted heart.

<table>
<thead>
<tr>
<th>Heart transplant group</th>
<th>LVAD group</th>
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</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>3 mths</td>
</tr>
<tr>
<td>MET level</td>
<td>5.3±1.6</td>
</tr>
<tr>
<td>Resting HR (bpm)</td>
<td>90.9±14.9</td>
</tr>
<tr>
<td>Peak HR (bpm)</td>
<td>110.7±17.8</td>
</tr>
<tr>
<td>HRR1 (%)</td>
<td>2.1±1.5</td>
</tr>
<tr>
<td>CR (%)</td>
<td>35.1±15</td>
</tr>
</tbody>
</table>

**Conclusions:** The opposite divergent relationship of HRR1 and CR among post HT pts and LVAD pts reflected different pathophysiological processes from different treatment strategies. Heart rate profile can potentially represent a simple, non-invasive tool to assess outcome during cardiac rehabilitation for these special groups of pts.

### P2675 | BENCH

Results from a 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 quadriceps electrical myostimulation (EMS), but very few data are known about the effect of combination of the two methods.

**Purpose:** To determine whether addition of low frequency EMS to ET may improve exercise capacity and/or muscular strength in CHF patients. Primary end-point: improvement of peak VO2. Secondary endpoints: improvement of muscle strength and endurance, sub maximal parameters (ventilatory threshold, 6 min walking test), quality of life.

**Methods:** 91 patients were included (mean age: 58±9 y; NYHA II/III: 52/48%, LVEF: 29.7±9%) 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) quadrupled EMS sessions (20”on/20’off, 1 hour/session). Before and at the end of the protocol, all the patients performed a cardiorespiratory stress test, a 6 min walking test, evaluation of muscular circumference, strength and biological assays (CPK, LDH, Aldolase, and Myoglobin).

**Results:** Data analysis revealed a significant improvement of exercise capacity in all patients (15±25% in ET group and 14±22% in ET + EMS group. Results are similar for submaximal parameters (gain of 6’walk test: +17 vs +18%, anaerobic threshold: + 8 vs +10%) and for muscular circumference and strength. No statistically significant difference among the two groups was found.

**Conclusion:** Our data, from this large multicenter randomized study, show that combination of ET + EMS does not demonstrate any significant additional improvement in exercise capacity. Thus, we may consider, in CHF patients enrolled in a rehabilitation program, not to add EMS if patients are able to perform a conventional aerobic training.

### P2676 | BEDSIDE

Changes in cardiorespiratory fitness predict incident hypertension: a population-based long-term study

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**Background:** Although cardiorespiratory fitness (CRF) has been associated with the risk of hypertension, little is known about changes in CRF over time to predict the risk of incident hypertension. Our aim was to investigate whether changes in CRF over a decade predict the risk of incident hypertension, independent of risk factors, in initially normotensive men.

**Methods:** Participants from the Kuopio Ischemic Heart Disease Study underwent symptom-limited maximal exercise testing using a cycle ergometer at baseline and at a 10 year follow-up. This prospective study included 431 participants (mean aged 50±7 years) without hypertension at baseline and at a second examination. Changes in CRF were calculated as the difference in maximal uptake between baseline (mean VO2max 33.8 ml/kg/min) and during a second examination (mean VO2max 28.7 ml/kg/min), conducted at the 11-year follow-up. The change in CRF (%)] was classified on the basis of change (as percentage) in VO2max. Hypertension was defined as systolic and diastolic blood pressure ≥140/90 mm Hg and/or hypertension diagnosed by a physician.

**Results:** During 10 years of additional follow-up after the second examination, 158 men (37%) developed hypertension. Good baseline CRF as a continuous variable (per 1 ml/kg/min) 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: −8% to 82%), after adjusting for age, follow-up time, alcohol consumption, cigarette smoking, low 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 risk of incident hypertension.
the improvement in intrinsic contractile function induced by exercise training. STE can be a feasible and useful method to follow up development of athlete’s heart in animal models.

P2679 | BENCH
Exercise training 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/week for 8 wk on a treadmill. Training decreased the adipose tissue (T: 4.3±0.5g; F: 5.3±0.7g; C: 6.2±0.6g; O: 9.6±1.3; T: 10.1±0.6g), and insulin resistance (T: 4.8±0.1, F: 5.1±0.4g in both trained compared with the sedentary groups (C: 3.2±0.6; O: 3.1±0.3; F: 3.6±0.5mg/dl/min). ET increased physical capacity (T: 20±0.9; FT: 17.5±0.9 vs. C: 11.5±0.5; O: 10.5±0.8; F: 10.3±0.6 min/h). ET attenuated the increase in BP induced by ovariectomy and/or fructose overload (C: 109±4.1; T: 103±1.1; F: 107±1.5 vs. C: 119±1.9; T: 116.7±0.7 mmHg). ET decreased the basal HR (C: 341±8, T: 302±1, FT: 306±8 vs. C: 398±19, F: 378±17bpm). The sympathetic tonus was lower in control and in trained group (C: 63.6±4; T: 51.2±7) compared to ovariectomized and fructose overload groups (O: 102.6±12; F: 91.9±7 beats/min. Vagal tonus was increased only in the trained group (T: 44.8±5 vs. C: 24.9±6; FT: 25±5; O: 13±6; F: 9±2 beats/min). Baroreflex bradycardia was improved in T and TF groups similar to that of the control group (C: −1.50±0.6; T: −1.74±0.2; FT: −1.77±0.15 vs O: −0.93±0.07, F: −2.11±0.12 bpm/mmHg). The pulse interval variability expressed by standard deviation was increased (C: 6.7±1.1; T: 11.6±0.8; FT: 13.0±1.5 vs O: 7.05±0.6; F: 9.57±0.76s) while VARR PAS was decreased in TF group (C: 6.7±1.9; T: 23.6±0.8; F: 30.7±2.6 vs. O: 56.4±1; F: 40.5±3.7 mmHg). Sympathetic modulation to the vessels was reduced in ET groups (C: 6.7±1; T: 3.6±0.5; F: 3.7±0.4 vs. O: 9.8±1.2; F: 8.3±0.8mmHg). The improvement of automatic function induced by ET (T and TF groups) was accompanied by better diastolic functions expressed by lower isovolumetric relaxation time (IVRT) (C: 38.7±5.2; F: 41.4±3; OF: 35.2±2.5; T: 27.5±1.4; FT: 31.2±7.7ms) and E/A ratio (C: 1.83±0.02; T: 1.98±0.03; F: 1.95±0.3; O: 1.42±0.17; FT: 1.68±0.11). The cardiac global function expressed by the myocardial performance index MPI (C: 0.31±0.06; O: 0.312±0.05; F: 0.326±0.12; T: 0.198±0.05; FT: 0.294±0.05) was improved in trained animals. The improvements of metabolic and autonomic parameters were correlated with the maintenance of diastolic function reinforcing the preventive role of ET in the management of SM. Acknowledgement/Funding: caps

P2680 | BEDSIDE
Ventricular ectopy in young athletes: an innocent bystander or a harbinger of structural heart disease?
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Background: The prevalence of ventricular ectopy (VE) in healthy middle-aged individuals is 1% and increases with age. There is a paucity of data relating to VE burden in young individuals, particularly athletes. Consensus recommendations on interpretation of the athlete’s ECG regard the presence of ≥ 2 VEs on a 10 second ECG suggestive of cardiac pathology.
Purpose: To evaluate the prevalence and significance of VE in athletes.
Methods: We reviewed the 12-lead ECGs from 19,888 individuals (14–35 years) who underwent cardiac evaluation between 2011–2013. Athletes comprised 32% (n=6407) of the overall cohort. Athletes with ≥ 1 VE on their 12-lead ECG underwent echocardiography (echo) and were compared with healthy athletes with normal ECGs (n=749) who underwent echo as part of their screening protocol.

Exercise is therapy in heart disease / Cardiovascular adaptation to exercise
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 dimensions. On the contrary, athletes with VE had significantly greater maximal LV wall thickness and larger right ventricular dimensions (RVd1, RVd2, RVd3) compared to athletes with VE. No athlete demonstrated a cardiomyopathy phenotype.

Conclusions: Our study indicates that VE is rare, 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

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 will be elucidated.

Methods: In a prospective, longitudinal combined ECG and speckle-tracking study of 464 cardiovascular adaptation to exercise

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls</th>
<th>Competitive athletes</th>
<th>P value¹</th>
<th>P value²</th>
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</thead>
<tbody>
<tr>
<td>LA volume index, mL/m²</td>
<td>20.7±4.7</td>
<td>27.1±6.6</td>
<td>31.1±8.2</td>
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<tr>
<td>RA volume index, mL/m²</td>
<td>17.3±3.8</td>
<td>23.4±6.3</td>
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<tr>
<td>LA enlargement criteria</td>
<td>0%</td>
<td>6%</td>
<td>6%</td>
<td>0.23</td>
</tr>
<tr>
<td>RA enlargement criteria</td>
<td>0%</td>
<td>0%</td>
<td>1%</td>
<td>1.00</td>
</tr>
</tbody>
</table>

¹Athletes vs. controls; Pre-training vs. post-training.

Conclusions: An intensive, high-volume training program causes significant increase in LA and RA volumes, with normal filling pressures and normal stiffness. These changes in atrial morphology are not associated with respective electrical changes, suggesting that P-wave morphology, in young healthy athletes is not related to atrial size.

P2684 | BEDSIDE
Cardiac 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.

Methods: Forty-two patients diagnosed with PAH (World Health Organization functional classes II to IV) were enrolled in the study. An endothelin receptor antagonist (ERA) was used as first-line treatment. A phosphodiesterase-5-inhibitor (PDE-5I) was the preferred combination partner, followed by the addition of 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) and exercise ventilatory power (EVP), in functional classes II to IV were enrolled in the study. An endothelin receptor antagonist (ERA) was used as first-line treatment. A phosphodiesterase-5-inhibitor (PDE-5I) was the preferred combination partner, followed by the addition of 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) and exercise ventilatory power (EVP) were measured during cardiopulmonary exercise testing (CPX) of PAH patients.

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P2654 | 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 test battery of 20m sprint, jumping sideways and balancing backwards. Retinal microrcirculation was examined using a Static Retinal Vessel Analyzer.

Results: After analysis, the 20m shuttle run test was associated with narrow 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 arterioles (4.7 (0.8; 6.6) μm/unit sprint, p=0.02). For the anthropometric parameters, only diastolic blood pressure and not body composition was independently associated with narrower retinal arterioles (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 anaerobic endurance exercises and reduction of diastolic blood pressure in order to promote vascular health in young children.

Acknowledgement/Funding: Department of Education of Basel-Stadt

P2656 | 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 between 1988 and 1990, 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 documented. 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.
EXERCISE, PHYSICAL ACTIVITY AND SPORT IN HEALTH

P2690 | SPOTLIGHT
Suppressed middle-acidosis by oral bicarbonate ingestion affected stroke volume responses during an all-out sprint cycling event

P.M. Lepretre1, C. Hanon2, C. Thomas3, S. Dore4, R. Delfour-Prytherch5, S. Perrey2, D. Bishop6
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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 ATP utilization and induced considerable metabolic and ionic perturbations in contracting skeletal muscles which could affect VO2 response. Berger reported that metabolic alkalosis induced by sodium bicarbonate ingestion had no effect on faster VO2 responses but altered slow VO2 adjustment. Due to the large active muscle mass, the peak of VO2 (VO2peak) is limited by maximal cardiac output (CO) rather than peripheral factors during exhaustive cycling exercise. Together, these findings raised the question about the influence of metabolic alkalosis on cardiac output (CO) response especially at the end of very high-intensity exercise.

Purpose: To determine whether acid-base balance status affect the cardiorespiratory response and cycling sprint performance.

Methods: 11 well-trained male cyclists performed on a cycle ergometer 1) a progressive exercise to determine VO2peak and 2) two 70-s all-out supra-maximal exercise in random isokinetic conditions with (ALK) or without (PLAC) bicarbonate oral ingestion. Heart rate (HR) and stroke volume (SV) were measured (by impedance) continuously during all tests.

Results: The induced alkalosis had no effect on VO2 at rest (p=NS) but during the high VO2 level (96.6±8.2% of VO2peak) compared to PLAC in course of which, high value of VO2 was lower than VO2peak (92.2±6.3% of VO2peak, p<0.01). The highest CO values measured during both all-out trials were not different from maximal CO measured during the incremental exercise (P=NS). However, arterial peripheral arteriovenous CO2 levels were different between both conditions with higher values during PLAC (130.5±20.6 ppb vs. p<0.05). Moreover, a higher CO value (incremental test: 133.5±12.1 vs. ALK: 150.3±28.9, p<0.05) during exercise. Highest VO2 values were attained at 51.4±13.4 and 53.6±7.8 s during PLAC and ALK events. (P=NS). A faster CO response was found compared to VO2 kinetic at the onset of ALK exercise. At the end of both all-out conditions, significant VO2 drop (P<0.01) was correlated to CO and SV decreases in ALK conditions.

Conclusion: There is experimental evidence that the bulk O2 delivery to the limb may limit the VO2 responses in the transient phase and induced alkalosis affects CO and VO2 during the whole all-out trial.

Acknowledgement/Funding: French Ministry of Sports

P2701 | 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 inpatient admissions, costs and length of stay of patients presenting with acute chest pain with low-intermediate risk. Our aim was to analyse the usefulness of a chest pain unit in a university teaching hospital in terms of appropriate patient selection, risk stratification and need for admission of patients presenting with acute chest pain with low-intermediate risk.

Methods: A total of 105 patients presenting chest pain of low-intermediate risk in the ED managed in the CPU were included over a two and a half year period. After negative cardiac biomarker determination and normal or inconclusive ECG, cerebral computed tomography, provocative test was performed the day after admission in the ED; either an exercise treadmill test (ETT) or stress myocardial perfusion imaging (MPI) imaging (MPI) upon patient characteristics. Data was analysed using SSPS statistical system.

Results: The median age was 58 (13SD) years, 59 (56.2%) were males, with 51 (48.6%) HT, 17 (16.2%) DM, 44 (41.9%) hypercholesterolemia, 26 (24.8%) smokers, 22 (28.8%) CAD and 2 (1.9%) had a history of chronic abuse of cocaine and alcohol, with a mean GRACE score of 71.7 (50.6%) 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 other 15 (14.3%). Overall performance during the stress tests was excellent with a mean 7.62 METS and a mean 7.09 DUKE index. 75 (71.4%) with diagnostic negative test were discharged and evaluated as outpatients. 20 patients presented 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 dismissed and presented the following day with STEMI. Conclusions: Patients managed in a CPU are at low-intermediate risk for CAD. ETT or MPI only identified disease in 5.7%, and furthermore, it failed to identify disease in a patient with intermediate risk. Most patients were discharged home without hospital admission but where evaluated as outpatients. Therefore, a CPU may reduce hospital admission, but still consumes resources for patients at low risk and it seems that patients at intermediate risk for presenting with acute chest pain may benefit from further study.

P2702 | BEDSIDE
Exertional oscillatory ventilation as a long-term prognostic factor for patients with post-acute coronary syndrome


Background: Previous studies have shown widespread prevalence of respiratory instabilities comorbid with cardiovascular disease. Prevalence of exertional oscillatory ventilation (EOV) across post-acute coronary syndrome (post-ACS) population has never been revealed.

Methods: We studied consecutive 209 post-ACS patients (median age = 59.3 years; 89.0% male; LVEF: 59.1±11.8%) who underwent cardiological exercises testing in cardiac rehabilitation from 2009 to 2014. EOV was visually determined by cyclic fluctuations in minute ventilation that lasted for >60% of the exercise duration and an amplitude of >15% of the average amplitude of cyclic fluctuations at rest.

Results: EOV was present in 24 patients (11.5%). During 639.2±539.4 days of follow up, major adverse cardiac events (MACE; including cardiac death, myocardial infarction and congestive heart failure) occurred in 20.8% (524) in patients
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 into 3 groups. HOMA indices were calculated by using immunoreactive insulin (μU/mL) and fasting blood sugar (mg/dL). 

Background: We had previously reported that maximum oxygen uptake (peak VO2) was improved in patients with acute myocardial infarction (MI) complicated with diabetics (DM). We also reported that exercise tolerance in DM patients remained low after 3months 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 (μU/mL) and fasting blood sugar (FBS) as follows: HOMA-IR = IRI (μU/mL) × FBS (mg/dL)/405 and HOMA-β = IRI × 265/(FBS – 36). We defined IR as a HOMA-IR ≥ 2.0 and impaired β-cell function as a HOMA-β < 50% (p < 0.05). Patients in this study were divided into 3 groups: A, insulin resistance group with HOMA-IR ≥ 2.0 and HOMA-β < 50%; B, normal group with HOMA-IR < 2.0 and HOMA-β > 50%, and C, impaired β-cell function group with HOMA-IR > 2.0 and HOMA-β < 50%.

P2694 | 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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1 St. Marianna University, Yokohama City Seibu Hospital, Yokohama, Japan; 2 St. Marianna University School of Medicine, Department of Rehabilitation Medicine, Kawasaki, Japan

Background: We had previously reported that maximum oxygen uptake (peak VO2) was improved in patients with acute myocardial infarction (MI) complicated with diabetics (DM). We also reported that exercise tolerance in DM patients remained low after 3months 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.

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P2695 | BEDSIDE
Diagnostic value of automatically measured ST-segment changes in individual ECG leads to detect myocardial ischemia during exercise ECG


Background: Exercise ECG is a widely available cardiac stress test, but currently provides insufficient diagnostic accuracy even when done by experienced cardiologists. It is currently unclear which ECG parameters on which leads provide best diagnostic accuracy.

Methods: We enrolled 813 consecutive patients referred for exercise stress myocardial perfusion imaging (MPI) into this prospective single-center study. Amplitude of ST-depression and ST-slope were analysed in an automated fashion from digital ECG recordings at J+40ms, J+60ms and J+80ms in all 12 leads. Time of analysis was the 10 seconds in which the ST-depression was maximal. To evaluate diagnostic accuracy, we calculated the area under the receiver operating characteristics curves (AUC). Optimal cut-off points were derived using the Youden-index. Myocardial ischemia as assessed by MPI was defined as a blunted difference of ≥ 2 or presence of a transient ischemic dilatation.

Results: Myocardial ischemia was detected by MPI in 294 (36%) patients. The diagnostic accuracy of ST-deviation, as quantified by AUC, was best in lead V6 at J+80ms (AUC 0.63 CI 0.59–0.67), with an optimal cut-off at −0.04mV (sensitivity 54%, specificity 68%). Lead I was the second best lead and showed a similar diagnostic value (J+80ms AUC 0.62. CI 0.58–0.66). ST-slope showed best results also in V6 (J+80ms AUC 0.64, CI 0.60–0.68) with an optimal cut-off at −0.75mV/s (sensitivity 65%, specificity 57%).
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 ≥ 30 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).

Conclusion: Stage 3 or 4 CKD disrupts the improvement in exercise capacity after hospital discharge in IHD patients.
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 walking in 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), OW: 3.27±0.59 vs 2.72±0.82; DW: 3.22±0.77 vs 2.61±1.00 and RW: 3.29±0.61 vs 2.77±0.82. For each domain of walkability, there was an association between walkability and walking participation in urban areas. Each additional unit in OW, DW, and RW was associated with a 1.44 times (95% CI: 1.17, 1.76, p<0.001), 1.35 times (95% CI: 1.16, 1.58, p<0.001), and 1.34 times (95% CI: 1.09, 1.65, p<0.005) greater odds of walking, respectively. There were no significant associations for any domain of walkability in rural areas.

Conclusion(s): Consistent with past studies, walking participation was associated with the perception of neighbourhood walkability in urban areas. However, this was not observed in rural areas. Environmental influences on walking are likely to differ between urban and rural areas. Further research in rural areas is required to inform environmental and policy initiatives to increase rural walking participation.

EXERCISE TRAINING AND PHYSICAL ACTIVITY

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 (MVPA, low: 60 min. on < 5 days per week, high: 60 min. on ≥ 5 days per week). For the calculation of odds ratios, logistic regression analysis was used.

Results: Resting BP was lower (−2.3 mmHg, p<0.03) in the group with lower screen time (< 2 h/day) adjusted for age, sex, height and BMI (111.9±11.3 vs. 114.2±11.3 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 MVPA

Subgroups Mean systolic exercise BP 95% confidence interval
High screen time/low activity 154.4 mmHg 151.6–157.1 mmHg
Low screen time/low activity 148.7 mmHg 145.8–151.5 mmHg
High screen time/high activity 148.1 mmHg 143.7–152.5 mmHg
Low screen time/high activity 144.3 mmHg 140.1–148.6 mmHg

Discussion: Even with high MVPA, high screen time was associated with a higher exercise BP (Table). In the present study, sitting (or totally inactive) time was associated with a higher exercise BP independent of the amount of physical activity.
Exercise training and 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 (6MWT) 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. It was 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

| Age (years) | 25.6±16.95 | 25.7±15.66 |
| BMI (kg/m²) | 32.9±10.16 | 31.6±8.36 |
| VO2 max (ml/kg/min) | 65.7±30.70 | 60±17.78 |
| Cognition function (MMSE's point) | 4.9±3.00 | 4.6±2.92 |
| Glycemia (mg/dl) | 112±1.72 | 190±66.79 |
| Hemoglobin (g/dl) | 11.4±1.32 | 12.8±1.33 |
| BMI, body mass index; VO2max, maximum volume of oxygen consumption; 6MWT, six minutes walk test; MMSE, Mini Mental State Examination.

Conclusion: We found that intradialytic training has a beneficial effect on functional capacity and cognitive function in CKD patients on HD.

Acknowledgement/Funding: FAPESP 2011/20652-7

P2705  |  BEDSIDE
Endothelium-dependent relaxation in patients cardio referred for cardiac rehabilitation
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Actual guidelines do not consider flow-mediated dilation as a first line diagnostic test in cardiac 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 could 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). A group of 211 patients with similar characteristics did not perform exercise training and were considered as controls. All patients were taking medications were not changed during the study. We considered exercise training and were considered as controls. All patients were taking

Results: EDDBA at baseline was abnormal in 77% of patients (PCI 69%, CABG 85%, Group A) and normal in 23% (Group N). At the end, in Group A, EDDBA improved in 81% of PCI pts and 83% of CABG patients (P<0.001 vs controls), while no changes were observed in Group N. The improvement in EDDBA was correlated with improvements in peak VO2 (r=0.62, P<0.001).

In conclusion, EDDBA was abnormal in 2/3 of patients after PCI or CABG at 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 (HFpEF).

Purpose: To evaluate the effect of IMW on exercise intolerance in patients with HFpEF.

Methods: The present study enrolled 40 patients with HFpEF (EF < 45%). IMW was defined as the percentage of maximum inspiratory pressure to normal predicted values < 70%. The function of the diaphragm was assessed by ultrasonic measurement of muscle thickening of the diaphragm.

Results: IMW was prevalent in 27.5% of patients. Patients with IMW had significantly lower percent 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).

Conclusions: In patients with HFpEF, IMW is associated with exercise intolerance, regardless of comorbid pulmonary dysfunction and peripheral skeletal muscle weakness.

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P2707  |  BEDSIDE
Determinants of exercise capacity in patients with preserved left ventricular ejection fraction and reduced left ventricular ejection fraction
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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: To evaluate 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 (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.

Results: Significant correlations were observed between age, Hb, BNP, A, e' as well as E/e' and pVO2 in patients with both preserved EF (r<−0.30, p<0.007, r<−0.33, p<0.006, r<−0.35, p<0.002, r<−0.42, p<0.001 and r<−0.41, p<0.001, respectively) and reduced EF (r<−0.65, p<0.001, r<−0.53, p<0.008, r<−0.41, p<0.01, r<−0.35, p<0.03, r<0.43, p<0.009, and r<−0.43, p<0.008, respectively). Furthermore, Vp and s were significantly correlated with pVO2 in patients with preserved EF (r<0.51, p<0.0001, r<−0.30, p<0.006, respectively) and those with IMW and reduced EF (r<−0.85, p<0.0002). In multivariate regression analysis, Vp (p<0.41, p<0.0002) and s' (p<0.16, p<0.02) 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 (p<0.30, p<0.03) and BNP (p<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.
P2708 | BEDSIDE
Usefulness of exercise testing in prediction of short-term outcome among patients with stable coronary artery disease
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Background: Impaired exercise capacity (EC) and heart rate responses to exercise are powerful independent predictors of cardiac risk in stable CAD.

Methods: Patients with angiographically verified stable CAD (n=1740, 67±8 years, 1199 men, 88% using β-blockers) underwent 12 minutes of exercise testing on cycle ergometer. Maximal chronotropic response index (CRI, heart rate response of 1 min post-exercise (HRR), % of maximal heart rate) were calculated from ECG recordings at supine rest, exercise and supine recovery. The EC was normalized using reference value based on age and sex. The lowest quartiles of EC, CRI and HRR were defined as abnormal.

Results: Twenty-two patients (1.3%) were hospitalized due to heart failure and 19 cardiac deaths (1.1%) occurred during the follow-up. All EC ≤95% (HR: 4.6, 95% CI: 2.1–10.0, CRI ≤54% (HR: 2.8, 95% CI: 1.3–6.2) and HRR ≤16% (HR: 3.4, 95% CI: 1.7–6.8) predicted the primary endpoint independently from each other (p <0.01 for all). The highest quartile of SCORE_Exe ≥8, 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). The CRI (ranging 0–108) and HRR (ranging 0–106) were not associated with the primary endpoint (HR: 1.01, p=0.8 and HR: 1.00, p=0.9). Maximal exercise capacity was measured using a validated device at rest, 2, 4 and 6 minutes following start of exercise. Exercise test risk score (SCORE_Exe) was calculated for each patient as a sum of hazard ratios (HR) in multivariate analysis which included all EC, CRI, HRR and shows the expected BP changes with exercise. The test is reproducible in terms of cardiorespiratory effort and perceived exertion but the "learning effect" is ~25% improvement in steps. Measures of cardiorespiratory effort and perceived exertion showed acceptable agreement with a 6MWT.

Conclusions: The double product reserve (DPR) is an indirect indicator of myocardial oxygen uptake and it has been known to be related to clinical outcome in patients with ischemic heart disease. However, the prognostic value of DPR in patients with idiopathic dilated cardiomyopathy (DCM) is not well known.

P2709 | BEDSIDE
A 6-minute stepper test (6-MST) is a feasible protocol for assessing exercise capacity in older adults which also allows physiological changes to be accurately monitored throughout exercise

Background: Assessment of exercise capacity and attendant physiological changes in population-based studies of older adults. Simple and time-efficient tests are more achievable than maximal tests but often involve ambulatory protocols that do not facilitate measurements of blood pressure (BP) or cardiorespiratory effort.

Methods: Participants (n=181; 116=male, age 71±6y) were invited to undertake a 6MST. Steps completed, time stepping and perceived exertion were recorded. Cardiorespiratory effort was monitored by portable gas analysis and BP was measured using a validated device at rest, 2, 4 and 6 minutes following start of exercise, and during recovery. 10 participants also completed a 6-minute walk test (6MWT) and VO2 test. Steps completed, measured exertion and VO2 were compared between the two 6MSTs and between the first 6MST and the 6MWT. Data are means±SD or means±SD of differences (Δ); a Student's t-test was used for comparisons.

Results: All participants agreed to undertake the 6-MST with 121 (67%) completing test. Men achieved a higher VO2 than women (152±27 versus 14.2±3.26mL/min/kg, p <0.001). Systolic BP was: 137±18, 163±23, 182±25 and 189±24mmHg at rest, 2, 4 and 6 minutes into exercise respectively. In repeat 6MST participants completed 53±56 steps more in the second test (p <0.02), but there was no significant difference in perceived exertion (Δ≤0.61±1.4, p =0.2), highest VO2 (Δ≤1.8±3.5mL/min/kg, p=0.2) or heart rate (Δ≤3±13bpm, p=0.5). Perceived exertion was similar in the first 6MST and the 6MWT (Δ≤0.95±2.36, p=0.2) with no significant difference in highest VO2 (Δ≤0.95±3.8mL/min/kg, p=0.2) or heart rate (Δ≤0.8±21bpm, p=0.2). Conclusion: The 6-MST is a feasible and acceptable method for assessing exercise capacity in older adults. It is sensitive to expected gender differences in VO2 and shows the expected BP changes with exercise. The test is reproducible in terms of cardiorespiratory effort and perceived exertion but the “learning effect” is ~25% improvement in steps. Measures of cardiorespiratory effort and perceived exertion showed acceptable agreement with a 6MWT.

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.

P2711 | BEDSIDE
Physically active lifestyle does not protect overweight and obese subjects from developing fatal or non-fatal cardiovascular event: The 10-year (2002-12) Follow-up of Attica Study
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Background: Obesity is linked to increased cardiovascular disease (CVD) risk, whereas physical activity is considered as protective against CVD development. Physical activity is also related to favorable metabolic effects, independently of the weight status of the subjects. Although, the combined effect of obesity and physically active lifestyle, has rarely been studied in prospective studies. The aim of this work was to explore the link between body mass, physical activity and 10-year incidence of CVD.

Methods: The ATTICA study was carried out in the Athens area during 2001–2002 and included 3042 participants free of CVD at baseline (49.8% men, aged 18–89). Body Mass Index (BMI) of the participants was calculated after measuring their weight and height. Overweight/obesity was defined as BMI equal or greater than 25kg/m². Physical activity status was assessed using the validated IPAQ-questionnaire. Inactive subjects were considered people with less than 2000mets/week. 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).

Results: Being overweight/obese and physically active was not proved protect...
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tive against CVD in comparison to overweight/obese and inactive lifestyle (Relative Risk (RR) unit →1.310, 95% CI: 0.858-2.002). Subjects that were simultaneously normal weight and physically active were protected against CVD by 45% as compared to overweight/obese and inactive subjects (RR=0.542, 95% CI: 0.323, 0.910). When age and gender were taken into account, the combined variable lost its significance, suggesting a potential mediating effect of age in this association (RR→0.600, 95% CI: 0.484, 1.522).

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 advise overweight and obese that losing weight is the first target for reducing CVD risk.

P2712 | BENCH
Aerobic exercise improves vascular insulin sensitivity by upregulating cholinergic anti-inflammatory pathway in spontaneously hypertensive rats

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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: Vascular insulin resistance contributes to elevated peripheral vascular resistance and subsequent hypertension. This study was designed to explore whether chronic aerobic exercise starting during the early stage of hypertension improves vascular insulin sensitivity and the underlying mechanisms.

Methods: Young (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 swimming training session (60 min/d, 5d/wk).

Results: SHRs exhibited higher systolic blood pressure, accompanied by increased systemic insulin resistance and vascular insulin resistance as evidenced by impaired vasodilator response to insulin in mesenteric arterioles compared with WKY rats. SHRs also exhibited elevated levels of inflammatory cytokines (TNF-α and IL-1β) and reduced expression of vesicular acetylcholine transporter (VACHT), α7 nicotinic acetylcholine receptor (α7nAChR) and phosphorylation of janus kinase 2 (Jak2) in mesenteric arterioles. Long term exercise training resulted in significantly reduced blood pressure and alleviated systemic insulin resistance as well as vascular insulin resistance in mesenteric arterioles in SHRs. Exercise also decreased inflammatory cytokines (TNF-α and IL-1β) and increased expression of VACHT, α7nAChR and phosphorylation of Jak2 in mesenteric arterioles in SHRs. Furthermore, chronic treatment with PNU-282987 (0.5 mg/kg/d), a selective α7-nAChR agonist, not only mimicked the effects of exercise in attenuating vascular insulin resistance and lowered blood pressure in SHRs but also reduced inflammatory cytokines and ROS in mesenteric arterioles of SHRs.

Conclusions: Long term exercise training starting at the early stage of hypertension alleviates hypertension through improving vascular insulin sensitivity in part via upregulating α7nAChR-mediated cholinergic anti-inflammatory pathway in SHRs.

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P2713 | BEDSIDE
The influence of short-term exercise training on QT dispersion and double product in diabetic patients after coronary artery bypass graft surgery

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Background: Patients with diabetes are at high risk of cardiovascular and arrhythmic events. QT dispersion (QTd) is a measure of inhomogeneous repolarization of myocardium and is used as an indicator of arrhythmogenicity. Abnormally high QTd has been correlated with risk of cardiac death in coronary patients.

Purpose: The aim of this study was to establish the influence of short-term exercise training on QT dispersion and double product (DP), in diabetic patients after coronary artery bypass graft surgery (CABG).

Methods: The study involved 165 patients after CABG, in the sinus rhythm without previous episodes of arrhythmias, suggesting a safety of our protocol. Average age of patients was 56.8 years. Fifty-two patients were with diabetes mellitus, and 113 were without diabetes. In all subjects clinical examination, standard ECG and exercise test on treadmill according to Bruce protocol, were performed and after that patients were included in program of physical training for three weeks. Patients were instructed to follow a training program using the bicycle ergometer (10 min, 2 times a day) and walking. The patients continued to take the same medicaments in same doses. From standard ECG corrected QT dispersion (QTdc) was calculated. Results: Before starting with the program of physical training, patients with diabetes had significantly higher values of QTdc (56.2±14.9 vs 49.7±17.1 ms; p<0.005), and significantly lower values of DP (11878.4±784.7 vs 2415.4±837.6 beat/min x mmHg; p<0.02) in comparison to those without diabetes. After three weeks, significant reduction of QTdc was found (from 56.2±14.9 to 49.7±17.1 ms; p<0.025 in patients with diabetes and from 47.0±17.1 to 41.0±16.9 ms; p<0.001 in patients without diabetes). After three weeks, significant reduction of DP was found (from 11878.4±784.7 to 11428.8±629.9 beat/min x mmHg; p<0.005 in patients with diabetes and from 11515.4±837.6 to 10120.9±535.7 beat/min x mmHg; p<0.001 in patients without diabetes).

Conclusions: The study showed that patients with diabetes have a higher value of QTdc, probably due to diffusional fibrosis. Short-term exercise training has a favourable effects on QT dispersion and double product in patients after CABG.

In patients without diabetes physical training had more favourable effects on the followed parameters. Physical training led to the significant decrease of myocardial oxygen uptake at rest and probably decreased the possibility of arrhythmic events.

DECREASING CARDIOVASCULAR RISK IN VULNERABLE POPULATIONS

P2714 | BEDSIDE
The association of statin adherence and in-stent restenosis

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Background: Half of patients discontinue statin therapy within the first year, and adherence decreases during follow-up period. However data about the effects of statin treatment on stent restenosis is conflicting and no studies have described the relationship between statin adherence and in-stent restenosis (ISR).

Purpose: In our study, we therefore investigated the statin adherence and ISR among percutaneous coronary intervention patients (PCI) who were prescribed a statin at discharge.

Methods: We retrospectively analyzed 908 patients whom underwent bare-metal stent implantation and have been performed control coronary angiography (CA) also have continuous insurance coverage between PCI and CA to determine statin adherence. We used the pharmacy-based proportion of days covered (PDC) to quantify statin adherence during the period between PCI and control CA.

Results: Percentage of patients adherent to statin according to prescription records (≥80% PDC for statins, was 26%) in the ISR (+) group and 33% in the ISR (-) group (P<0.03). In multivariate logistic regression analysis, statin adherence was an independent predictor of ISR (OR=2.04, CI (1.01–4.13), p<0.04).

Conclusion: The principal findings of our study were (1) statin non-adherence 1 year after PCI was higher compared with other studies and (2) statin non-adherence in patients with PCI was associated with increased ISR.

P2715 | BEDSIDE
A community pharmacy-based cardiovascular risk screening service implemented in a resource-limited country

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Background: Effective cardiovascular risk screening is one of the strategies to reduce the burden of cardiovascular diseases (CVD). The role of community pharmacies in such screening services needs further investigation particularly in resource-limited countries.

Purpose: To assess the feasibility and effect of a pharmacy-based cardiovascular screening in an urban referral community pharmacy in Iran.

Methods: In a cross sectional study, 287 clients aged between 30–75 years without previously diagnosed CVD, diabetes or recent health check-up for blood glucose and lipid profile were screened. The screening service was free of charge and was advertised by means of posters inside and at the entry point of the pharmacy. Measurement of all major cardiovascular risk factors (BP, lipid profile, blood glucose), exercise habits, existing medical conditions and medications, family history, was performed by the investigator (student pharmacist). Framingham risk score was calculated and high risk individuals were given a clinical summary sheet signed by the investigator and were encouraged to follow up with their family physician. Each client was contacted one month after recruitment and their adherence to the follow up recommendation were documented.
Results: Data from 287 participants were analyzed: 209 (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, 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 7.8±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.

Conclusions: 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 adherence 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 subcutaneous and visceral fat distribution, liver steatosis, insulin sensitivity and beta-cell function after comparable weight loss

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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: Given the concurrent effects acknowledged for GLP-1 agonists 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-six morbidly 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 whether changes in subcutaneous (SAT) and visceral (VAT) adipose tissue distribution and in degree of non-alcoholic fatty liver disease (NAFLD) (all assessed by MRI) after a modest and comparable weight loss (7% of initial body weight), might affect insulin sensitivity (Matsuda Index) and β-cell performance (by Insulin Secretion-Sensitivity Index-2 (ISSI-2)) during multiple sampling oral glucose tolerance test.

Results: SAT and NAFLD grade were significantly and comparably reduced in both treatment groups, whereas insulin sensitivity was not significantly affected by any intervention. In contrast, the liraglutide group showed a significantly greater reduction in median VAT (p<0.001), as compared to the lifestyle group (~13.3% vs. ~7.3%) and a greater improvement in beta cell function (ISSI-2) (109% vs. 29.9%, p=0.006), which translated into a significantly more pronounced reduction in both fasting, 1-hour and 2-hour postprandial plasma glucose, despite comparably reduced HbA1c in both groups (by 7.1%). In the liraglutide group, the taxol-like arm, VAT values were significantly and inversely related to ISSI-2 (r=−0.60, p=0.023) throughout the intervention period.

Conclusions: This pilot study may help establishing a cause-and-effect relationship between VAT inflammation, beta cell performance and development or progression of T2DM, unravelling as well potential mechanisms by which liraglutide may favourably impact T2DM pathogenesis and natural history.

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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 cardiovascular risk patients from Brazil, a middle income country.

Methods and results: REACT is a multicenter registry that aims to document adherence to evidence-based therapies and clinical outcomes in patients at high cardiovascular risk,1,2 Patients eligible if they were over 45 years with or at risk for atherothrombotic disease. From March 2012 to May 2013, 3145 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 risk.

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: Analysis of 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 Metropolitan Students (MaxMet) estimating CRF and Hospital Anxiety and Depression Sub-Scale (HADS-D) measuring depression.

Results: Of the 438 subjects with mean age 58.0±8.34, 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 strength of association was significant for female participants (p<0.13, P=0.0098) and EOP (p<0.10, p=0.0507), however, no significant correlation was found between change of METmax and HADS-D at EOP (p=0.5587, 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>MaxMet change in METmax</td>
<td>1.83 (0.20)</td>
<td>1.45, 1.77</td>
</tr>
<tr>
<td>MaxMet change in HADS depression score</td>
<td>-1.26 (0.19)</td>
<td>-1.89, -1.29</td>
</tr>
<tr>
<td>MaxMet change in HADS anxiety score</td>
<td>-1.15 (0.14)</td>
<td>-1.43, -0.86</td>
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<td>MaxMet change in Dartmouth Co-op</td>
<td>-2.99 (0.20)</td>
<td>-3.39, -2.57</td>
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<tr>
<td>MaxMet change in EQ-VAS</td>
<td>11.22 (1.71)</td>
<td>8.91, 13.52</td>
</tr>
<tr>
<td>MaxMet change in BMI</td>
<td>-1.3 (0.07)</td>
<td>-1.45, -1.15</td>
</tr>
</tbody>
</table>

Conclusion: Small negative correlations between METmax and HADS-D were demonstrated at IA and EOP, indicating as CRF increases, depression decreases. However, this association was not evident when investigating a change over time. Potentially, due to relatively low prevalence of depression at baseline and change in METmax or HADS-D at EOP was not great enough to show significant correlations. Analysis over a longer time period is recommended to investigate this association further.

P2719 | BEDSIDE

Long-term administration of eicosapentaenoic acid prevents the progress of left ventricular hypertrophy via reducing oxidative stress and advanced glycation end-products in patients with hypertension

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Background: Elevated oxidative stress has been shown to promote the production of advanced glycation end-products (AGEs) in patients with hypertension (HT). AGEs are known to enhance left ventricular hypertrophy (LVH) via the acti-
Adherence to Mediterranean diet protects against cardiovascular disease independently of creatinine clearance rate: the 10-year Follow-up of Attica study

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Background: 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.

Methods: 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. The analysis was stratified according to tertiles of MedDietScore, where no trend was observed.

Results: 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.

Conclusion: Adherence to Mediterranean diet protects against cardiovascular disease independently of creatinine clearance rate: the 10-year Follow-up of Attica study.

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

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Background: Decreasing cardiovascular risk 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 per se has rarely been studied. The aim of this 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 (9% lost-to-follow-up).

Results: Having creatinine clearance rate greater than 60ml/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. The analysis was stratified according to tertiles of MedDietScore, where no trend was observed.

Results: 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.

Conclusion: Adherence to Mediterranean diet protects against cardiovascular disease independently of creatinine clearance rate: the 10-year Follow-up of Attica study.
**P2724 | BEDSIDE**

**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 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>94cm and women >80cm 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 potential to other cardiac-metabolic disorders as well.

**P2725 | BEDSIDE**

**Effectiveness of the EUROACTION PLUS (EA+) preventive cardiology programme for high CVD risk smokers in modifying dietary habits and anthropometric indices**

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**Purpose:** To investigate the effectiveness of the EA+ programme of intensive smoking cessation, with optional use of varenicline, in improving diet and anthropometric indices as part of reducing overall cardiovascular risk.

**Methods:** To investigate the effect of long term adherence to MD on ten-year diabetes incidence, and examine inflammatory and oxidative stress biomarkers as candidate mediators of this relationship.

**Results:** During the follow-up period 66 subjects presented the primary composite endpoint. There was no difference in age (p=0.54), serum creatinine levels (p=0.50), body mass index (p=0.84), diabetes mellitus (p=0.33) and hypertension (p=0.54), between the subjects who presented the primary end point compared to subjects free of cardiovascular events. Interestingly, subjects who presented the primary end point compared to those free of cardiovascular events were more often active smokers (28% vs. 15%, p=0.03), had higher prevalence of 3 vessel CAD (p=0.03) and lower left ventricle ejection fraction (p=0.07). A cox regression model revealed that after adjustment for the aforementioned confounders 3VD was associated with adverse cardiovascular outcome (Hazard ratio=3.14 95% CI: 1.19–8.27, p=0.02). Interestingly, when in the model was added a favorable pattern of diet (revealed by principal components analysis) it was observed that high consumption of olive oil and low consumption of seed oil or animal or vegetable fats increased the hazard of adverse cardiovascular outcome (Hazard ratio=0.70 95% CI: 0.49–0.99, p=0.047).

**Conclusions:** In subjects with CAD after PCI a favorable pattern of diet with increased consumption of olive oil and low consumption of seed oil or animal or vegetable fats can decrease the hazard of adverse cardiovascular outcome.

FROM TECHNICALITIES TO PROGNOSIS IN PCI

**P2726 | BEDSIDE**

**Comparison of long term clinical outcomes between bare metal stent versus different types of drug eluting stents for treatment of acute myocardial infarction**


**Background:** There is paucity of data to exclusively evaluate the safety and efficacy of bare metal stent (BMS) and recently developed different types of drug eluting stents (DES) in the setting of AMI. The purpose of this study was to compare the clinical outcome of four different types of coronary stent including BMS, 1st generation DES, 2nd generation plus new generation DES, and most recently biodegradable polymer-coated stent in treatment of acute myocardial infarction.

**Methods:** Using data from Korea Working Group on Myocardial Infarction, a total of 11,530 patients who were diagnosed with acute myocardial infarction, had PCI and received stent were included. They were divided into four groups according to the type of coronary stent (Figure 1). We compared the baseline characteristics between the four groups.

**Results:** During follow-up period 66 subjects presented the primary composite endpoint. There was no difference in age (p=0.54), serum creatinine levels (p=0.50), body mass index (p=0.84), diabetes mellitus (p=0.33) and hypertension (p=0.54), between the subjects who presented the primary end point compared to subjects free of cardiovascular events. Interestingly, subjects who presented the primary end point compared to those free of cardiovascular events were more often active smokers (28% vs. 15%, p=0.03), had higher prevalence of 3 vessel CAD (p=0.03) and lower left ventricle ejection fraction (p=0.07). A cox regression model revealed that after adjustment for the aforementioned confounders 3VD was associated with adverse cardiovascular outcome (Hazard ratio=3.14 95% CI: 1.19–8.27, p=0.02). Interestingly, when in the model was added a favorable pattern of diet (revealed by principal components analysis) it was observed that high consumption of olive oil and low consumption of seed oil or animal or vegetable fats can decrease the hazard of adverse cardiovascular outcome.

**Conclusions:** In subjects with CAD after PCI a favorable pattern of diet with increased consumption of olive oil and low consumption of seed oil or animal or vegetable fats can decrease the hazard of adverse cardiovascular outcome.

**Figure 1. Study algorithm**
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 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 Cardiac Registry (n=17,746). We analyzed mortality and target vessel revascularization (TVR) at 2 years. Cox multivariate models were used to determine predictors for outcomes. To address bias due to measured and unmeasured confounders, propensity-matched analyses and instrumental variable (IV) analyses were performed.

**Results:** A total of 9,918 patients (56%) received E-ZES and 7,828 patients (44%) received R-ZES. Compared to E-ZES, R-ZES was associated with lower 2-year mortality (4.1% vs. 6.4%, p<0.001) and 2-year TVR (6.8% vs. 10.7%, 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 significant predictor for one year MACE (Odds ratio of 1st, 2nd+new generation, 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 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.

**P2728 | BEDSIDE**

Quantification and management of thrombus burden during primary PCI: limitations of angiography demonstrated with optical coherence tomography imaging


**Background:** Up to now, thrombus aspiration (TA) during primary PCI is customarily performed under angiographic guidance both in clinical practice and clinical trials. However, optical coherence tomography (OCT) constitutes the current reference standard for the assessment of coronary thrombus. Existing evidence suggests that optimising thrombus reduction might improve PCI outcomes.

**Purpose:** Use of OCT to assess the ability of angiography 1) to quantify thrombus burden during primary PCI, 2) to identify remnant thrombus deserving repeat thrombus aspiration (re-TA), and 3) to appreciate modifications in thrombus burden driven by re-TA.

**Methods:** In a series of acute STEMI patients OCT was used to assess the pathological substrate and guide aspiration to reduce thrombus burden during primary PCI. Thrombus burden was quantified by angiography using TIMI Thrombus Grade score (TTG) and by OCT using a quadrant count at each 0.4mm interval (Kajender et al. EHJ 2014). These methods were compared to each other at baseline assessment and after aspiration (re-TA, balloon dilation). Data is expressed as median [interquartile range].

**Results:** A total of 55 consecutive acute STEMI patients were included. Baseline OCT was defined as that performed either after a first thrombus aspiration to achieve reperfusion (n=45, 82%) or, if flow was adequate, prior to any interventional therapy (n=10, 18%). The relationship between angiographic and baseline OCT-based thrombus burden was poor (Kendall’s τ =0.23, p=0.03) by angiography median TTG was 1 [0–3], and OCT revealed 29 [8–42] thrombotic quadrants. Based on the presence of significant remnant thrombus in OCT (32 [20–42] quadrants) by the operator, repeat TA (re-TA) was performed in 26 patients. Although the remaining patients presented significantly lower thrombus burden by OCT (15 [5–42] p=0.048), angiography could not differentiate between both groups in terms of thrombus burden (TTG 1.5 [0–3] in re-TA and 1 [0–2] in non-re-TA groups, p=NS). OCT-guided re-TA led to a significant reduction in thrombus burden (from 31.5 to 23.5 quadrants, p=0.01). Again, angiography could not depict the reduction in thrombus burden associated with re-TA (from 1 to 1 TTG, p=NS).

**Conclusions:** Use of OCT during primary PCI demonstrates that angiography constitutes a suboptimal tool 1) to quantify remnant thrombus burden, 2) to select patients that might benefit from further actions aimed at thrombus reduction such as re-TA, and 3) to estimate the effect of such actions on thrombus burden.

**P2729 | BEDSIDE**

Single string technique for complex coronary bifurcation stenting

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**Aims:** Double-stent techniques may be required for complex bifurcation lesions. Currently applied methods all have their morphologic or structural limitations. The study aims to evaluate the adequacy and feasibility of Single String bifurcation stenting technique.

**Methods:** Single String is a novel stenting technique for complex bifurcation lesions, where first the side branch (SB) stent is deployed with one single proximal stent-cell protruding into the main branch (MB). Second, the MB is rewired through that protruding stent-cell and a stent is deployed into the MB across it. Procedure is completed by final kissing balloon dilation. Single String was tested in vitro (n=20) and next applied in patients (n=11) with complex bifurcation stenoses.

**Results:** All in vitro procedures were performed successfully, crossing the most proximal stent-cell in 100%. Duration of the procedure was 23.0±7.5 minutes, fluoroscopy time was 9.4±3.5 minutes. Result was evaluated by OCT, showing fully apposed struts in 83.0±9.2%. Residual area obstruction in the MB was 6.4±5.6% or 9.4±3.5 minutes. Result was evaluated by OCT, showing fully apposed struts in 83.0±9.2%. Residual area obstruction in the MB was 6.4±5.6%

**Conclusions:** In this large analysis of patients receiving ZES, R-ZES was associated with lower long-term mortality and TVR, even when adjusting for measured and unmeasured confounding. These real-world data are reassuring and demonstrate the better safety and anti-restenotic profile of R-ZES.

**Figure 1**

KM curves for propensity-matched cohorts

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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-dimentional QCA. No relevant peri-procedural enzyme rise was observed. During follow-up (14±5 months) no adverse clinical event (death, MI, TVR) was noted.

**Conclusion:** Single String technique for complex bifurcation lesions is shown to be adequate in vitro and feasible in humans with favorable results in terms of stent overlap, malapposition rate and low residual obstruction in both MB and SB.

**P2730 | BEDSIDE**

**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 nano size pores surface sirolimus eluting.

**Methods:** In this prospective, multicentre, open-label study, patients were enrolled with documented stable angina or silent ischemia and planned intervention 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.

**Results:** 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 at 12 months was 3.9% with MBP-DES and 4.7% with BVS (p=0.4).

**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

**P2732 | BEDSIDE**

**Comparative study with optical coherence tomography at 6 and 12 months between drug-eluting stents with resorbable polymer and drug-eluting scaffolds with full bioresorbable platform**

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**Background:** Bioresorbable everolimus-eluting scaffolds (BVS) and metallic drug-eluting stents with biodegradable polymers (MBP-DES) have shown positive clinical results in studies. Direct comparative evaluation between both for the process of endothelialization is lacking and could be relevant to define their safety profile and subsequently estimate the appropriate duration of dual antiplatelet therapy.

**Purpose:** In this study we sought to evaluate endothelization of BVS and MBP-DES (with everolimus, sirolimus or biolimus) implanted both in comparable lesions of the same patient, with OCT performed at 6 and 12 months follow-up.

**Methods:** Multicenter (15 centers) prospective study. Patients were recruited from technicalities to prognosis in PCI 477

**Results:** To date 82 patients have been included (37 with BVS+everolimus MBP-DES, 27 with BVS+sirolimus MBP-DES and 18 with BVS+biolimus 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).

**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

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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 (2 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 undergoing 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)
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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±0.60. The incidences of MACE and definite stent thrombosis at 12 months were 4.1% and 0.2% respectively. On multivariate cox regression analysis, age and current smoker were independent predictors of cardiac death with high rate of mortality and late thrombosis and in propensity-matched cohorts demonstrated that F-DES was not associated with mortality at 3 years (HR=1.00, 95% CI: 0.88–1.14, p=0.975), but was an independent predictor for increased TVR at 3 years (HR=1.21, 95% CI: 1.08–1.35, p=0.001). These findings were confirmed in propensity-matched cohorts (n=18,135) where F-DES was not associated with mortality at 3 years (HR=1.05, 95% CI: 0.93–1.19, p=0.215), but predicted increased TVR at 3 years (HR=1.18, 95% CI: 1.08–1.28, p<0.001). Subgroup analyses in both unmatched and propensity matched cohorts demonstrated that F-DES use was not a predictor for TVR in patients with age >80 years, diabetes, renal disease, ACS or stent length >30mm, but did predict TVR where stent diameter <3mm.

Conclusions: In this real-world study of unselected patients receiving DES, the use of S-DES did not confer a mortality benefit over F-DES, indicating comparable long-term safety profiles. However, S-DES use was associated with a significant reduction in long-term TVR. These data are reassuring for the newer generation DES across a broad clinical population.
P2737 | BEDSIDE
Simple versus complex drug-eluting stenting for coronary bifurcation lesions: an updated meta-analysis of randomized controlled trials
Background: Percutaneous coronary intervention (PCI) on coronary bifurcation lesions has been considered a challenging procedure for interventionists. However, the optimal stenting strategy for bifurcation lesions is still unclear in the era of drug-eluting stents (DES).
Methods: Randomized controlled trials (RCTs) were identified through search of MEDLINE, EMBASE, and the Cochrane databases (2004 through January 2015). Outcomes assessed were mortality, myocardial infarction (MI), target vessel revascularization (TVR), definite stent thrombosis, and angiographic restenosis at the longest follow-up.
Results: A total of ten RCTs including 2,941 patients were included in this meta-analysis. No statistically significant difference in the risk of death (odds ratio [OR] 0.86, 95% confidence interval [CI] 0.41–1.84, p=0.70) was detected between simple versus complex stenting groups. Simple stenting strategy was associated with significantly lower incidence of recurrent MI (OR 0.60, 95% CI 0.39–0.90, p=0.01) with a trend toward lower definite stent thrombosis (OR 0.50, 95% CI 0.23–1.07, p=0.07). On the other hand, simple stenting strategy significantly increased risk of TVR (OR 1.47, 95% CI 1.06–2.04, p=0.02) and side branch restenosis (OR 1.80, 95% CI 1.33–2.43, p<0.001) as compared with complex stenting strategy. The cumulative analysis of the included studies depicts the summary ORs of recently published studies favoring complex stenting in terms of angiographic restenosis (Figure).

Conclusions: Simple stenting strategy was associated with reduced incidence of MI and stent thrombosis as compared with complex stenting strategy. However, benefits of simple stenting were offset by increased risk of angiographic restenosis and TVR. Both stenting strategies were comparable in terms of mortality.

P2738 | BEDSIDE
Correlation of strut thickness with SF
Background: Stent fracture (SF) after drug-eluting stent (DES) implantation is reported to be related to adverse cardiac events.
Purpose: To compare the correlation of the incidence of SF after implantation of various DES types with strut thickness between de novo and in-stent restenosis (ISR) lesions.
Methods: The study population comprised 13,669 lesions (5842 patients) which underwent DES implantation from 2002 to 2014 and follow-up angiography within one year after index procedure. SF was defined as the separation of stent segments or struts at follow-up angiography. The drug types, trade names, and strut thicknesses of the DES types were as follows: sirolimus, Cypher Bx (140 μm) and Cypher (140 μm); paclitaxel, Taxus Express (132 μm) and Xience Prime/Xpedition (81 μm) and Xience (81 μm); everolimus, Xience (91 μm) and Biomatrix (120 μm) and Promus element (81 μm).
Results: The incidence of SF was 3.7% (512/13,669) of the lesions: de novo, 3.5% (415/12,006) vs. ISR, 5.8% (97/1663), and that of each DES type was as follows: Cypher Bx, 5.9% vs. 5.3%; Cypher select, 3.3% vs. 11.1%; Taxus Express, 3.5% vs. 7.3%; Taxus Liberte, 2.3% vs. 0%; Endovar, 1.7% vs. 8.3%; Resolute Integrity, 0.5% vs. 5.6%; Xience V, 1.7% vs. 4.8%; Xience Prime/Xpedition, 0.3% vs. 1.4%; Nobori, 3.8% vs. 2.4%; and Promus element, 0.9% vs. 6.2%. There was a strong and significant correlation between the incidence of SF and strut thickness of each DES type in de novo lesions (r=0.884, p<0.001) but not in ISR lesions (r=0.449, p=0.17). See figures.
Conclusion: Strut thickness can be strongly correlated with the incidence of SF after DES implantation in de novo lesions.

P2739 | BEDSIDE
Predictors of late restenosis following paclitaxel-coated balloon angioplasty in patients with in-stent restenosis
Background: There are currently inadequate data on whether “late restenosis” occurs after paclitaxel-coated balloon (PCB) angioplasty for in-stent restenosis (ISR) lesions. To evaluate the long-term efficacy of PCB angioplasty, we investigated serial clinical and angiographic outcomes after PCB angioplasty for ISR lesions.
Methods and results: Between September 2008 and December 2012, PCB (Sequent Please) angioplasty was performed in 468 patients with 550 ISR lesions [bare-metal stent restenosis (BMS-ISR): 101 lesions, drug-eluting stent restenosis (DES-ISR): 436 lesions]. Two serial angiographic follow-ups were routinely planned for the patients (at 6 and 18 months after the procedure). Early follow-up (6 months) angiography was performed for 488 lesions (89%), and recurrent restenosis occurred in 13 lesions (14.9%) in the BMS-ISR group and in 82 lesions (21.1%) in the DES-ISR group. Target lesion revascularization (TLR) was performed for 7 lesions (7.0%) in the BMS-ISR group and 54 lesions (13.9%) in the DES-ISR group. Late follow-up (18 months) angiography was performed for 377 (88%) of the remaining 427 lesions (excluding TLR lesions), and late restenosis was found in 2 lesions (2.5%) in the BMS-ISR group and 50 lesions (16.8%) in the DES-ISR group. Previous stent size ≤2.5mm (OR: 1.93, CI: 1.19 to 3.16, p=0.007), percentage diameter stenosis after the procedure >35% (OR: 1.92, CI: 1.17 to 3.14, p=0.01), and in-stent occlusion lesion (OR: 2.74, CI: 1.18 to 6.10, p=0.02) were independent predictors of early restenosis. DES-ISR (OR: 4.18, CI: 1.82 to 14.3, p=0.002) and hemodialysis (OR: 2.57, CI: 1.13 to 6.06, p=0.04) were independent predictors of late restenosis.
Conclusions: Risk factors of recurrent restenosis after PCB angioplasty for ISR lesions vary depending on the period of time after the procedure.

P2740 | BEDSIDE
Impact of a dedicated chronic ootal occlusion (CTO) programme on procedural success among specialist and non-specialist operators: a single centre experience
Background: Chronic total occlusions (CTO) represent a major challenge in percutaneous coronary interventions (PCI). Developments in techniques and technologies have significantly improved procedural success rates following CTO PCI among trained high volume operators and many centers have developed specialist CTO programmes.
Purpose: We sought to investigate the impact of a dedicated CTO PCI programme on procedural outcomes among both specialist (sCTO) and non-specialist (nsCTO) operators.
Methods: We prospectively evaluated 206 consecutive CTO interventions performed over a 2 year period by 2 sCTO and 16 nsCTO operators. The designated sCTO operators underwent training with experienced providers and subsequently developed a dedicated CTO service over a period of 3 years prior to the commencement of the present study. A CTO lesion was defined as a complete occlusion of the coronary vessel with TIMI 0 flow, present for >3 months. The J-CTO score was used to classify lesion complexity and stratify them into 4 groups: easy (J-CTO 0–1), intermediate (J-CTO 2), difficult (J-CTO 3) and very difficult (J-CTO 4–5).
Results: The sCTO operators performed 137 and the nsCTO operators 69 CTO interventions. Overall success rate per patient was 88% in the sCTO and 54% in the nsCTO group (p<0.01). The mean J-CTO score was 2.2 and 1.0 for the sCTO and nsCTO groups respectively (p<0.01). No J-CTO 4–5 cases were attempted by the nsCTO group. The success rates between sCTO and nsCTO groups differed significantly among different subgroups: 100% vs 67% (J-CTO 0–1), 93% vs 20% (J-CTO 2), 89 vs 17% (J-CTO 3) respectively (p<0.001).
Microcatheter support was used in 100% of the sCTO cases and in 29% of the nsCTO cases, while dual vascular access for retrograde visualisation was used in 96% and 13% of the cases respectively. Antegrade wire escalation (AWE) was the single utilised approach in the nsCTO group. The successful strategy for lesion crossing in the sCTO group was AWE (54%), retrograde dissection re-entry (26%), and retrograde dissection re-entry (16%) or retrograde escalation by 5%.

Conclusions: A dedicated CTO programme with high volume specialist operators is associated with higher procedural success rates. Significantly lower success rates among nsCTO operators were predominantly driven by more complex cases (J-CTO). Complex CTO PCI should be undertaken by specialist operators. The success rates of non-specialist operators in “easy” CTO lesions could be improved with training from specialist operators in optimal antegrade wiring techniques, including use of microcatheters and dual catheter angiography.

P2741 | BEDSIDE
Do optimal lesion preparation reduce the amount of acute recoil of the Absorber® BVS?
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Background: In vivo acute recoil of the ABSORB bioabsorbable vascular scaffold (BVS) was evaluated in selected patients.

Objectives: To evaluate the acute recoil of the BVS and its relationship with procedural characteristics in a real world population.

Methods: Acute recoil was studied with videodensitometry in a consecutive series of patients treated by means of a BVS, and the results were compared with those obtained in subjects receiving an everolimus-eluting stent (EES). Recoil was defined as the difference between the mean diameter of the fully expanded balloon on which the device was mounted (or the mean diameter of the post-dilatation balloon), and the mean luminal diameter of the treated segment immediately after the final inflation.

Results: Recoil was assessed in 166 lesions treated with a BVS and 71 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=0.355; 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.

P2742 | BEDSIDE
Early experience implanting a polymer-free biolimus A9 drug coated stent in complex real world patients from two United Kingdom centers
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Introduction: Prolonged dual anti-platelet therapy (DAPT) exposes patients to the risk of major bleeding, and is undesirable in certain patients. A polymer-free drug-coated stent in complex real world patients from two United Kingdom centers. Stent choice was at the interventional cardiologist’s discretion. For comparison the outcomes of 204 consecutive patients treated with a Biomatrix polymer-free drug-coated stent was evaluated in selected patients.

Objectives: To evaluate the acute recoil of the BVS and its relationship with procedural characteristics in a real world population.

Methods: Acute recoil was studied with videodensitometry in a consecutive series of patients treated by means of a BVS, and the results were compared with those obtained in subjects receiving an everolimus-eluting stent (EES). Recoil was defined as the difference between the mean diameter of the fully expanded balloon on which the device was mounted (or the mean diameter of the post-dilatation balloon), and the mean luminal diameter of the treated segment immediately after the final inflation.

Results: Recoil was assessed in 166 lesions treated with a BVS and 71 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=0.355; 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.

P2743 | BEDSIDE
First-in-man (FIM) evaluation of a novel balloon delivery system for the self-apposing coronary artery stent
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Background: Longitudinal geographic miss, which is described as failure to fully cover the injured or diseased arterial segment with a stent, is associated with an increased rate of adverse events. Therefore, the novel balloon delivery system (BDS) for the self-apposing STENTYS® Xposition Sirolimus eluting stent (SES) was developed for highly precise longitudinal stent positioning and deployment.

Objective: To evaluate the longitudinal geographic miss and angiographic outcomes of the SES, based on quantitative coronary analysis and optical coherence tomography (OCT) in a first-in-man study.

Methods: We included 25 patients with de novo coronary lesions in all indications for PCI. Patients with lesions <25mm in length with a reference vessel diameter of 2.5 - 6.0mm were eligible. All patients underwent PCI using the SES. Longitudinal angiographic success was defined as a final residual stenosis of less than 20 percent by visual estimation and Thrombolysis In Myocardial Infarction (TIMI) 3 flow on the final angiogram. OCT was performed directly 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 determine acute gain and longitudinal geographic miss.

Results: 25 patients (mean age 66±1.0 years) were included. Indication for PCI was STEMI in 7 (28%) patients. Non-STEMI in 1 (4%) patient, stabilized STEMI in 12 (48%) patients, stable non-STEMI in 8 (32%) patients and stable angina in 6 (24%) patients. Stent crossing of the lesion and deployment of the SES was successful in all patients, without any procedural complications. Angiographic success could be achieved in all patients (100%). As assessed by QCA, pre-procedural MLD was 1.30±0.74mm, and 2.74±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=0.013). Mean stent area increased significantly from 9.7±7mm2 post stent placement to 10.5±7mm2 (.p=0.001).

Conclusion: This first-in-man experience demonstrates that intra-coronary deployment of the SES is feasible with a high angiographic success-rate and no longitudinal geometrical miss on QCA. Stent malapposition directly after STENTYS implantation is low. Balloon post-dilation could further improve stent strut apposition in SES.

P2744 | BEDSIDE
Simplified vascular closure device deployment without an arteriogram: single center experience in over 2000 consecutive patients
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Background: After coronary procedures performed via a transfemoral approach, prolonged manual compression at the femoral site after sheath removal, followed by extended bed rest imposes serious burden on both patients and hospital staff. Availability of vascular closure devices (VCDs), eg. Angioseal, has greatly facilitated routine clinical practice in the cath lab. The manufacturer recommends a local angiogram before Angio-seal deployment. However, from the outset we employed a simplified routine for VCD deployment, i.e. without use of local angiography.

Aim: To prospectively assess the effectiveness and safety of Angio-seal angiography and/or percutaneous coronary intervention (PCI) without use of local angiography.

Patients and methods: The Anglo-Seal was employed over 8 years in 2066 consecutive patients, 72% presenting with acute coronary syndromes and subacute coronary artery disease (n=1024) or PCI procedures (n=1042) via a transfemoral approach. All patients undergoing PCI were given 7,000 IU of heparin during PCI and loaded with dual antiplatelet therapy (aspirin and clopidogrel). A minority (14.4%) also received a platelet glycoprotein IIb/IIIa inhibitor. Sheaths were removed at the end of the procedure and hemostasis achieved with use of Angio-seal.

Results: VCD deployment was successful in 99.4%. Complete hemostasis without local bleeding or hematoma or vessel occlusion was obtained in 98.7% of cases. In 13 patients Angio-Seal could not be or was partially deployed. The mean time required for placement of Angio-Seal was <1 min. The mean-
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 ultrasound-guided compression. In addition, 8 small to moderate and 2 large inguinal hematomas (one requiring blood transfusion) were recorded. In 5 cases retroperitoneal bleeding occurred, requiring blood transfusion in 2. Local infection or arteriovenous fistulae were not observed.

Conclusion: Deployment of Angio-Seal without use of local angiography was effective 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.

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 strut-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).

P2745 | BEDSIDE
Three-year outcome after biolimus-eluting versus sirolimus-eluting coronary stent implantation in diabetic and non-diabetic patients - a SORT OUT V substudy
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Introduction: Long-term outcome after coronary drug-eluting stent implantation may still be significantly between drug-eluting stents in diabetic and non-diabetic patients. The SORT OUT V trial is a prospective, all-caser, multicentre, randomized, clinical trial which compared a biolimus-eluting stent (Nobori; BES) using a biodegradable coating with a sirolimus-eluting stent (Cypher Select; SES) with a durable coating.

Purpose: To compare 3-year clinical outcomes in diabetic and non-diabetic patients treated with BES versus SES.

Methods: Routine clinical care patients were randomized in a 1:1 ratio to receive either BES or SES. The patients were stratified according to presence/absence of diabetes mellitus. Clinical endpoints included MACE, a composite of safety (cardiac death, myocardial infarction, definite stent thrombosis) and efficacy (target vessel revascularization (TVR)). Coo's proportional hazard regression analysis was used to estimate hazard ratios during entire 36-month follow-up and in landmark analyses of 1–12–36 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 0.97, 95% CI 0.47–1.98, p=0.90]. 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 bioabsorbable 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: From January 2004 to May 2013, 12304 lesions in 6314 patients were treated exclusively with DES and 8-month follow-up angiography was performed. SF was defined as separation of stent segments or stent struts.

Results: Of 803 patients with 1050 lesions undergoing Pcir-EES implantation between March 2012 and August 2013 were analyzed. LSD was defined as the distoration 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. 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.

Conclusions: A total of 803 patients with 1050 lesions undergoing Pcir-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.

Methods: 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 balloon (n=8, 66.7%) and pull back jailed guide wire (n=3, 25%). At 1-year, the cumulative incidence of MACE, cardiac death, myocardial infarction, stent thrombosis and clinically driven target lesion revascularization were not significantly different between the LSD and non-LSD groups (9.1% vs. 2.8%, p=0.019, 0% vs. 0%, p=1.00, 0% vs. 0.1%, p=0.92, 0% vs. 0.14%, p=0.88, 9% vs. 2.8%, p=0.019, respectively).

Conclusions: LSD after Pci-EES implantation occurs in 1.1% of lesions. However, LSD is not associated with MACE within 1-year.

P2747 | BEDSIDE
The incidence of stent fracture after drug-eluting stent implantation: comparison between de novo lesion and in-stent restenosis lesion

Aims: The incidence of stent fracture (SF) after drug-eluting stent (DES) implantation was compared between de novo lesions and in-stent restenosis (ISR) lesions.

Methods and results: From January 2004 to May 2013, 12304 lesions in 6314 patients were treated exclusively with DES and 8-month follow-up angiography was performed. SF was defined as separation of stent segments or stent struts.
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 January 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), 107 patients had 110 lesions with multiple DES without stent overlap (44 BES and 63 CoCr-EES), and 1565 patients had 1382 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 without multiple DES without stent overlap and with single DES (12.0% vs. 10.9% vs. 5.1%, p<0.001 and 1.6% vs. 0.0% 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**

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. Methods: A total of 121 patients (89 RCA and 32 LCA) with de-novo aorto-ostial lesions treated with first (Sirolimus/ Paclitaxel) or second (Zotarolimus/ Everolimus/ Biolimus) generation DES in our institute between 2004 and 2013 were investigated.

**Results:** Prevalence of target lesion revascularization (TLR) was significantly higher in RCA than in LCA (20.2% vs. 3.1%, p=0.02). In a subgroup of RCA-ostial lesions, prevalence of in-stent restenosis and TLR were significantly lower in second generation DES (table).

**Conclusion:** Clinical outcome of LCA (LMT) ostial lesion treated with DES is acceptable, whereas that of RCA ostial lesion is still poor. However, second generation DES, compared to first generation may improve the prognosis.

**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, TRA may be used as initial choice of vascular access for CTO lesions.

**Methods:** We retrospectively analyzed a cohort of 325 cases of PCI for CTO, all performed by antegrade route, in a single high-volume PCI center.

**Results:** From January 2006 to August 2013, 7860 PCI were performed in our center, being 325 (4.13%) for CTO. Of these, 82.6% (269) were performed by TRA and 17.2% (56) by TFA. Baseline characteristics were similar in both groups except for the presence of hypertension, more frequent in the TFA group (57.8% vs 73.2%, p=0.032). There were no differences in LVEF (53.8% vs 46.9%), mean lesion length (30.8 vs 28.2mm), calcified lesions (51.5% vs 40%) and mean contrast volume (251±122 vs 251±122mL). Compared to TFA, TRA patients had shorter fluoroscopic time (251±14 vs 33±20 minutes, p=0.008) and shorter total procedural time (58±29 vs 76±33 minutes, p=0.001). Angiographic success rates and final flow TIMI III were achieved more frequently in the first attempt in the TRA group (78.5% vs 63.6%, p=0.02). Logistic regression analysis demonstrated 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 1.162–4.663]) 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 TRA in CTO, this vascular approach use in first attempt of PCI for CTO showed a comparable, if not higher success than TFA, with a decrease in the mean fluoroscopy and mean procedure times in selected cases. Short and non-calcified lesions remain the main predictors of success in PCI for CTO.
plaque recoil. Minimal Lumen Diameter (MLD) and Minimal Lumen Area (MLA) were obtained from Optical Coherence Tomography (OCT) imaging.

Results: MLA in the model after BVS and metallic DES implantation was respectively 4.9±2.0 and 5.4±0.2 mm^2 (p=0.02) at Nominal Pressure (NP) and 5.4±0.20 and 6.07±0.25 mm^2 (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±3.0% in BVS and 20±4±1.7 in the Xience stent at NP (p=0.03) compared to 29±4±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 trabecular stent method in treatment of coronary bifurcation lesions M.A.R. Akorariaraj, Pondicherry Institute of Medical Sciences, Pondicherry, India

Aim: A novel stent was designed for the treatment of coronary bifurcation lesion, and it was investigated for its performance by finite element analysis. This study was performed in a novel method of treatment of bifurcation lesion with provisional stenting.

Methods and results: A bifurcation model was created with the proximal vessel of 3.2 mm diameter, and the distal vessel after the side branch (2.3 mm) was 2.7 mm. A novel stent was designed with connection links that had a profile of a tram. Laser cutting and shape setting of the stent was performed, and thereafter it was crimped and deployed over a balloon. The contact pressure, stresses on the aortic wall, stresses on the stent, the maximal principal log strain of the main artery and the side-branch were studied. The study was performed in Abaqus, Simulia. The stresses on the main branch and the distal branch were minimally increased after deployment of this novel stent. The side branch was preserved, and the stresses on the side branch were lesser; and at the confluence of bifurcation on either side of the side branch origin the von-Mises stress was marginally increased. However, the stresses at the bifurcation were significantly lesser than the stresses of the currently existing techniques used in the treatment of bifurcation lesions. Parametric modifications of the tram area was performed, and the variations were studied for effective crimping. The observed stresses are summarized in the figure.

Stress observed after stent deployment.

Conclusions: There is a potential for a novel Tram-stent method in the treatment of coronary bifurcation lesions.

P2754 | BENCH Fraction of reserve assessed by pressure wire could predict proper stent deployment A.A. Elasfar, H.A. Remah, O.S. Elshahawy. Tanta University Hospital, Adult Cardiology, Tanta, Egypt

Background: There are different methods for assessing the results of coronary intervention, some are morphological and the others are physiological. Myocardial fractional flow reserve (FFRmetry) is a lesion specific index relating maximum myocardial blood flow in the presence of stenosis to its normal value if there is no stenosis.

Objective: The aim of our study is to assess the results of coronary stenting before and after post-stenting balloon dilation by measuring myocardial fractional flow reserve using intracoronary pressure wire.

Methods: FFRmetry and quantitative coronary angiography (QCA) were obtained before PCI, after stent placement and after post-stenting balloon dilation in 120 patients (LAD in 76 patients, RCA in 36 patients and LCX in 8 patients). FFRmetry was calculated as the ratio of Pd/Pa during intracoronary adenosine (50 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 dilation produced non-significant more reduction in the percent diameter stenosis (6±5% with P value <0.05). FFRmetry after PCI was significantly higher than that at baseline conditions before intervention (0.4±0.18 at baseline versus 0.89±0.09 after stenting, p<0.05). There was significant increase in FFRmetry after post-stenting balloon dilation (0.9±0.05 versus 0.89±0.09).

Conclusions: Post-stenting Balloon dilation produced non-significant trend towards better lumen diameter by quantitative coronary angiography but with significant increase in Myocardial fractional flow reserve assessed by pressure wire.

P2755 | BENCH 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 (GPI) due to “bail-out” situations or thrombotic complication (lia C recommendation by ESC guideline 2014).

Methods: The Clotinab application in high risk Acute Coronary Syndrome under GP IIb/IIIa (CAP) registry is a prospective, 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 endpoint 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 hemostasis, intracranial hemorrhage and other bleeding complications.

Results: After propensity score matching, there were no differences in baseline characteristics between two groups except history of atherosclerosis (7.7% vs. 13.4%, p=0.024). The primary endpoint occurred in 7 (2.4%) of 298 patients in TRI 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.

P2756 | BENCH Effect of a novel peptide and sirolimus-coated stent on re-endothelialization and anti-restenosis

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Drug-eluting stent (DES) still has limitations such as thrombosis and inflammation. These limitations can be occurred by the lack of endothelialization. This study was undertaken to investigate the effects of WKYMVM- and sirolimus (SRL) coated stent on re-endothelialization and anti-restenosis. The WKYMVM, specially synthesized peptide for homing of endothelial colony-forming cells, was coated to bare metal stent (BMS) with hyaluronic acid (HA) through simple dip coating (designated as HA-Pep). Thereafter, SRL was coated to HA-Pep, consecutively (designated as Pep/SRL). The cellular response of stents on human aortic smooth muscle cell (SMC) was examined by XTT assay. Stents were implanted to rabbit iliac artery and were isolated at 6 weeks of post-implantation. And then they were subjected to histological analysis. The peptide was well-attached to surface of BMS and the surface was smoothed by SRL coating. The release pattern of SRL was similar to commercial SRL-coated stent (57.2% within 7 days, followed by an additional releasing was continued to 28 days). The proliferation HUVEC was enhanced in HA-Pep group at 7 days of culture (38±7.62%, compared to BMS group). On the other hand, the proliferation HUVEC was inhibited in Pep/SRL group at 7 days of culture (40.7±6.71%, compared to BMS group). In animal study, the re-endothelialization and anti-restenosis were obtained from Optical Coherence Tomography (OCT) imaging.

Conclusions: Post-stenting Balloon dilation produced non-significant trend towards better lumen diameter by quantitative coronary angiography but with significant increase in Myocardial fractional flow reserve assessed by pressure wire. These results suggested that the coating of WKYMVM could promote the endothelial healing.

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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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Purpose: To study the impact of bifurcation angle on immediate results and long term outcomes in patients treated with the crush or simple approach.

Methods: From February 2009 to November 2012, 372 patients with true bifurcation lesions treated with rotational atherectomy through the radial (TR) artery were retrospectively analyzed (183 procedures). Choice of TR was more frequent 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 87.8%, p<0.05). 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 53% vs 68% (p=0.05). In the subgroup of patients without TF at discharge, indicating that consecutive coating of the WKYMVm and SRL to BMS have no additional benefit vs the BMS alone.

Conclusions: TF is safe, feasible and widespread associated with good long term clinical outcome. It is used in the majority of patients with true bifurcation lesions and the crush or simple approach. TF and RA is associated with a better long term result, especially in the subgroup of patients without TF at discharge.

P2779 | 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 2.25–4.4 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). Rate of procedural success at 12 months was 87% in TF vs 84% in RA (p=NS). There were no differences regarding in-hospital/long term all-cause mortality or MACE but a trend was observed showing more TLR in this registry. In this real-world population, the everolimus DES Xience Prime performs extremely well in long lesions, with a very low rate of MACE at 12 months and very low stent thrombosis.
Conclusions: among women receiving longer stents, associations were attenuated and no adverse events up to 3 years.

Background: Stent length is a correlate of adverse events, including stent thrombosis, after PCI with drug-eluting stents (DES). Whether a similar pattern exists for other drug-eluting stents (DES) is unknown. The purpose of this study was to investigate the influence of stent length on adverse events after PCI with everolimus-eluting bioresorbable vascular scaffold (BVS), which could provide theoretical advantages at mid-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 analysed and treated percutaneously in our center. From them, 42 patients with 46 CTO were successfully treated by 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 DES diameter was performed. A computed tomography (CT) scan was scheduled for all patients at least 6 months after treatment.

Results: The mean age of 76 (91%) patients and 41 (98%) 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-CTO score of complexity, 21 (46%) CTO were difficult or very difficult. An antegrade therapy approach was chosen in 29 (55%) and a retrograde approach in 12 (23%). 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 TR in T-treatment tend 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.

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the Group 1 vs 5.9±1.7 mm² in the Group 2, p=0.774) as well as Proximal Edge Area (7.5±2.6 mm² in the Group 1 vs 7.8±2.0 mm² in the Group 2, p=0.706) and Distal Edge Area (6.33±2.4 mm² in the Group 1 vs 6.5±2.0 mm² in the Group 2, p=0.717). Importantly, a lower distal edge malapposition rate was reported in favour of the "latest" procedures (11.8% in the Group 1 vs null in the Group 2).

**Conclusion:** OCT confirmed to play a pivotal role in procedural decision-making during BVS implantation and represents an important tool in order to improve the procedural outcomes overtime.

**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 pro-

**Results:** Of the 68 [t 100 patients who had been treated with implantation of DES with mini-crush technique for the treatment of true CBL, Clinical follow-up 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.

**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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**Background:** The only difference between the first and second generation zotarolimus-eluting stent (ZES) is the coated polymer, which controls drug-eluting rates. Although the second generation, slow releasing ZES (SR-ZES, Endeavor Resolute), has been shown to be superior to the first generation, fast-releasing ZES (FR-ZES, Endeavor Sprint) in short term outcomes, there are no study comparing the long-term clinical outcomes between the two stents.

**Method:** A total of 714 patients (pts) receiving FR-ZES or SR-ZES were pooled from our percutaneous coronary intervention (PCI) registry. To adjust potential confounders, a propensity score matched (PSM) analysis was performed, and clinical outcomes compared between the two groups up to 3 years.

**Results:** After PSM analysis, 2 propensity-matched groups (214 pairs, n=428, C-statistic=0.767) were generated, and all baseline characteristics were well balanced. The SR-ZES were superior to FR-ZES for 6-month angiographic outcomes with reduction in in-stent restenosis (22 (15.1%) vs 6 (5.5%), p=0.015). The incidence of mortality, myocardial infarction and stent thrombosis was not different between the two groups; however, the incidence of target vessel revascularization (TLR) and target vessel revascularization (TVR) were lower in pts receiving ZES compared to the FR-ZES group up to 3 years (TLR; HR: 0.342, 95% CI: 0.129–0.916, p=0.039; TVR; HR: 0.413, 95% CI:0.177–0.962, p=0.041). There was a trend toward lower incidence of TLR and TVR-major adverse cardiac events (MACE) in the SR-ZES group (Table).

**Conclusion:** As compared with FR-ZES, the use of SR-ZES was associated with lower rate of repeat revascularization than FR-ZES during 3-year follow-up, suggesting slow-releasing drug-eluting kinetics would be better for long-term clinical outcomes.

**P2767 | BEDSIDE**

**Procedure related platelet activation in long lesions treated with bioresorbable vascular scaffold versus xience xpedition implantation (prospective trial)**

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**Background:** Significant procedure-related platelet activation and myonecrosis has been reported with increasing stent length despite dual anti-platelet therapy. The aim of the study was to investigate the impact on microvascular function and possible myocardial damage.

**Methods:** Between December 2013 and December 2014, 22 patients with stable coronary artery disease and long lesions (to be treated with >25 mm stent/scaffold) were randomized (1:1) into the open-label, non-inferiority pilot study (Proactive” trial either to Absorb BVS (11 patients) or Xience Xpedition EES (11 patients). All patients with ACS, bifurcation lesions with a side branch >2.0 mm and severely calcified stenosis suitable for rotational atherectomy were excluded. All patients were loaded with 500 mg aspirin and 600 mg clopidogrel at least 12 hours before the procedure. The primary endpoint was the immediate periprocedural (post-PCI - pre-PCI) variations in platelet reactivity assessed by high sensitivity ADP (hs-ADP) in the 2 groups. Secondary endpoints were: peri-procedural changes in the index of microvascular resistance (IMR post-PCI – IMR pre-PCI), peri-procedural myocardial injury as assessed by increase in high sensitivity troponin (hs-Tn) at 24 h, and changes at 30 days in hs-ADP within and between groups.

**Results:** Clinical and angiographic characteristics of the patients were not different in both groups. Scaffold/stent length was 36±12.2 in the BVS and 31±7.5 in the EES group (p=0.58). A significant periprocedural reduction of hs-ADP was observed in the BVS group (from 22.5±9.1 to 14.4±4.6, p=0.01), but not in the EES group (from 19.1±11.2 to 15.8±13.6; p=0.35). IMR did not significantly change in both groups (BVS, from 22.7±12.1 to 16.2±4.7, p=0.106; EES, from 18.7±6.6 to 18.8±10.3; p=0.52). A peri-procedural myocardial injury occurred in 3 (27%) patients of the BVS and 2 (18%) patients of the EES group (p=1.00). At 30 days, there was no difference in hs-ADP as compared to post-PCI between and among the 2 groups.

**Conclusions:** In long lesions, peri-procedural platelet reactivity was unchanged with EES and even decreased with BVS implantation with no further changes at 30 days. Peri-procedural myocardial infarction occurred in less than 30% of the patients similarly in both groups, without a significant impact on microvascular resistance.

**P2768 | BEDSIDE**

**Acute performance of second generation everolimus-eluting bioresorbable vascular scaffolds for percutaneous treatment of chronic total coronary occlusion**

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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.

**Methods:** Three-arm, non-randomized, single-center trial. Device and procedural success rate of BRS use in percutaneous coronary intervention (PCI) of CTO lesions performed at a single center were prospectively evaluated. Patients with reference vessel diameter (RVD) <2.25 mm and ≥3.8 mm, heavy calcification within the CTO segment and target lesion in bifur-
cation involving a side branch >2 mm in diameter were intentionally excluded. De-
vice acute success was defined as 1) successful BRS delivery and implantation
2) post-procedural residual diameter stenosis <30% within the treated segment;
3) restoration of Thrombolysis in Myocardial Infarction (TIMI) grade 3 antegrade
flow. Procedural success was defined as device success with no in-hospital major
adverse cardiac events (MACE).
Results: Between May 2013 and May 2014, 51 patients underwent intended
CTO-PCI with BRS. Wire crossing of the CTO lesion was achieved successfully
in 42 cases and the Absorb BRS implanted in 32 of them. At least one exclu-
sion criterion was encountered in 10 patients. Most of the procedures (30/32) were
performed via the default antegrade approach, whereas switching to a retrograde
approach was needed in two cases (6.2%). A total of 90 BRSs were successfully
implanted with a mean number per patient of 2.81±1.28 and a mean scaffold
length of 54.9±16.33 cm. Eight of 32 patients (25%) received both BRSs and drug-
eluting stents (due to shelf unavailability in seven cases and delivery failure in
one case). Intravascular ultrasound evaluation was carried out in 21/32 patients
(65.6%). Device and procedural success were 78.1% and 78.1% respectively. In 7
of 32 patients (21.9%) a maximum residual stenosis >30% persisted. In hospital
stay was uneventful in all cases. OCT assessment was performed post-PCI in 26
of 32 patients (81.2%). Among 63 scaffold analyzed, under-expansion was noted
in 14 (22%) while both sub-medial dissection and BRS fracture were observed in
2 cases (3% respectively). Mean scaffold area was 8.25±2.52 and 9.52±2.54 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-
egripeligible rate of device failure. Adequate lesion preparation together with ex-
pected device ameliorations will be key to enable routine usage of BRS in the
CTO setting.

P2769 | BEDSIDE
Clinical and angiographic outcome of excimer laser coronary angioplasty (ELCA) + paclitaxel coated balloon for patients with second generation drug-eluting stent restenosis
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 debulking (vaporizing).
Methods: Consecutive 57 ISR patients with second generation DES were ran-
domly assigned to PCB (n=28) or ELCA+PCB treatment group (n=29).
In ELCA group, coronary arterectomy with 1.4 to 2.0mm ELCA catheter was per-
formed prior to PCB dilatation. 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 divided
by stent area for entire stented segment, was also calculated by OCT.
Conclusions: Excimer laser coronary angioplasty + PCB strategy for second gen-
eration drug-eluting stent restenosis appears to be comparably safe and effective
as conventional PCB. However, adjunctive debubling therapy did not reach the chronic benefit possibly due to small sample size.

P2770 | SPOTLIGHT
Temporal trend in the incidence of stent thrombosis—is it the impact of improved antiplatelet regimen and evolving coronary stent technology?
Background: The incidence of stent thrombosis (ST) may have declined over
the past several years, perhaps due to a combination of continuously improving
antiplatelet regimen (AR) and coronary stents. We studied the temporal change
in the incidence of ST.
Methods: We retrospectively examined the percutaneous coronary interven-
tion (PCI) database at our large academic medical center between 1/1/2006 and
12/31/13. Patients with ST within 1 year of index PCI were identified (as per Aca-
demic Research Consortium definition). The AR and characteristics of CS at the
time of index PCI were recorded for pts developing ST.
Results: The study sample included 4460 patients. Of those, 210 patients
(4.7%) developed ST (71: definite, 22: probable, 117: possible). Patients with ST
were older (68±13 vs 62±13, p<0.0001), higher smoking rate (53% vs 32%,
p<0.0001), more diabetes (67% vs 28%, p=0.009), more STEMI (43% vs 33%,
p<0.005), higher stent/patient (1.8±0.9 vs 1.6±0.9, p<0.0001), lesser drug elut-
ing stents (due to shelf unavailability in seven cases and delivery failure in
one case). Intravascular ultrasound evaluation was carried out in 21/32 patients
(65.6%). Device and procedural success were 78.1% and 78.1% respectively. In 7
of 32 patients (21.9%) a maximum residual stenosis >30% persisted. In hospital
stay was uneventful in all cases. OCT assessment was performed post-PCI in 26
of 32 patients (81.2%). Among 63 scaffold analyzed, under-expansion was noted
in 14 (22%) while both sub-medial dissection and BRS fracture were observed in
2 cases (3% respectively). Mean scaffold area was 8.25±2.52 and 9.52±2.54 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-
egripeligible rate of device failure. Adequate lesion preparation together with ex-
pected device ameliorations will be key to enable routine usage of BRS in the
CTO setting.

P2771 | BEDSIDE
Anatomical and functional assessment of Tryton bifurcation stent before and after final kissing balloon dilatation: evaluations by three-dimensional coronary angiography, optical coherence tomography
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Aims: Current experience and retrospective analysis suggest clinical benefit of
final kissing balloon dilatation (FKB) in patients undergoing bifurcation dilatation
using the Tryton Side Branch Stent (Tryton-SBS), but the reasons for these obser-
vations remain speculative. In this study we sought to assess the anatomical
and functional impact of FKB after implantation of this dedicated bifurcation stent
system.
Methods and results: An unselected group of 10 patients with complex bi-
curcation coronary lesions undergoing percutaneous coronary intervention (PCI)
with Tryton-SBS underwent paired anatomical assessment with two- and three-
dimensional quantitative coronary analysis (2D- and 3D-QCA), and optical co-
herence tomography (OCT), including 3D reconstruction with dedicated software,
before and after FKB. Functional assessment was performed in the main branch
(MB) and side branch (SB) before and after FKB using fractional flow reserve
(FFR). At 2D-QCA, a significant decrease in SB diameter stenosis was observed
after FKB (from 27.6±15.6% to 15.4±15.9%, p<0.045). At 3D-QCA, no significant
variations were detected after FKB. By OCT imaging, FKB increased both the SB
ostial area (+2.5±2.8 mm², p<0.001) and the SB maximum diameter (+0.7±0.9
mm, p<0.003). These findings were associated with a significant increase in FFR
in the SB (delta FFR +0.04±0.13 mm, p=0.011), with no significant change in the
MB (delta FFR +0.01±0.04 mm, p=0.470).
Conclusions: In patients with complex bifurcation stenosis undergoing PCI with
a dedicated bifurcation system, FKB is associated with improved procedural
anatomical and functional results at the SB level, without compromising outcomes
of the MB.
Purpose: The aim of this abstract is to report our experience using extracorporeal membrane oxygenation assistance (ECMO) in an effort to improve outcomes in high-risk percutaneous interventions. Methods: Between October 2013 and December 2014, 10 adult patients were treated with extracorporeal membrane oxygenation (ECMO) during percutaneous coronary intervention (PCI). Consecutive 11 patients who were scheduled for DES implantation surgery 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 in response to the endothelium-dependent and independent vasodilators (acetylcholine (Ach) and adenosine tri-phosphate (ATP)) was evaluated as an index of epicardial endothelial function. Microvascular endothelial function measured in response to Ach and isosorbide dinitrate was also analyzed as an index of microvascular endothelial function.

Introduction: There is no enough evidence regarding safety and efficacy of extracorporeal membrane oxygenation (ECMO) during percutaneous coronary intervention (PCI) amongst high-risk patients with non-ST-segment elevation acute coronary syndrome (NSTE-ACS).

Aim: To compare the results of PCI during ECMO and coronary artery bypass graft (CABG) surgery amongst patients with NSTE-ACS.

Materials and methods: Retrospective analysis of 30-day follow-up of high-risk patients with NSTE-ACS who underwent either PCI during ECMO or CABG surgery. Study sample included 69 patients, and all of them had significant co-morbidity along with high risk according to EuroScore scale and with high SYNTAX score. 16 patients underwent PCI during ECMO (PCI-ECMO), and other 53 patients underwent CABG surgery. PCI was carried out in patients who were restricted to CABG surgery. Average risk according to GRACE score did not differ significantly between these two groups (PCI-ECMO group 100±22.9, CABG surgery group 95±14.6, p=0.39). There was no statistically significant difference concerning clinicopathological features. Both groups did not differ significantly regarding EuroScore scale (PCI-ECMO group 12.2±19.9, CABG surgery group 7.5±5.2%, p=0.12) and SYNTAX score (PCI-ECMO group 30.5±9.3, CABG surgery group 30±8.2, p=0.8). However, PCI-ECMO group included significantly more patients with unprotected left main stenosis (CABG surgery group 0 vs. PCI-ECMO group 25%).

Study endpoints included successful intervention, death, myocardial infarction (MI), stroke, repeat revascularization, and bleeding. There was also combined endpoint which included death, MI, stroke, and repeated revascularization.

Results: Intervention was successful in all cases. During the 30-day period of follow-up, case fatality rate was 12.5% in PCI-ECMO group (2 patients) and 7.5% (4 patients) in CABG surgery group (p=0.53). There were two cases (3.8%) of MI and one (1.9%) MI-related death postoperative period in CABG surgery group. In addition, 7 (13.2%) patients from CABG surgery group had heavy bleeding (according to TIMI classification) versus 1 (6.2%) patient in PCI-ECMO group (p=0.44).

There were no statistically significant differences in prevalence of endpoints during the 30-day period of follow-up. The prevalence of combined endpoint did not differ significantly between groups (12.5% in PCI-ECMO group, 9.4% in CABG surgery, p=0.72).

Conclusion: PCI-ECMO may be an alternative technique of myocardial revascularization in high-risk patients with multivessel coronary artery disease and NSTE-ACS.

Purpose: The aim of this abstract is to report our experience using extracorporeal membrane oxygenation assistance (ECMO) in an effort to improve outcomes in high-risk patients undergoing percutaneous interventions in the catheterization laboratory. Methods: Between October 2013 and December 2014, 10 adult patients were placed on veno-arterial (VA) ECMO (CardiohelpTM, Maquet Cardiopulmonary AB, Solna, Sweden) for primary PCI. In 4 patients VA-ECMO was placed as hemodynamic support during high-risk percutaneous interventions in the catheterization laboratory. Underlying diseases included high-risk angioplasty (3 patients) of unprotected left main or multiple vessel revascularization in the context of severe left ventricular (LV) dysfunction; and during aortic valvuloplasty in a patient with severe aortic valve stenosis, two- vessel disease and very severe LV dysfunction with heart failure symptoms at rest. All 4 cases were discussed in the heart- team and were rejected for surgery. Intervventional cardiologist and cardiothoracic surgeons made the implantation of cannulas and a percutaneous assisted the VA-ECMO during percutaneous intervention. In two patients prior to percutaneous insertion of the arterial cannulas a Prostar XL device was implanted for achieving arterial haemostasis.

Results: All patients, except one, required invasive mechanical ventilation during intervention due to heart failure and shortness of breath. Arterial and venous access was performed percutaneously except for a patient with severe peripheral arterial disease to whom axillary artery was cannulated by surgery to complete the ECMO circuit. During the procedures pump flow was 2.5–3.0 l/min. ECMO was placed immediately before percutaneous interventions and implantation was performed immediately after finishing the intervention except for a patient who was supported for three days because weaning in the catheterization laboratory was not successful. None of the patients required blood transfusion or had complications such as stroke or limb ischemia. Arterial haemostasis with Prostar XL sutures at the end of the procedure was successful in both attempted patients.

Conclusions: We believe that ECMO support is a viable mode of hemodynamic support in high-risk percutaneous interventions. Percutaneous ECMO implantation in the catheterization laboratory and immediate implantation after percutaneous intervention is feasible and safe.
Conclusion: DES impaired microvascular endothelial function rather than epicardial endothelial function of coronary artery distal to the DES. Our results support a long-term worsening of microvascular function by DES implantation.

P2776 | BEDSIDE
Modified stent platform favorably affects longitudinal stent strength and stent deformation of the platinum chromium everolimus-eluting stent: an in vivo frequency domain optical coherence tomography study
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Background: Several studies have suggested that platinum chromium (PtCr) everolimus-eluting stent (EES) with 2 links between stent hoops have higher incidence of longitudinal stent deformation than cobalt chromium EES with 3 links between hoops. A recent bench test suggested that increased numbers of links (from 2 to 4) at the proximal part of the PtCr-EES may improve longitudinal stent strength and therefore decrease the incidence of longitudinal stent deformation.

Purpose: The aim of this study was to investigate the impact of the modified stent platform of the PtCr-EES on the longitudinal stent strength and the incidence of stent deformation by using frequency domain optical coherence tomography (FD-OCT) in vivo.

Methods: Fifty-two lesions treated with PtCr-EES (Promus Element; n=29, Promus Premier; n=23) were studied. After successful stent implantation, FD-OCT was performed to measure actual stent length in vivo. Percent longitudinal stent shortening 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 (1.3±4.7% and 2.8±6.7%) 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 affects the longitudinal strength of the PtCr-EES. Longitudinal stent deformation may not be an issue anymore for the modified version of the PtCr-EES.

P2777 | BEDSIDE
Use of protective ballooning technique with provisional stenting for treatment of non-left coronary bifurcation lesions
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Background and objective: Percutaneous coronary intervention (PCI) of bifurcation lesions is associated with a higher risk of adverse events. Recent studies support the use of provisional side branch (SB) stenting, but the risk of SB closure after main vessel (MV) stenting remains an important concern. We sought to compare the incidence and preliminary efficacy of a novel protective ballooning technique (PBT) for SB protection and treatment during MV stenting.

Methods: The rationale of PBT for SB protection is to preposition a small balloon (2.0/0.20 mm) in the SB before MV stenting while the proximal makers of the balloon and the MV stent are aligned. During deployment of the MV stent (14–16 atm), the uninflated jailed balloon under the stent struts serves to reduce both carina and plaque shifts due to its spatial occupation in the SB ostium. Thereafter, the inflated balloon is inflated at 8–14 atm to dilate the ostium. After removing the jailed balloon MV stent’s balloon is inflated again at 14–16 atm to correct stent deformation or malapposition. If SB flow is preserved after MV stenting, the jailed wire will be removed from SB; otherwise it could be used as a marker to facilitate rewiring SB, and further kissing balloon inflation or provisional SB stenting will be performed to restore SB flow. Final intravascular ultrasound (IVUS) examinations were selectively performed in some patients to check the MV stent. Procedural and immediate clinical outcomes were recorded and reviewed.

Results: This novel technique was successfully adopted in 41 patients with 49 bifurcation lesions. The majority of patients had Median class 1, 1 bifurcation lesions (81%). Final TIMI 3 flow was achieved in 100% of MV and 98% of SB. IVUS revealed optimal deployment of MV stent after final inflation in all checked cases (n=13). Only one patient (2%) had lesions that required rewiring and provisional stenting (0.8撕3.7% and 2.96±6.7%) 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 PtCr-EES. Longitudinal stent deformation may not be an issue anymore for the modified version of the PtCr-EES.
Longitudinal neointimal distribution after drug-eluting stent implantation: an optical coherence tomography study

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) 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=25) or NEVO™ stent (n=9), were analyzed. 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, medial or distal coronary segment; p=0.016) and stent diameter (<3.0 mm or ≥3.0 mm; p=0.007). NIT of instent segments were not different between three groups (p=0.677).

Conclusions: NIT after DES implantation may depend from some clinical and angiographic factors. In particular it seems that it is homogenously distributed within the stent segment.

P2781 | BEDSIDE
Dedicated side branch stent versus mini-crushing stenting: comparison between two techniques in the 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, 1, 1; 1, 0, 1; or 1, 1, 1; account for approximately 15% of all treated lesions and are associated with a lower procedural and long-term success when compared with non-bifurcation lesions. Therefore, several dedicated bifurcation 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 stenting 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 comparison with 23 CBL in 23 patients 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 m in the TR-group vs 84±10 in the MCT-group (p=ns); the fluoroscopy time was 21±10 vs 28±7.7,5 (p=0.003); contrast medium was 235±45 vs 248±62 ml (p=ns); procedural MI was absent in both group.

Conclusions: Tryton Side branch stent and mini-crushing technique provides excellent angiographic and procedural success. Procedural time and contrast dose are acceptable for both; fluoroscopy time is higher for MCT.

P2782 | BEDSIDE
 Favorable clinical long-term follow-up of mini-crushing technique for treatment of true bifurcations

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Background: Percutaneous treatment of coronary bifurcations lesions (CBL) is associated with a low procedural success rate and high incidence of target lesion revascularization (TLR), and stent thrombosis. The provisional approach is accepted as the default technique, but stent implantation on both branches of the bifurcations is still required in 15%-30% of cases. The “mini-crush” technique (MCT) is one of the techniques used to implant stents on both branches of a CBL and provides complete coverage of the ostium of the side branch, while minimizing the length of the crushed stent.

Purpose: The aim of this study is to evaluate the long-term clinical outcomes associated with the treatment of CBL with MCT.

Methods: Between January 2006 and December 2011, all consecutive patients who underwent MCT (59 patients with mini-crush™ technique) for the treatment of true CBL were admitted to this observational study. The measured end-points were cardiac death, follow-up myocardial infarction (MI), TLR, target-vessel revascularization (TVR) and major adverse cardiac events (MACE) defined as combination of cardiac death, MI and TVR. Three-year follow-up was obtained in all of the cases. One episode of definite stent thrombosis was documented 10 days after the index procedure (DIRT discontinuation).

Results: In the study period we treated 90 CBL in 90 patients with “mini-crush” technique. Clinical presentation was an ACS-NSTEMI in 40% and STEMI in 16%. Impacted left main was included into the patient population. Two-step kissing balloon inflation and final kissing balloon inflation was systematically performed. Second generation DES was used in 7% of the patients. Immediate procedural success was obtained in all of the cases. One episode of definite stent thrombosis was documented 10 days after the index procedure (IRLST discontinuation).

Conclusion: Our results suggest that the treatment of CBL by means of mini-crush technique has acceptable angiographic and procedural success and provides acceptable long-term outcomes in a high-risk patients population.

P2783 | BEDSIDE
Anti-CD34 capturing in coronary stenting leads to improved endothelial coverage: COMBO vs. Xience Prime

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Introduction: Drug-eluting stents (DES) reduce neointimal hyperplasia (NIH) by inhibition of vascular smooth muscle cell (VSMC) proliferation. Because of their non-selective anti-proliferative effect, stent re-endothelialization is also inhibited, which may increase the risk for stent thrombosis. The COMBO stent combines an abluminal sirolimus-eluting coating with endothelial progenitor cell (EPC) capturing technology to combine initial intimal hyperplasia reduction with improved re-endothelialization.

Purpose: The aim of our study was to compare the novel COMBO stent with current standard treatment.

Methods: Twelve New-Zealand White (NZW) rabbits were subjected to iliac artery stent placement. Twenty-eight days after implantation, optical coherence tomography (OCT) was performed (n=4) and tissue was harvested from the animal.(n=6). Lumen loss ratio was defined as angiographic stent diameter directly after implantation/stent diameter at twenty-eight days of follow-up. Intimal hyperplasia was assessed by both histology and OCT. Additionally, scanning electron microscopy (SEM) was performed for the treatent stent coverage.

Results: Comparisons to EES, strut coverage was significantly higher in the COMBO stent (78.5±16.8% vs. 96.6±3.5%; p=0.043). Intimal hyperplasia did not differ between the EES and COMBO stent as assessed by OCT (0.227±0.025 mm2 vs. 0.188±0.044 mm2; p=NS) or histology (0.823±0.200 mm2 vs. 0.891±0.312 mm2; p=NS). No differences were observed in late lumen loss ratio between both EES and COMBO stent (0.95±0.027 vs. 0.94±0.024; p=NS).

Conclusion: Re-endothelialization was significantly improved in the COMBO stent as compared to EES with equal inhibition of intimal hyperplasia. As stent endothelialization is a major determinant of stent thrombosis, this may reduce thrombotic events after DES implantation.

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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 patients 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.

Changes in Heart Failure, Epidemiology and Management

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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 [80%]; 70±14 yr (range 40–94 yr)); current smoking (3/20 [13%]); with comorbidities (in 20/23 [87%]) or AF 3/23 (13%), were classed as new onset TCM. Of these 6/23 (26%) had suggested acute MI; 20/23 (86%) had HBP; 15/23 (65%) had diabetes mellitus (DM). As a consequence, we observed a significant reduction in exercise capacity in parallel to decreasing haemoglobin levels (r=0.24, p < 0.001). In patients with ID and anaemia together (n=63, 19%) exercise capacity was significantly lower than in patients with ID or anaemia alone. Cox regression analysis showed higher risk of mortality in patients with microcytic anaemia (hazard ratio [HR]: 2.434, 95% CI: 1.10–5.38, p = 0.02) and with higher NYHA class (HR: 1.935, 95% CI: 1.41–2.67, p = 0.0001) and lower risk in patients without anaemia (HR: 0.46, 95% CI: 0.31–0.70, p = 0.003), with higher TSH (HR: 0.976, 95% CI: 0.956–0.99, p = 0.001) with out renal failure (HR: 0.38, 95% CI: 0.25–0.57, p < 0.0001), with higher LVEF (HR: 0.938, 95% CI: 0.92–0.96, p < 0.0001), with higher peak VO2 (HR: 0.856, 95% CI: 0.75–0.97, p = 0.001). After adjusting for NYHA, age, BMI and hsCRP anaemia is an independent predictor of mortality in patients with heart failure.

Conclusions: Anaemia and ID are associated with reduced exercise capacity. The impact of anaemia on reduced exercise capacity and on mortality is stronger than that of ID. Patients with microcytic anaemia showed a 2 fold higher risk of death.

P2786 | BEDSIDE
The impact of iron deficiency and anaemia on exercise capacity and outcomes in patients with chronic heart failure

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Background: Anaemia and iron deficiency are important co-morbidities and both may lead to reduced exercise capacity.

In a total of 331 patients with stable chronic HF (mean age: 64±11 y, 77% female, left ventricular ejection fraction [LVEF] 35±13%, body mass index [BMI] 28.5±5.2 kg/m2, New York Heart Association class 2.2±0.7, chronic kidney disease 35%, glomerular filtration rate 61.7±20.1 mL/min) were enrolled from 2010 and followed until April 2014 or death. Anaemia was defined according to World Health Organization criteria (Hb < 13 g/dL in men, <12 g/dL in women). Hypokinesia in the context of standard therapies and had an available EF measurement in their medical records. MHS databases were used to collect data on other demographic and clinical characteristics. Patients were according to their EF level at diagnosis.

Conclusion: Demographic and clinical characteristics of male and female patients with preserved ejection fraction in a large health organization.

Demographic and clinical characteristics of male and female patients with preserved ejection fraction in a large health organization

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Introduction: Congestive heart failure (CHF) with preserved ejection fraction (EF) has been reported to be more common in females than in males. However, the contribution of other demographic and clinical characteristics to this difference has rarely been analyzed in real-world settings. The study aim was to characterize male and female CHF patients according to their EF level at diagnosis.

Methods: Included in the study were adult members of a public health organization who were diagnosed with CHF between January 2006 and December 2012 and had an available EF measurement in their medical records. MHS databases were used to collect data on other demographic and clinical characteristics.

Results: A total of 3076 patients were eligible for analysis (62.3% males). Although males were significantly (p<0.001) younger (mean age 70±7 y) at CHF diagnosis compared to females (74±1 y), they were more likely to have a reduced ejection fraction (40.6% vs. 22.0%), ever have been a smoker (24.5% vs. 10.2%), and have a history of ischemic heart disease (69.9% vs. 44.5%). Females had a higher mean BMI (30.2±6.4 vs. 29.0±5.1 kg/m2) despite having a higher proportion of patients being treated with diuretics (46.4% and 38.6% among females and males, respectively).

Conclusions: Male and female CHF patients are clinically and statistically significantly different in important clinical characteristics that may affect survival. While ischemia is more common in male CHF patients, female CHF patients substantially more often have preserved ejection fraction. Whether and how clinical characteristics or gender determinants may drive disease etiology and/or prognosis should be further assessed.

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P2787 | 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 outcome of consecutive patients with AMI admitted to all hospitals in Sweden. In-hospital HF was defined as presence of cracks, use of iv diuretics or use of iv inotropic drugs. Late-onset HF was defined as readmission within 2 years because of HF in patients without prior HF and no in-hospital HF. (n=230,408).

Results: The incidence of in-hospital HF and late onset HF decreased from 48% to 26% (p<0.001) and from 15% to 13% (p<0.001), respectively. Changes in baseline characteristics are shown in Table 1. In multivariable analyses, female gender (OR [95% CI]), 1.14 (1.1–1.2), diabetes mellitus 1.3 (1.25–1.3), STEMI 1.5 (1.4–1.5) and prior HF (2.1 [2.0–2.2]) were strongest associated with in-hospital HF, whereas diabetes (OR [95% CI]), 1.8 (1.4–1.7), prior AMI 1.4 (1.1–1.8) and periferal arterial disease 1.3 (1.1–1.7) were strongest associated with late-onset HF. Calendar-year reduced the odds of in-hospital HF (OR [95% CI], 0.85 (0.8–0.9) as well as late-onset HF 0.8 (0.6–0.9).

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.

Table 1. Changes in baseline characteristics of patients with in-hospital and late onset HF after an index AMI

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>In-hospital HF</th>
<th>Late-onset HF (at 2 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>73.8</td>
<td>76.1</td>
</tr>
<tr>
<td>Female (%)</td>
<td>39.5</td>
<td>43.1</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>21.4</td>
<td>31</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>34.6</td>
<td>53.3</td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>23.1</td>
<td>17.4</td>
</tr>
<tr>
<td>Prior Stroke (%)</td>
<td>17.6</td>
<td>17.6</td>
</tr>
<tr>
<td>RAD (%)</td>
<td>7.4</td>
<td>7.3</td>
</tr>
<tr>
<td>Renal failure (%)</td>
<td>5.0</td>
<td>1.9</td>
</tr>
<tr>
<td>STEMI/LBBB (%)</td>
<td>36.3</td>
<td>51.1</td>
</tr>
</tbody>
</table>

Changes in heart failure, epidemiology and management 491

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Heart failure mortality: evolution from 2003 to 2012
B. Sredniawa1, A. Lekston1, M. Zembala1, L. Polonski1, M. Gasior1.

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 demonstrated that the 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 significantly from 77.5 to 80.1 years. Our findings showed that mortality risk in females was age-dependent (<0.05) during all study period. Male gender was associated with higher mortality for the whole sample of the study, however, gender ceased to be a significant contributor to the mortality risk in 2012.

Conclusion: HF is the most common cause of hospitalization due to cardiovascular disease. The progress in treatment of HF has achieved to lengthen the life of expectancy of HF patients but the mortality rate still remains high. Female HF incidence rates have increased recently.

Acknowledgement/Funding: This study was supported by an unconditional grant from Menarini.

Heart failure mortality: evolution from 2003 to 2012
B. Sredniawa1, A. Lekston1, M. Zembala1, L. Polonski1, M. Gasior1.

Heart failure (HF) is the main cause of hospital admissions in patients over 85 years in developed countries. The incidence of re-admissions in the first 30 days after being discharged with the diagnosis of HF is 20–30%, which accounts for a significant increase in health costs. Several hospital strategies to lower re-admission rates have been developed. However, the age of mortality increased significantly by 50% over the study period. The risk adjusted in-hospital mortality rate due to HF decreased slightly from 10.8% in 2003 to 10.0% in 2012. However, the mean age of mortality increased significantly from 77.5 to 80.1 years. Our findings showed that mortality risk in females was age-dependent (<0.05) during all study period. Male gender was associated with higher mortality for the whole sample of the study, however, gender ceased to be a significant contributor to the mortality risk in 2012.

Conclusion: HF is the most common cause of hospitalization due to cardiovascular disease. The progress in treatment of HF has achieved to lengthen the life of expectancy of HF patients but the mortality rate still remains high. Female HF incidence rates have increased recently.

Acknowledgement/Funding: This study was supported by an unconditional grant from Menarini.

Oral presentations reduce 30-day re-hospitalization rate
C. Pachas, M. Domingo, R. Nunez, M. Rodriguez, R. Cabanes, B. Gonzalez, C. Rios, P. Barroso, J. Lupon, A. Bayes-Genis. Germans Trias i Pujol Hospital, Badalona, Spain

Introduction: Heart failure (HF) is the main cause of hospital admissions in patients over 85 years in developed countries. The incidence of re-admissions in the first 30 days after being discharged with the diagnosis of HF is 20–30%, which accounts for a significant increase in health costs. Several hospital strategies to lower re-admission rates have been developed. However, the age of mortality increased significantly by 50% over the study period. The risk adjusted in-hospital mortality rate due to HF decreased slightly from 10.8% in 2003 to 10.0% in 2012. However, the mean age of mortality increased significantly from 77.5 to 80.1 years. Our findings showed that mortality risk in females was age-dependent (<0.05) during all study period. Male gender was associated with higher mortality for the whole sample of the study, however, gender ceased to be a significant contributor to the mortality risk in 2012.

Conclusion: HF is the most common cause of hospitalization due to cardiovascular disease. The progress in treatment of HF has achieved to lengthen the life of expectancy of HF patients but the mortality rate still remains high. Female HF incidence rates have increased recently.

Acknowledgement/Funding: This study was supported by an unconditional grant from Menarini.
Heart transplantation (HTX) is an established therapy for end-stage heart failure. However, the rate of heart failure (HF) hospitalizations and its consequent cost-reduction is a significant concern. In Spain, the average length of hospital stay for HF patients is 7.6 days, and the cost of a HF hospitalization is €10,000.

Methods: This was a single-center, prospective study conducted at a tertiary care hospital in Spain. We included patients with acute decompensation of HF who were admitted to the ICU during the study period. The primary outcome was the number of hospitalizations and the number of days spent in the ICU.

Results: A total of 120 patients were enrolled in the study. The mean age was 67.5 years, and 70% of the patients were men. The primary diagnosis was ischemic heart failure in 80% of the cases. The mean length of stay was 5.8 days, and the median number of hospitalizations was 1.5 per patient. The majority of patients (85%) were discharged from the hospital within 7 days.

Conclusions: This study demonstrates the importance of improving the management of HF hospitalizations to reduce costs and improve patient outcomes.
Conclusions: This study showed that the severity of OSAS and the total number of arhythms decreased significantly in semi-recumbent sleep position in patients with CHF. The maximal decrease in arhythms 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 and no single therapy is currently available to significantly modify HF progression. Iron deficiency (ID) is known to be common in HF patients. However, the role of ID in HF management remains controversial.

Methods: This meta-analysis on individual patient data is performed using all available completed trials conducted in systolic CHF patients with ID (FER-CARS, FAIR-HF, EFFICACY-HF) comparing intravenous (iv) iron therapy with FCM and placebo (saline). All trials were designed as double-blind, multi-centre, prospective, randomized trials and enrolled ambulatory patients with symptomatic CHF (NYHA class II/III) with LVEF <50% and with echocardiography ID (defined as ferritin <100 ng/dl or ferritin 100-300 ng/dl if transferrin saturation (TST) <20%). FER-CARS-01 and FAIR-HF were randomised 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 1000 mg of iv iron up to 1000mg as injection at baseline and at weeks 12, 24, 36 and 48. Patients received a maintenance dose of 500 mg iv iron up to 1000mg as injection at baseline and at 48 weeks. Safety endpoints are change from baseline in PGA, 6MWT distance, NYHA, EQ5D and Hb measurements. Patients received a 500 mg maintenance dose during the maintenance period at Weeks 12, 24 and 36 if ID is still present. FAIR-HF and EFFICACY-HF lasted 24 weeks, FER-CARS-01 12 weeks, respectively. During the correction phase of these trials weekly iv injections of 200 mg were administered to achieve cumulative dose calculated by the Ganzoni formula. Patients received a 200 mg maintenance dose of 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 cause. The secondary endpoints include the rate of and time to first hospitalisation(s) due to worsening HF or death for any cardiovascular reason, hospitalisation(s) due to 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 G ACH, GEDसय 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 iv iron therapy with iv FCM in CHF patients with ID in regards to these clinically primordial and important endpoints. Results of the current study 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.

Methods: The present study investigates the effects of various types of PAP therapy on oxygen saturation, desaturations and hypoxemia within the first night of usage.

Results: A total of 232 patients (25 female, 68±10 years, BMI 29.7±5.1, NYHA 2±0.5, NT-proBNP 2774±7618 pg/ml, LVEF 34±18%) 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 importantly, none of the patients developed hypoventilation and oxygen saturation was below 90% (T<90%) during at least 3 minutes during both the first and second night of therapy (Table: p<0.05).

Conclusion: PAP therapy of SDB is able to significantly reduce nocturnal hypoxia in HF patients. Important and robust outcome parameters like T<90% improved markedly with PAP therapy.

P2798 | BEDSIDE Exercise cardiac power and the risk of heart failure in men

S. Kuri1, S.Y. Jou2, F. Zaccardi3, J. Kauhanen1, K. Ronkainen1, J.A. Laukkanen1.

1 University of Eastern Finland, Institute of Public Health and Clinical Nutrition, Kuopio, Finland; 2 University of Seoul, Seoul, Korea, Republic of; 3 Catholic University of the Sacred Heart, 3Internal Medicine and Diabetes Care Unit, Policlinico Gemelli Hospital, Catholic University of Sacro, Rome, Italy

Background: Heart failure (HF) is among the most common causes of death in developed countries.

Purpose: The aim of this study was to examine the relationship of exercise cardiac power (ECP), defined as a ratio of directly measured maximal oxygen uptake with peak systolic blood pressure during exercise, with the risk of heart failure in general population.

Methods: 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 participating in exercise stress test 313 cases of HF occurred.

Results: Men with low ECP (<9.8 mL/min/kg, lowest quartile) had a 2.36-fold (95% CI 1.7–3.3, p<0.0001) risk of HF as compared with men with high ECP (>13.9 mL/min/kg, highest quartile) after adjusting for age and examination year. 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

S. Suda1, T. Kasa12, H. Matsumoto2, A. Murata1, S. Yatsu1, T. Kato1, M. Hiki1, H. Daida1.

1 Juntendo University, Cardio-Respiratory Sleep Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan; 2 Juntendo University, Cardio-Renal Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan

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.

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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 (for those 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 results. Results: Overall, 114 patients including 76 SDB (30 with PAP treatment) and 38 without SDB were enrolled. At a median follow-up of 6.8 months, 44 patients had clinical events (39%). In the stepwise multivariable analysis including age, etiology of LV dysfunction, NYHA class, cardiac resynchronization therapy (CRT), use of beta blockers, hemoglobin, INR, creatinine, protein level, 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, presence of SDB was associated with increased risk of poor prognosis. However, there are no reports regarding the impact of decompensated 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 arterial 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±15 vs. 69±14 years), male gender (57% vs. 58%), BNP (213.8±(50.1–441.2) vs. 133.2±(73.9–914.9) pg/ml), calculated as a percent change in %DLCO between the PFT. There were no significant differences in baseline characteristics for HF admission (%DLCO was associated with HF admission (P=0.03, Table 1).

Table 1. Analyses of % change in characteristics between the two points of PFT for HF admission

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>odds ratio P</td>
<td>odds ratio P</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.97 (0.94–1.01)</td>
<td>0.97 (0.93–1.01)</td>
</tr>
<tr>
<td>Estimated GFR</td>
<td>0.99 (0.97–1.01)</td>
<td>0.99 (0.97–1.02)</td>
</tr>
<tr>
<td>Log BNP</td>
<td>1.03 (1.00–1.06)</td>
<td>1.02* (1.00–1.06)</td>
</tr>
<tr>
<td>% VC</td>
<td>0.98 (0.94–1.00)</td>
<td>1.001 (0.94–1.05)</td>
</tr>
<tr>
<td>FEV1.0%</td>
<td>1.06 (0.99–1.14)</td>
<td>1.02 (0.93–1.11)</td>
</tr>
<tr>
<td>% DLCO</td>
<td>0.96 (0.92–0.99)</td>
<td>0.95 (0.90–0.99)</td>
</tr>
</tbody>
</table>
| VC, vital capacity: FEV1.0, forced expiratory volume in one second: DLCO, diffusing capacity for carbon monoxide.

Conclusion: DLCO is decreased following decompensated HF. Pulmonary congestion resulting hospitalization may cause irreversible reduction of DLCO.

P2801 | BEDSIDE
Exercise therapy in heart failure with reduced ejection fraction is safe but did not improve mortality, cardiac death or hospitalisation - a meta-analysis

S. Sze, V. Algar, K.Y.K. Wong. Castle Hill Hospital, Hull, United Kingdom

Background: European and American guidelines recommend exercise training to improve the quality of life in stable heart failure patients. However, there is conflicting evidence regarding whether exercise reduces mortality and hospitalisation in patients suffering from heart failure.

Methods: We conducted a systematic review and meta-analysis of prospective studies which investigated the efficacy and safety of exercise therapy in stable chronic heart failure patients with reduced ejection fraction. Using a predefined search strategy, electronic databases (MEDLINE and Embase) were searched for randomised controlled trials (RCTs) published between 1946 and 2013. Five eligible studies which investigated the relationship between exercise therapy and all-cause mortality, cardiac mortality and all-cause hospitalisation were identified and appraised using set criteria. Heterogeneity test was considered significant if p<0.10. If significant, random effect model was used to allow generalisation of the results and sources of heterogeneity were investigated. If there is no significant heterogeneity, then the fixed effect model would be used.

Results: Combined, these 5 RCTs recruited a total of 2581 patients (Table 1).

Compared with usual care, the pooled risk ratio of all-cause mortality, cardiac mortality and all-cause hospitalisation after exercise therapy in chronic HF EF patients was 0.85 (95% CI = 0.80–1.14, p=0.61) (Figure 1). 0.06 (95% CI = 0.34–1.24, P=0.20) (Figure not shown) and 0.95 (95% CI = 0.90–1.10, P=0.13) (Figure 2) respectively.

Conclusions: Exercise training in patients with stable chronic heart failure due to left ventricular systolic dysfunction is safe, but there is no evidence that exercise training improves all-cause mortality, cardiac mortality or all-cause hospitalisation.

P2802 | BEDSIDE
The inverse correlation of sympathetic activity and daytime sleepiness in patients with heart failure and sleep apnea

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Background: It has been demonstrated that sleep apnea syndrome (SAS) is associated with cardiovascular morbidity and mortality. Various mechanisms link SAS to an increase in heart failure (HF). But patients with HF and SAS are less sleepy than patients with SAS but without HF. Furthermore, unlike the general population, in the HF population, the degree of daytime sleepiness is not correlated with the apnea-hypopnea index (AHI). This makes the treatment of SAS with HF patients by positive airway pressure more difficult. The aim of this present study is to investigate the interaction between daytime sleepiness and sympathetic nerve system activity in patients with HF with or without PAP.

Methods: We studied 220 SAS patients, all underwent polysomnography in our institutes. Subjects were divided into 2 groups based on cardiac function (Ejection fraction 40% below or not) (HF group 84, NonHF group 176). Daytime sleepiness was assessed by the Eyworth Sleepiness Scale (ESS) and overnight urinary catecholamines were measured.

Results: HF group was less sleepy compared with NonHF group (ESS score 6.1±1.7 vs 7.1±2.5, p<0.004). HF group had significantly increased overnight urin ary adrenaline, noradrenaline and dopamine levels compared to NonHF group. Sleepiness was inversely correlated to urinary catecholamine levels.

Conclusions: In patients with HF, the degree of daytime sleepiness was inversely correlated to urinary catecholamine levels. This may help to explain the lack of daytime sleepiness in SAS patients with HF.

P2803 | BEDSIDE
Impact of adaptive servo ventilation therapy on cardiovascular event free survival in heart failure patients

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Background: Adaptive Servo Ventilation (ASV) is considered beneficial to heart failure (HF). However, not all patients show good response to ASV. In the Canadian Continuous Positive Airway Pressure (CPAP) for Patients with Central Sleep Apnea (CSA) and HF trial, CPAP did not improve prognosis in CSA unsuppressed heart failure patients.

Abstract P2803 – Table 1. Safety of exercise training in CHF patients

<table>
<thead>
<tr>
<th>Author</th>
<th>Ex</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>9/50 (18%)</td>
<td>20/49 (40.8%)</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>5/50 (10%)</td>
<td>14/49 (29%)</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>2/50 (4%)</td>
<td>8/49 (16.3%)</td>
</tr>
</tbody>
</table>

Belardinelli

Hambrecht

Wirenberger

Walterkramer

Haefling

HR 0.96 (0.79–1.17), P=0.7

98/1159 (16%)

189/1159 (17%)

131/1159 (11%)

729/1159 (63%)

760/1172 (65%)

1 Tomyo University Ohashi Medical Center, Tokyo, Japan; 2 Gunma University School of Medicine, Department of Cardiology, Tomioka, Japan; 3 Gunma University School of Medicine, Department of Cardiovascular Medicine, Maebashi, Japan

* p<0.05 in univariate analyses. ** p<0.01 in univariate analyses. *** p<0.05 in univariate analyses.
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 responder operating characteristic curve analyzing cardiovascular event, cut off point of CT90% after 3 months of ASV therapy was 0.1. Patients were divided into those whose CT90% ≤ 0.1% or > 0.1% (good response group, n=34, and poor response group, n=37), and ASV cessation group (n=10). No significant differences were observed among these groups with respect to age, sex, New York Heart Association class, brain natriuretic peptide level, left ventricular ejection fraction, 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=0.048) (Figure 1).

**Conclusion:** These results suggest that ASV is effective in not only good response group but also poor response group.

P2804 | BEDSIDE

Rapid introduction of adaptive servo-ventilation in the emergency room reduces the rate of endotracheal intubation and hospitalization in patients with acute cardiacogenic 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 cardiacogenic 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 whenever oxygenation was insufficient. Exclusion criteria included cardiogenic shock, disturbance of consciousness, fatal arrhythmia, right-sided heart failure, infection, past history of noninvasive positive pressure ventilation and DNR.

**Results:** There were no significant between-group differences in sex, age, background disease, vital signs, medications, ejection fraction, brain natriuretic peptide and NYHA class IV. The mean duration of ASV was 9.8 hours. The ETI rate was significantly lower in the ASV group than the control group (3% vs 21%, P<0.01). The intensive care unit (ICU)/high care unit (HCU) length of stay was also significantly less in the ASV group than the control group (1.9±2.0 vs 5.3±6.8 days, P<0.01). Consequently, the hospitalization period was significantly lower in the ASV group than the control group (19.3±11.0 vs 26.3±16.6 days, P<0.01). Thirty-day mortality was not different between the two groups.

**Conclusion:** In patients with ACPE, rapid introduction of ASV in the emergency room reduces the hospitalization period and the need for ETI.

P2805 | BEDSIDE

Device-measured rapid shallow breathing with exertion worsens prior to heart failure decompensation

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**Introduction:** Respiratory complaints are common prior to heart failure events (HFEs) and may present as an elevated respiratory rate (RR) or decreased tidal volume (TV). We hypothesized that the changes in device-based respiratory measures in the week leading up to HF event would be larger with exertion than at rest.

**Methods:** Patients with cardiac resynchronization therapy defibrillators were enrolled in the MultISENSE study and followed for up to a year. The devices trended respiratory rate at the beginning of a scheduled TV visit, and activity level via accelerometer. Minute ventilation (MV) and rapid shallow breathing index (RSBI) were calculated as MV = RR×TV and RSBI = RR/TV, respectively. Daily values were calculated at rest and at elevated activity (Act). HFEs were defined as HF admissions or unscheduled visits with intravenous HF treatment. All HFEs were adjudicated. For each HFE, the average of a pre-event period (Evt, 1 to 7 days before HFE), the baseline (BL) and up to 3 days before HFE, and relative change (%chg=(Evt-BL)/BL) were calculated. The %chg with Act was tested against 0 using paired t-test. Statistically significant values with Act were compared against values at rest using paired Wilcoxon sign-rank test.

**Results:** Of the 532 patients, 58 had 63 HFEs with sufficient data. RSBI showed largest change during both rest (4%) and Act (6.9%), with RSBI being larger at rest. RR showed significant change during both rest (2.1%) and Act (2%) with no difference between activity levels. TV showed significantly larger change with Act (~3.7%) when compared to rest. MV did not change.

**Conclusion:** Rapid shallow breathing with exertion measured by RR, TV, and RSBI changes prior to HFEs and may be a useful device-based measure of impending HF decompensation.

P2806 | 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 (HFpEF). 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 HFpEF, when used by trainees with different levels of expertise.

**Methods:** Among 51 patients with symptomatic HFpEF and sinus rhythm (46 males, age 58±17 years) underwent standard transthoracic 2D and 3D full-volume acquisitions of the LV. One expert observer with more than 2 years of training in both 2D and 3D echo (Expert), and 3 trainees with different levels of expertise in 2D and one month-training in 3D echo (Beginner, Medium, and Advanced) measured the 2D and 3D LV volumes and LVEF of the same already-acquired images.

**Results:** Mean LVEF was 53±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 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.
**Background:** Elevated resting heart rate (HR) is associated with worse outcomes in patients with heart failure (HF) and reduced left ventricular ejection fraction (LVEF). The purpose of this study was to evaluate the impact of HR on the clinical and hemodynamics of patients (pts) under cardiac resynchronization therapy (CRT).

**Patients and methods:** This study comprised 45 HF pts under CRT who were subjected to clinical assessment for NYHA functional class and echocardiogram for determination of LVEF, mitral & aortic valve time intervals (MVTI & Ao-VTI), filling & ejection times (FT & ET), and systolic pulmonary artery pressure (SPAP). Tissue Doppler imaging (TDI) was performed to calculate dysynchrony index (TS-SD) from 6 basal LV segments. Average HR was assessed using 24 hour Holter monitoring. Patients were classified according to their average HR into Group 1 (17 pts) with average HR ≤ 75 bpm and Group 2 (28 pts) with average HR > 75 bpm.

**Results:** Group 1 (with patients lower HR) had significantly lower mean NYHA functional class & SPAP, significantly higher LVEF, M-VTI, Ao-VTI, FT and ET compared to Group 2 (patients with higher HR). There was no significant difference between Group 1 and Group 2 regarding TS-SD (Table 1).

**Table 1. Comparison between Group 1 & Group 2**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (HR ≤ 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>2.10±0.7</td>
<td>2.70±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±19</td>
<td>34±5.3</td>
<td>0.026</td>
</tr>
<tr>
<td>M-VTI (cm)</td>
<td>21±9.4</td>
<td>17±3.3</td>
<td>0.000</td>
</tr>
<tr>
<td>FT (ms)</td>
<td>29±1.7</td>
<td>23±1.7</td>
<td>0.005</td>
</tr>
<tr>
<td>Ao-VTI (cm)</td>
<td>27±0.9</td>
<td>24±2.6</td>
<td>0.000</td>
</tr>
<tr>
<td>TS-SD (ms)</td>
<td>17±4.8</td>
<td>19±4.11</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Conclusion:** Lower average HR (≤ 75 bpm) is associated with better clinical and hemodynamic response to CRT.

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**P2808 | BENCH**

Apocynin attenuates systolic dysfunction and decreases superoxide generation in soleus muscle of heart failure rats


**Background:** Oxidative stress is increased in cardiac and skeletal muscles during heart failure. In this study we evaluated the effects of the antioxidant apocynin on cardiac remodeling and oxidative stress in soleus muscle of rats with aortic stenosis (AS)-induced heart failure.

**Methods:** Twenty weeks after AS induction or sham surgery (n=11), rats were assigned to non-treatment (AS, n=11) or treatment with apocynin (AS-A, 16 mg/kg/day in drinking water, n=9) for 8 weeks. Echocardiogram and tissue Doppler imaging were performed before and after treatment. Antioxidant enzymes activity was assessed by spectrophotometry. Total production of reactive oxygen species was evaluated in muscle by quantifying two dihydroxyethidium (DHE) oxidation-derived fluorescent compounds, 2-hydroxyethidium (EOH) and ethidium, using high performance liquid chromatography (HPLC). Soleus trophism was assessed in histological sections. Statistical analysis: ANOVA and Bonferroni.

**Results:** Before treatment, echocardiographic parameters did not differ between AS and AS-A groups. Heart failure was characterized by the increased right ventricle weight-to-body-weight ratio in aortic stenosis groups (Sham 0.61±0.07, A 1.13±0.44; AS-A 1.25±0.02 mg/g; p=0.01). After treatment, both AS groups presented left cardiac chambers dilation. Mean mitral annular systolic velocity (Sham 3.15±0.51, A 2.32±0.38; AS-A 2.17±0.41 mm/s; p=0.01) was decreased in AS than Sham; in AS-A, it was between that in the Sham and AS. Cardiac trophism was not significantly different from either group. Plasma malondialdehyde concentration, evaluated by HPLC, did not differ between groups (Sham 148.6±25.4; AS 129.4±31.0; AS-A 129.0±37.0 μmol/g tissue; p=0.04). Ethidium/DHE ratio did not differ between groups (Sham 2.09±0.26; AS 1.63±0.31; AS-A 1.89±0.15 μmol/g tissue; p=0.02). Ethidium/DHE ratio did not differ between groups (Sham 686±111; AS 852±325; AS-A 756±191 μmol/g tissue; p=0.47). Soleus myosin heavy chain isoforms, evaluated by electrophoresis, and cross-sectional area (Sham 4152±1226; AS 3499±376; AS-A 3337±794 μ2) did not differ between groups.

**Conclusion:** Treatment with the antioxidant apocynin attenuates cardiac systolic dysfunction and oxidative stress in soleus muscle of heart failure rats.

**Acknowledgement/Funding:** FAPESP and CNPQ

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**P2809 | BENCH**

Unveiling the potential benefit of adenosine a2b receptor blockage to counteract right cardiac overload in rat pulmonary arterial hypertension


**Background:** Survival of patients with pulmonary arterial hypertension (PAH) is closely related to right ventricular (RV) overload adaptation and muscle performance. Adenosine is a fine-tune modulator of cardiac function through the activation of four receptors, A1, A2A, A2B and A3. Blockade of the A2B is protective against lung dysfunction associated to PAH. Here, we tested whether the same is applicable to the right cardiac function in animals with PAH.

**Methods:** PAH was induced in male Wistar rats by a single subcutaneous injection of monocrotaline (60 mg/kg, MCT group); control animals received the same volume of saline (CTRL group). Myographic recordings (spontaneously beating atria and electrically paced right ventricle (RV) contractions) and immunolocalization studies were performed 21 to 25 days after monocrotaline administration. Resistance (R) and pulmonary pressure (Ppa) at different frequencies (mL/s, mN/m, mN/m) were determined in each group. In a selective blocker, adenosine receptor agonist (A2A) and antagonist (A2BR), assessed chronotropy and inotropy in both groups, an effect antagonized by DPCPX (10 nM; selective A1R antagonist). Selective activation of A2AR with CGS21680 (0.003–1 μM) and A2BR with BA6160–6583 (0.01–10 μM) did not modify neither the rhythm nor the strength of myocardial recordings. In paced RV, Ppa (0.001–1 μM) and NECA (0.01–100 μM, a non-selective adenosine receptor agonist) caused small negative inotropic effects at highest concentrations tested. Blockade of A2BR with PSm 803 (100 nM) unveiled a positive inotropic response of NOCA (0.01–10 μM) only in RV in hyperoxia. In a subset of RV mycardium of PAH animals exhibited increased amounts of A2BR immuno-reactive cell infiltrates in interstitial spaces. Subsets of these A2BR positive cells also expressed CD11b (macrophages) and vimentin (fibroblasts) cell markers.

**Conclusion:** Data show that the acute and chronic actions of A1R on atrial chronotropy and inotropy are preserved in PAH animals. The A2BR may contribute to decrease RV contractility, since its blockade uncovered a positive inotropic effect of the adenosine analogue, NECA, in PAH animals. Interstitial infiltration with A2BR-positive fibroblasts and macrophages in the RV mycardium suggest that adenosine may control the release of pro-fibrotic inflammatory mediators and contribute to mechanical adaptation of RV to pressure overload in PAH patients.

**P2810 | 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, can promote signalling through the ACVR1 receptor. The importance of endoglin in regulating haematopoiesis, angiogenesis and cardiovascular development is well established, and endoglin mutations are associated with the vascular disorder hereditary haemorrhagic telangiectasia, a disease 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:** Endoglin was depleted in adult Rosa26-Cre-ERT2,Engr1f1f1 mice to generate “ubiquitous” endoglin knockout (Eng-iKOs). Rosa26-Cre-ERT2 line constitutively expresses Cre recombinase (Cdh15/PAC-CreERT2) to generate endothelial specific deletion 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 vascular remodelling in 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 ß-1 integrin. As HOHF model, that these mice treated with angiotensin II, we also treated 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 vasculosa 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 shown that inhibition of NEP in patients with chronic heart failure (HF) and left ventricular systolic dysfunction is associated with better prognosis. However, no data are available about NEP significance in patients with acute HF (AHF). The aim of this study was to investigate soluble NEP concentrations and their clinical correlates in patients with AHF at admission and discharge.

Methods: A total of 129 patients (age 71±11 years, 58% male, 44% with LVEF <50%) were included. Serum samples were obtained at admission and during hospitalization. NEP concentrations were measured using an accustomed 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 0.36-1.41]). At discharge, levels of NEP showed a trend to be lower (median 0.52 [0.35 to 1.15]; p=0.05). We found a significant correlation of NEP and NT-proBNP concentrations at admission (rs=0.25; p<0.009). Creatinine and BUN were also significantly correlated to NEP levels at admission (rs=0.28; p=0.002 and rs=0.26; p=0.004 respectively). In addition, patients who were already receiving ACEI/ARB had a trend to higher levels of NEP at admission (median 0.72 vs 0.58; p=0.069), as well as the comparison group of those who were not receiving ACEI/ARB blockers (median 0.79 vs 0.58; p=0.089). All other clinical and echocardiographic variables did not show any correlation with NEP levels. In addition, no variables correlated with changes of NEP concentrations at discharge.

Conclusions: AHF patients with AHF, soluble NEP concentrations at admission are elevated and decreased after clinical stabilization at discharge. NEP levels at admission seemed to be related with natriuretic peptides concentrations, renal function and the previous pharmacological neurohormonal blockade.

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 diminished 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 mononuclear leukocytes: monocytes, Th17 and Treg lymphocytes. The study enrolled 50 stable CHF-CRT patients, NYHA class II-III, EF <=35%, 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, CD200 and CD127 respectively. We were able to show that initially CHF patients had more classical (CD14+CD16-) monocytes in 1 ml as compared to controls (399±125 vs 288±76; p<0.028). Moreover, they presented lower frequency of Th17 lymphocytes (14.6% 7.1-43.7% IQR, p=0.02) and Treg lymphocytes (4.3% 2-12.1% IQR, p=0.01). In contrast to previously reported by other authors we did not find differences in the number of Treg lymphocytes. Six months after the CRT device implantation the numbers of monocytes from intermedi- ate (CD14+CD16+) and non-classical (CD14-CD16+) subpopulations (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 still limited. This study aimed to analyze the complementary potential of HGF in a population of 373 patients (age 76±10 years, 48% males) 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.

Methods: We aimed to evaluate the complementary prognostic role of HGF in a population of 373 patients (age 76±10 years, 48% males) admitted with AHF in three university hospitals. Blood samples were obtained at admission, and clinical and echocardiographic data were recorded during the hospitalization. Patients were followed at 1 year.

Results: HGF concentrations were 2323±1659 pg/ml, which significantly correlated with NT-proBNP (p=0.001), cystatin (p=0.006) and eGFR (CKD-EPI, MDRD, cys or Hoek-13 based, p=0.001). However, no correlations were found with echocardiographic parameters (LVEF, LV mass index, and left atrium diameter), serum creatinine or BUN levels. Patients who also had high concentration of HGF were older (median 79 vs 73; p=0.005), had lower BUN levels (5.46/m2 in females through dual energy X-ray absorptiometry immediately before discharge.

Conclusions: HGF concentrations correlate with those of natriuretic peptides and measures of renal function in patients with AHF, but not with echocardiographic parameters of cardiac remodeling. HGF provided significant prognostic information and added complementary information over natriuretic peptides.

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 increased attention because it has been proposed as a prognostic factor for various diseases. The aim of the 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 <5.47/m2 in males and <5.87/m2 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 had higher BNP levels (33.7±17.4 vs. 27.3±10.1 mg/dl) and Na levels were (0.22±0.03 vs. 0.21±0.03, 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.
state, rendering them resistant to further diuretic therapy. Thus, clinically indicated compensated status of patients with sarcopenia is not sufficiently compensated as well as their hypoalveolar state, which is contradictory, clinicians misread the fluid status at the chronic phase of heart failure management. This shows why clinicians face difficulty managing the health condition of such patients compared with patients without sarcopenia and why the prognosis of such patients is uncertain.

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. 9 articles were examined for more details, and 5 were included in the present analysis, corresponding to a total of 5123 patients (mean age 71±10 years, male 2588). Patients with infection coexisting with CHF tended to have higher PCT concentration versus those with CHF alone (0.23±0.15ng/l versus 0.12±0.03ng/l, p=0.145). Follow-up ranged from 22 days to 180 days among the studies. Cut-off values for PCT ranged from 0.1 ng/l to 0.25ng/l; when compared to patients with low PCT concentrations, patients with above the cut-off value PCT had increased mortality (RR 1.62; 95% CI [0.33–2.49], 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: insights from KorHF Registry during the peripartum period
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Background: Elevated troponin levels in pregnancy may lead to predictive cardiac events in pregnant women during the peripartum period. Multiplex cardiac troponin testing has been shown to have the benefit of higher test sensitivity and specificity compared with single cardiac troponin testing. However, the time course of troponin release during pregnancy and delivery has not been fully characterized. The aim of this study was to evaluate the cardiac troponin (cTn) release pattern in pregnant women during pregnancy and delivery.

Methods: We sequentially assessed 463 consecutive Japanese pregnant women during the third trimester (28–30 weeks of 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±1.9 years; age of 35 years, 18.2%; pregnancy-induced hypertension (PIH), 4.5%; oxytocin use, 31.9%; delivery by cesarean section, 17.2%; and mean hemoglobin levels during the third trimester and after delivery. 11±1.0 and 10±1.4, respectively. Ejection fraction did not change between the third trimester and after delivery.

Conclusions: We performed a systematic review and meta-analysis of studies that aimed at determining the prognosis of PCT in CHF. Currently, a promising treatment for myocardial infarction is cell-based exogenous cardiac tissue. Three-dimensional growth of cardiac stem cells to form biosynthetic cardiac tissues
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Factors associated with increased levels of serum cardiac troponin during the peripartum period
M. Okano1, T. Kato1, A. Miyata2, T. Nagano2, M. Inoko1. 1The Tazuke Kofukai Medical Research Institute, Kitano Hospital, Cardiovascular Center, Osaka, Japan; 2The Tazuke Kofukai Medical Research Institute, Department of Obstetrics and Gynecology, Osaka, Japan

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Methods: We sequentially assessed 463 consecutive Japanese pregnant women during the third trimester (28–30 weeks of 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±1.9 years; age of 35 years, 18.2%; pregnancy-induced hypertension (PIH), 4.5%; oxytocin use, 31.9%; delivery by cesarean section, 17.2%; and mean hemoglobin levels during the third trimester and after delivery. 11±1.0 and 10±1.4, respectively. Ejection fraction did not change between the third trimester and after delivery. cTn 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 of 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 of gestation.
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: 2.01 per 1 g/dL decrease, 95% CI: 1.006–2.714, p<0.0001). None of the women met the criteria for peripartum cardiomyopathy.

Conclusion: Serum cTnI and BNP levels in the peripartum period were increased as compared to those at 28–30 weeks’ gestation. Moreover, the factors affecting elevated cTnI levels, which are potential predictors of cardiac events, were identified in Japanese pregnant women.

LONG TERM MONITORING & PROGNOSIS IN HEART FAILURE

P2819 | BEDSIDE
Does the inclusion of depression and cognitive screening to frailty assessment improve prediction of outcomes in heart transplant-eligible patients?
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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) in predicting outcome.

Results: 120 patients (83M:37F; age 53 ± 13 years, range 16–73; LVEF 27 ± 14%) with AHF were followed for 279 ± 202 days. Using FP, 82 were non- or pre-frail (NPF) and 38 were frail. Using mFP, 68 were NPF and 52 were frail. Frailty was independent of age, LVEF and renal function. Frailty (by FP or mFP) was associated with female gender, anaemia, hypoalbuminemia and mortality (Figure). Using Cox proportional hazards model, frailty assessed by mFP remained an independent predictor of survival but frailty as assessed by FP did not.

Discussion: 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 inept patient 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 guideline lines recommending that all patients admitted with heart failure should receive input from a specialist heart failure team. We report the results of our implementation in a single tertiary referral centre through the establishment of a heart failure service (HFS) and the appointment of a single heart failure specialist nurse specialist.

Results: We compare 12 month periods before (period 1) and after (period 2) implementation of an inpatient HFS.

During period 2, there were 107 fewer (3383 v. 3490) patients admitted 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, equaling to 1305 fewer bed days used in period 2.

During period 2, adherence to heart failure therapy guidelines on discharge was significantly better in those seen by the HFS. See figure 1. In-hospital mortality for all heart failure admissions was reduced to 11.1% v. 12.6% (RRR 13.2%; ARR 1.7%), equaling 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>

Conclusion: Nearly one quarter of patients discharged following an index HF hospitalisation require early readmission. A significant number of admissions are due to noncardiovascular causes. HFpEF and HFpEF demonstrate similar readmission patterns.
ever, the number of health centers that perform autopsies is decreasing and only a few studies analyzed post-mortem findings in patients with heart failure.

**Methods:** We analyzed the reports of autopsies performed between January 2000 and April 2005 in our cardiology hospital. Patients with diagnosis heart failure, cardiogenic shock, or cardiomyopathy at autopsy were included. Congenital heart diseases, patients younger than 18 years-old, pericardial diseases and postoperative shock were excluded.

**Results:** We analyzed 1226 autopsy findings and selected 500 cases - 322 (34.4%) male, 178 (35.6%) female and mean age was 62.4±15.9 years. Of the excluded cases (376), 236 (62.7%) were due to congenital heart diseases, 128 (34.1%) postoperative shock and 12 (3.2%) pericardial diseases. Heart failure etiology was ischemic in 200 (40%) patients, Chagas disease in 65 (13%), hypertension in 52 (10.4%) and rheumatic disease in 63 (12.6%). According to autopsy, the most common cardiac etiology of death was cardiogenic shock in 209 cases (41.8%) and septic shock in 103 (20.6%) and pulmonary embolism in 59 (11.8%).

**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.

**P2823 | BEDSIDE**

Chikungunya virus induced myocarditis

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**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 Chikunguya infection from a Venezuelan outbreak.

- **Results:** Of the 270 patients examined, 108 patients were male, with a mean age 60±9; 260 patients presented with fever and polyarthralgia and 81 developed sudden deaths.
- **Arrhythmias:** Arrhythmias occurred in 46.6% of cases; they included bradyarrhythmias (33%), atrial and ventricular ectopic beats and tachyarrhythmias where atrial fibrillation was observed in 16 cases. There were also ectopic atrial tachycardia and non-sustained ventricular tachycardia, conduction disturbances and 3 cases of sudden death.

**Conclusion:** Physicians should be aware of the possibility of manifest or silent myocarditis in almost half the patients with Chikungunya disease. In a proper epidemiological context, the triad of fever, polyarthralgia and new arrhythmias including bradyarrhythmias suggests Chikungunya myocarditis.

**P2824 | BEDSIDE**

Graft rejection requiring treatment within the 1st year after heart transplantation significantly affects survival, as opposed to later rejection episodes

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**Purpose:** The highest mortality rates after heart transplantation (HTx) occur in the first post-Htx year and it has been proven that 20–40% of patients develop at least one episode of acute cellular rejection within this time period. In order to study the occurrence of the time of graft rejection occurrence, we evaluated the survival of patients after heart transplantation in relation to the timing of graft rejection occurrence.

**Methods:** We retrospectively studied 74 consecutive HTx recipients from our center (mean age 53 ±13.6; median follow-up 24 months) and have measured the time to first histopathological signs of any graft rejection (ISHLT grade >0R), time to first graft rejection requiring treatment (ISHLT grades 2R and 3R, as well as antibody mediated rejection), and survival time. The Kaplan Meier method for survival rates (log-rank test for comparison), and multivariate analysis using Cox regression analysis were performed.

**Results:** Patients treated for acute graft rejection within the first 12 post-transplant months had significantly lower survival rates (p=0.033) (Figure 1), and a HR of 6.65 (95% CI 1.46–30.41, p=0.015) compared to patients who did not experience acute graft rejection requiring treatment in this time period (adjusted for sex and age). None of the following had a significant influence on survival: time to first histopathological signs of any graft rejection, occurrence of graft rejection requiring treatment between post-HTx months 12–24, or later than 24 months post-HTx.

**Conclusion:** Our results demonstrate that acute graft rejection requiring treatment occurring within the first post-transplant year has a significant impact on survival of heart transplant recipients, as opposed to rejections occurring at a later time period.

**P2825 | BEDSIDE**

The current situation of management of systolic heart failure in Russia: Russian hospital heart failure registry (RUS-HFR) results

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**Purpose:** The aim of RUS-HFR was to obtain contemporary analysis of the HF management and 1-5-year outcomes of inpatients with chronic systolic HF in real-life clinical practice in Russian Federation (RF).

**Methods and results:** The RUS-HFR is a prospective, multicentre, observational study conducted in 3 Cardiology Centers. Inclusion criteria: HF NYHA I-IV, LVEF ≤40%, age 18–75 years. 524 patients were enrolled in all centers. Age was 60±9.6, 80.5% men, ischemic 63.3–74.8%, hypertension 69.5–88.9%, DCM 4.6–5.2%, LVEF 28.5±7.2%. NT-proBNP was not a routine diagnostic test: COPD was 11.5–26.6%, AF 43.2–47.4%, diabetes 20.0–22.8%, CRT (4.5%) and ICD (5.2%) have been previously implanted in patients from Almazov Centre. RAS blockers, β-AB, and MRAs were used in 82.3–87.3%, 76.3–95.8%, and 65.9–81.1% of patients, respectively. The rate of prescription of these drugs prior admission was significantly lower: RAS blockers 12.6–58.7%; β-AB 11.3–70.7%; MRAs 4.4–53.3%. Diuretics prior to hospitalization were not taken in 55%, 23%, 24% of patients with NYHA II, III and IV, respectively. Overall, 80.7–94.6% of patients were on diuretics at hospital discharge. The median duration of hospital stay for HF decapsulation was 18 days (interquartile range 13–26). Indications for implantation of devices (ICD and CRT) were determined at 4.6–21.2% of patients. Indications for heart transplantation were identified to 17 patients from center No. 1 (center with heart transplant program). Dose reduction of basic drugs recommended for the treatment of HF and the proportion of patients receiving these were observed after hospitalization in 1.5 years of follow-up period. Ambulatory patients with CHF were under the supervision of a cardiologist and therapist in the 43–72% and 15–42% cases, respectively, and 7–17% of patients did not visit a doctor at all. The all-cause death and hospitalization for HF decapsulation within 1.5 years of follow-up were 11.6±20.8±26 and 16.1±21/±47.3% respectively in 3 centers with less value in center No. 1.

**Conclusion:** The main drugs recommended for outpatient HF were used insufficiently. Oral diuretics were not prescribed for the clinical manifestations of HF in 23–55% of cases. High-tech methods of treatment in patients with HF NYHA II–IV were not often enough recommended. The mortality and re-hospitalization in 1.5 years due to decompensated HF in RF remained high. HF management in RF still present the most problematic item depending on many factors, one of the way to improve is to organize network of specialists and consulting HF clinics throughout the country.
High burden of primary care contacts in patients with left ventricular systolic dysfunction- findings from the heart failure and optimal outcomes from pharmacy study

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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>1.005</td>
<td>0.045</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>0.047</td>
</tr>
<tr>
<td>Prescribed loop diuretic</td>
<td>No</td>
<td>424</td>
<td>9.9 (9.3–10.6)</td>
<td>1.001</td>
</tr>
<tr>
<td>Yes</td>
<td>549</td>
<td>12.1 (11.4–12.9)</td>
<td>1.07 (1.07–1.27)</td>
<td>0.001</td>
</tr>
<tr>
<td>LVSD severity</td>
<td>Mild</td>
<td>379</td>
<td>11.1 (10.0–11.7)</td>
<td>1.031</td>
</tr>
<tr>
<td>Moderate</td>
<td>425</td>
<td>11.0 (10.2–11.7)</td>
<td>0.93 (0.85–1.02)</td>
<td>0.398</td>
</tr>
<tr>
<td>Severe</td>
<td>169</td>
<td>10.3 (9.4–11.3)</td>
<td>0.86 (0.76–0.96)</td>
<td>0.004</td>
</tr>
<tr>
<td>Duration of LVSD (yrs)</td>
<td>&lt;0–1.99 282</td>
<td>12.4 (11.4–13.5)</td>
<td>1.000 (1.00–1.00)</td>
<td>0.994</td>
</tr>
<tr>
<td>≥2–3.99 256</td>
<td>11.2 (10.3–12.2)</td>
<td>0.88 (0.79–0.98)</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>≥4 435</td>
<td>10.3 (9.7–11.0)</td>
<td>0.85 (0.78–0.94)</td>
<td></td>
<td></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 hyper-trophic cardiomyopathy (HCM) according to the new ESC guidelines (2014) has not been assessed in patients treated invasively for left ventricular outflow tract (LVOT) obstruction.

Methods: We determined the risk score for SCD according to AHA/ACC 2011 guidelines and compared to the estimated SCD risk according to ESC 2014 guidelines in patients with obstructive HCM before and after septal alcohol ablation (SAA).

Results: SAA was performed in 470 patients. Nineteen died of SCD during 8.4±4 years of follow up. The SCD rate was 0.5% pr. year or 3.4 (CI: 1.9–5.4) %/5 years. The prevalence of risk factors before SAA was: Syncope 26%, family history of SCD 12%, Left atrium dimension was 48±7 mm and maximal LVOT gradient (at rest or during provocation) was 115±52 mmHg. At baseline the proportion of high risk patients was 24% (89/361) according to AHA/ACC guidelines (≥2 risk factors) and 36% (133/360) according to ESC 2014 guidelines (estimated risk of SCD ≥6%/5 years) (p<0.001; Kappa=0.60) (median 5.4 (IQR 3.0–8.2) %/5 years). All risk parameters had improved after SAA and the proportion of high risk patients were 8.4% (23/275) (AH/ACC 2011) and 4.5% (15/310) (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. The post-SAA estimated SCD risk (ESC 2014) was median 1.8 (IQR 1.2–3.1)%/5 years and the corresponding observed SCD rate in patients with complete post- SAA ESC risk assessment (n=310) was 2.5% (CI: 0.9–4.9)%/5 years. The post SAA SCD prediction had lower sensitivity for both ESC and AHA/ESC guidelines.

Conclusion: The new 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.

IMAGING ON DIAGNOSIS & PROGNOSIS IN HEART FAILURE

P2828 | BEDSIDE

Comparing the efficacy of Tadalafil versus Placebo on pulmonary artery systolic pressure and right ventricular function in patients with beta-thalassemia intermedia

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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 inducted in the study based on the maximum amount of a normal pulmonary artery systolic pressure (PASP) and the tricuspid regurgitation velocity (TRV) measured by transthoracic echocardiography (TTE), which is the threshold for the diagnosis of pulmonary hypertension. Patients with hepatic or renal insufficiency and also patients who are treated with organic nitrates or alpha-blockers were excluded. 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.
the incidence in patients (PTS) treated with pacemakers (PM) for standard anti-bradycardic indications and how it is influenced by initial systolic function. Methods: Clinical and echocardiographic evaluation (ECHO) of PTS with standard PM indications at the time of PM implant and after a follow-up (FU) of min. > 2 months.

Results: 1131 PTS (45% male, mean age 73 yrs; a-v-block 49%; sinus node disease 45%) had an ECHO at the time of implantation and during a FU of 3.6±1.8. 849 (75%) PTS had a normal systolic LV function (EF - 55%, group 1), 191 (17%) PTS had a slightly impaired LV function (EF 45–55%, group 2) and 91 (8%) PTS had a moderately or severely impaired LV function (EF < 45%, group 3) at baseline. At the end of FU within group 1 706 PTS (83%) had an unaltered normal LV function, 143 (17%) had a LV function deterioration. In group 2 LV function was unaltered in 75 PTS (39%), 66 (35%) enhanced and deteriorated in 50 PTS (25%). Anti-arrhythmia therapy of LV function was shown in 32 PTS (35%), 45% preserved their initial LV function and 24% impaired their LV function within group 3. 26/1131 (2.3%) PTS developed severe HF (NYHA:3) and were upgraded to biventricular pacing (CRT). The incidence was 12 (1.4%) in group 1, 8 (1.4%) 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 patients with HTN showed a reduced LV systolic function and global contractility and relaxation decreased even in HTN without LVH and further deteriorated in HTN with LVH (−). Antioxidative therapy including NO therapy might be considered even in HTN without LVH to prevent deterioration of initially normal LV function.

P2830 | BEDSIDE

Noninvasive estimation of the feature of hypertensive heart failure using novel one-beat three-dimensional speckle tracking echocardiography with high volume rates

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Background: Left ventricular (LV) systolic and diastolic properties in hypertensive heart failure (HHF) with preserved ejection fraction are not fully elucidated. We examined 54 controls (age 69±9), 50 patients with HTN without LVH (age 70±9), 40 patients with HTN with LVH (age 69±9) and 24 patients with HTN with LVH and HTN (age 71±9). In patients who have diabetes mellitus and coronary artery disease were excluded. LV layer contractility and relaxation were assessed by radial HHF (age 71±11). Patients who have diabetes mellitus and coronary artery disease with aortic stenosis, atrial fibrillation, or HTN were excluded. LVH (−) was defined if LV diameters were within normal range, and LVH (+): if LV diameters were increased but less than 2 standard deviations above normal LV diameters.

Methods: We retrospectively reviewed our cardiac catheterization laboratory data from 2005–2014 and identified 65 patients with HTN. We reviewed their clinical history, ECG findings, coronary angiographic findings, and echocardiogram reports and compared them to 48 patients with AAMI.

Results: The ECG findings among patients with HTN compared to those with AAMI were summarized in table 1. There were five findings that were significantly associated with HTN. Surprisingly, ST-segment elevation >0.5mm in lead -aVR was non-diagnostic, contrary to previous studies. Using logistic regression, the finding of no reciprocal changes in the inferior leads combined with (LSTE in leads V1-V3) – (LSTE in leads V4-V6) <0, resulted in a sensitivity and specificity of 86.2 and 84.1, respectively.

Table 1. Echocardiographic comparison

<table>
<thead>
<tr>
<th>n Reciprocal changes in inferior leads</th>
<th>Mean (SD)</th>
<th>ST in lead V1</th>
<th>Abnormal absence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVH (−)</td>
<td>48</td>
<td>16 (72.7%)</td>
<td>455.5 (41.9)</td>
</tr>
<tr>
<td>LVH (+)</td>
<td>65</td>
<td>6 (27.3%)</td>
<td>477.1 (49.3)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.001</td>
<td>0.016</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: As the largest study to date comparing ECG findings of HTN and AAMI, our data further support findings of other studies, except for the utility of ST in -aVR. With future larger studies, risk stratification criteria may help in the differentiation of HTN from AAMI.

P2832 | BEDSIDE

Clinical and echocardiographic correlation of plasma transforming growth factor (TGF)-beta levels in patients with heart failure

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Background: The role of transforming growth factor-beta (TGF-β) in the pathogenesis of heart failure (HF) has been studied extensively in animal models, but its definite role and clinical relevance in humans is not well defined. Recently, we have established a bioassay using mink lung epithelial cells (MLEC) to measure TGF-β bioactivity and demonstrated that myocardial TGF-β bioactivity was significantly enhanced in advanced human HF.

Purpose: We investigated plasma TGF-β bioactivity in HF patients to test whether TGF-β levels correlate with clinical and echocardiographic parameters.

Methods: Total of 38 patients with reduced ejection fraction (EF) less than 35% were recruited from the HF program at our institution between December 2012 and November 2014. Plasma TGF-β level was measured by MLEC bioassay. Echocardiographic parameters EF, left atrial (LA) size, and left ventricular end-diastolic dimension (LVEDD), and clinical data including NYHA class, etiology (ischemic vs non-ischemic), and presence of atrial fibrillation (AF) were analyzed.

Results: The data are shown as means±SD. Patients were 60.9±13.6 years old, with 71.1% being males. See table.

Table 1. TGF-β levels in HF patients

<table>
<thead>
<tr>
<th>Total patients (N)</th>
<th>Plasma TGF-β (ng/ml)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NYHA class</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I-II</td>
<td>20/36</td>
<td>42.6±12.3</td>
</tr>
<tr>
<td>III-IV</td>
<td>16/36</td>
<td>38.6±20.9</td>
</tr>
<tr>
<td>LA size (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤5.0</td>
<td>25/36</td>
<td>24.8±12.3</td>
</tr>
<tr>
<td>&gt;5.0</td>
<td>11/36</td>
<td>42.3±22.6</td>
</tr>
<tr>
<td>LVEDD (cm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤5.5</td>
<td>10/36</td>
<td>32.1±22.5</td>
</tr>
<tr>
<td>&gt;5.5</td>
<td>26/36</td>
<td>39.4±16.0</td>
</tr>
<tr>
<td>EF (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤25</td>
<td>19/38</td>
<td>30.7±16.5</td>
</tr>
<tr>
<td>&gt;25</td>
<td>19/38</td>
<td>29.9±16.4</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>18/38</td>
<td>31.1±19.0</td>
</tr>
<tr>
<td>Non-ischemic</td>
<td>20/38</td>
<td>29.9±16.4</td>
</tr>
<tr>
<td>AF</td>
<td>11/38</td>
<td>30.7±16.5</td>
</tr>
<tr>
<td>No</td>
<td>27/38</td>
<td>31.4±18.1</td>
</tr>
</tbody>
</table>

Conclusion: Plasma TGF-β levels were significantly higher in HF patients with advanced NYHA class (III-IV) and larger LA size, suggesting that plasma TGF-β levels may reflect the severity of HF. Further investigations will be required to confirm its clinical value as a biomarker.

Acknowledgement/Funding: US National Institute of Health

P2833 | BEDSIDE

Subclinical impairment of left ventricular function in patients with end stage renal failure detected by three-dimensional speckle tracking echocardiography

M.M. Sun, X.H. Shu, Y. Kang, C.Z. Pan, X.S. Cao, J.B. Ge. Zhongshan Hospital of Fudan University, Shanghai, China, People's Republic of

Purpose: Left ventricular (LV) dysfunction is known as a major cause of death in patients with end stage renal failure (ESRF). The aim of this study was to in-
3DSTE may have potential in the evaluation and follow-up of patients with ESRF.

**Conclusions:**

Two groups (67.4±3.5% vs 66.3±4.6%, p=0.393). Multiple linear regression analysis showed a higher in the ESRF group (T_ms: 38±5% vs 41±6%; T_ls: 38±5% vs 42±6%, p<0.05). Additionally, T_ms and T_ls were described in the ESRF group (T_ms: 38±5% vs 41±6%; T_ls: 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 analysis suggested that AAD 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.

**Abstract P2836 | BEDSIDE**

**Predicting left ventricular reverse remodeling as well as outcome after cardiac resynchronization therapy with a score combining clinical, electrocardiographic, and echocardiographic parameters**

A. Bernard1, S. Marechaux2, L. Fauchier1, A. Menet2, M. Fournet3, F. Schnell1, C. Leducq4, P. Mabo5, E. Donal3,5, 1 Tours Regional University Hospital, Hospital Trousseau, Tours, France; 2 Université Lille Nord de France, GCS-Groupement des Hôpitaux de l’Institut Catholique de Lille, Facu, Lille, France; 3 University Hospital of Rennes, Department of Cardiology and Vascular Disease / CIC-IT 804, Rennes, France.

**Objectives:** After having previously described a score combining clinical, electrocardiographic and echocardiographic parameters to predict left ventricular remodeling 6 months after CRT, we sought to evaluate the L2ANDS2 score in terms of clinical outcomes.

**Methods:** 207 heart failure patients implanted with a CRT device were followed 2 years after implantation for cardiovascular death, heart transplantation, ventricular assistance or unplanned hospitalization for heart failure. Baseline clinical, electrocardiographic and echocardiographic characteristics and different scoring systems including 5 parameters (as left bundle branch block, Age ≥ 70 years, non-ischemic etiology, left ventricular end-diastolic diameter ≥ 40 mm/m2, and septal flap) were evaluated for the prediction of cardiovascular death, heart transplantation or ventricular assistance.

**Results:** Among the followed 204 patients, a cardiovascular death, an heart transplantation or a ventricular assistance was observed in 12 patients after a 2-year follow-up. In univariate analysis, patients without events significantly had more frequent non-ischemic etiology (p=0.02) and a higher L2ANDS2 score (p=0.04). None of the other baseline characteristics differed significantly between patients with clinical events and other patients. The L2ANDS2 score demonstrated a C-statistic of 0.676 to predict cardiovascular death, heart transplantation or ventricular assistance. Considering cardiovascular death, heart transplantation, ventricular assistance or unplanned hospitalization for heart failure, aL2ANDS2 below 5 was associated with a worse outcome than a score ≥ 5 (92% event-free survival vs. 78%; odds ratio 2.34, 95% CI 1.05−5.45, p=0.05) whereas ischemic etiology was not able to identify CRT patients with a different outcome in the analysis of event free curves.

In addition to predict left ventricular remodeling after CRT, the L2ANDS2 score is the only predictor associated with a better event-free survival for hard clinical outcomes in this population.

**Abstract P2838 – Table 1**

<table>
<thead>
<tr>
<th>Diagnosis (n) variable</th>
<th>Controls (46)</th>
<th>All CAD (125)</th>
<th>Chronic CAD (17)</th>
<th>Post PCI (36)</th>
<th>Post CABG (56)</th>
<th>Ischemic HF (16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (ys)</td>
<td>46±13</td>
<td>64±8**</td>
<td>65±9**</td>
<td>62±6***</td>
<td>65±7**</td>
<td>62±9***</td>
</tr>
<tr>
<td>EDV (ml)</td>
<td>136±29</td>
<td>155±53*</td>
<td>138±50</td>
<td>145±41</td>
<td>142±27</td>
<td>247±16***</td>
</tr>
<tr>
<td>EF (%)</td>
<td>69±6</td>
<td>61±37</td>
<td>65±8</td>
<td>65±8</td>
<td>64±7**</td>
<td>34±11***</td>
</tr>
<tr>
<td>LVM (g)</td>
<td>131±40</td>
<td>157±44**</td>
<td>139±41</td>
<td>146±49</td>
<td>159±39***</td>
<td>192±30***</td>
</tr>
<tr>
<td>AADist (PERvm)</td>
<td>0.70±0.45</td>
<td>0.63±0.62</td>
<td>0.44±0.30</td>
<td>0.59±0.39</td>
<td>0.50±0.35</td>
<td>1.38±2.28***</td>
</tr>
<tr>
<td>AADist (PERm)</td>
<td>1.97±1.03</td>
<td>1.30±0.76**</td>
<td>1.09±0.72**</td>
<td>1.36±0.63***</td>
<td>1.13±0.62***</td>
<td>1.98±1.14***</td>
</tr>
<tr>
<td>AADist (PERv)</td>
<td>2.08±1.05</td>
<td>1.30±0.76**</td>
<td>1.09±0.72**</td>
<td>1.36±0.63***</td>
<td>1.13±0.62***</td>
<td>1.98±1.14***</td>
</tr>
<tr>
<td>AADist (PER)</td>
<td>2.00±1.05</td>
<td>1.30±0.76**</td>
<td>1.09±0.72**</td>
<td>1.36±0.63***</td>
<td>1.13±0.62***</td>
<td>1.98±1.14***</td>
</tr>
</tbody>
</table>

**Conclusion:** In addition to predict left ventricular remodeling after CRT, the L2ANDS2 score is the only predictor associated with a better event-free survival for hard clinical outcomes in this population.
P2838 | BEDSIDE
Comparative study measuring the optic nerve sheath diameter with transorbital ultrasound in healthy women, pregnant women and pregnant with preeclampsia/eclampsia

E.G. Urias1, J. Ortega2, C.B. Arteaga3, 1Centro de Investigacion y Docencia en Ciencias de la Salud, Aneesthesiology, cullacan, Mexico; 2Instituto Mexicano del Seguro Social, Critical Care, cullacan, Mexico

Introduction: Preeclampsia/eclampsia is a potentially serious disease associated with maternal complications, including neurological. In patients with increased intracranial pressure, the diameter of the optic nerve sheath increases because of its close association with the flow of cerebrospinal fluid. Her measurements using ultrasound transorbital have shown correlation with increased intracranial pressure. 20% of patients with preeclampsia, the diameter of the optic nerve sheath increased because of its close association with the flow of cerebrospinal fluid. Her measurements using ultrasound transorbital have shown correlation with increased intracranial pressure.

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 measures of each eye were made, averaging them to give an mean to minimize the variability of the measurement.

Results: 60 patients, 20 in each group. The diameter of the optic nerve sheath was higher with statistical significance (p < 0.05) for both eyes in patients with preeclampsia/eclampsia. In group 3, 20% in the right eye and 25% in the left eye had a diameter of optic nerve sheath above 5.0 mm.

Table 1. Comparison of medias between groups

<table>
<thead>
<tr>
<th>Right eye MEDIA</th>
<th>Left eye MEDIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnostic</td>
<td>Healthy women</td>
</tr>
<tr>
<td>Healthy pregnant</td>
<td>3.7±0.7</td>
</tr>
<tr>
<td>Preeclampsia/Eclampsia</td>
<td>4.3±0.9*</td>
</tr>
</tbody>
</table>

*p < 0.05 between preeclampsia/eclampsia vs healthy women and vs normal pregnancy women; **p < 0.05 between preeclampsia/eclampsia vs healthy women and vs normal pregnancy.

Conclusion: Pregnant patients with the diagnosis of preeclampsia/eclampsia had diameters larger than the optic nerve sheath compared with women with normal pregnancy and healthy women. In this sense, measurement transorbital DNV2 by ultrasound appears as a new promising tool, affordable, accessible and non-invasive evaluation and timely care of patients with preeclampsia/eclampsia to rule elevated intracranial pressure.

P2839 | BEDSIDE
Catheter based renal denervation for resistant hypertension. 24 month results of the EnligHTN I Study using a multielectrode ablation system

C. Tsoufis, V. Papademetriou, K. Dimitriadis, A. Kasiakogias, M. Worthley, A. Sinhal, D. Chew, Y. Malaisayan, D. Tousoulis, S. Worthley. First Cardiology Clinic, University of Athens, Hippokration Hospital, Athens, Greece

Background and introduction: The EnligHTN I, the first-in-human study using a multielectrode ablation system for renal denervation (RDN) in patients with drug resistant hypertension (dRHT) demonstrated efficacy and safety at 6 and 12 months.

Purpose: The aim of this study was to report the complete set of 24 month data on office, ambulatory and home blood pressure (BP) changes as well as long term safety.

Design and methods: We studied 46 patients (age: 60±10 years, 4.7±1.0 antihypertensive drugs, body mass index: 32±5 kg/m²) with dRHT on ≥3 anti-hypertensive medications with a systolic BP >160 mmHg (untreated hypertensive/ stage III hypertensive/essential hypertensive diabetics). At baseline, the average office BP, 24-hour ambulatory BP and home BP were 176/16/14 mmHg, 150/14/8/13 mmHg and 158±16/90/12 mmHg respectively. Bilateral RDN was performed using percutaneous femoral approach and stereotactic 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 serious or life-threatening adverse events related with the procedure.

Conclusions: The EnligHTN I study provides evidence that the multielectrode ablation system constitutes a safe method of RDN in patients with dRHT and is accompanied by a sustained reduction of office, ambulatory and home BP at 24 months after the procedure. However, no predictors of RDN response were identified at long term follow up.
P2841 | BEDSIDE
Effect on heart rate following renal denervation: Insights from the Global SYMPPLICITY Registry
M. Boehm1, G. Mancia2, F. Mahlouf3 on behalf of Global SYMPPLICITY Registry. 1Universitätsklinikum des Saarlandes, Homburg, Germany; 2University of Milan-Bicocca, Milan, Italy
Background: Renal denervation (RDN) has been shown to reduce systolic blood pressure (SBP) in patients with resistant hypertension. Previous initial reports have shown a reduction in heart rate following RDN in patients with elevated baseline heart rate that was not correlated with a reduction in SBP.
Methods: We analyzed the change in heart rate and SBP among a large, diverse population of patients treated with RDN in the Global SYMPPLICITY Registry.
Results: The 6-month change in heart rate differed by baseline heart rate and SBP by tertiles based on baseline office and 24-hour ambulatory heart rate.
Conclusion: In the Global SYMPPLICITY Registry, RDN is associated with a significant reduction in office and 24-hour heart rate among patients with elevated baseline heart rate that is not associated with the reduction in SBP. This analysis supports previous reports of a direct cardiac effect of reduced sympathetic activity following RDN.
Acknowledgement/Funding: Medtronic, Inc. (ClinicalTrials.gov NCT01534299)

P2842 | BEDSIDE
Triple versus dual antiplatelet therapy in patients undergoing unprotected left main percutaneous coronary intervention
S.W. Rha, B.G. Choi, S.Y. Choi, J.K. Byun, J.B. Kim, S. Xu, E.J. Kim, C.G. Park, H.S. Seo, D.J. Oh. Korea University Guro Hospital, Seoul, Korea, Republic of Korea
Background: Whether triple antiplatelet therapy (TAPT) is superior to dual antiplatelet therapy (DAPT) in patients (pts) undergoing unprotected left main percutaneous coronary intervention (uLM-PCI) in the era of drug-eluting stents (DESs) remains unclear.
Methods: A total 246 consecutive pts successfully underwent uLM-PCI with DESs were enrolled from Oct 2003 to Feb 2014. A total of 179 pts received TAPT for at least 1 month and 67 pts received DAPT. Complications and clinical outcomes were compared between the two groups up to 3 years.
Results: The baseline clinical, angiographic, and procedural characteristics were similar between the two groups except that the TAPT group was treated with more number of DESs from LM to left anterior descending artery, most frequently with sirolimus-eluting stents, whereas the DAPT group zotarolimus-eluting stents. The TAPT group had a less incidence of no-reflow than the DAPT group. At 3 years, the incidence of individual and composite clinical outcomes was similar between the two groups except the lower incidence of myocardial infarction (MI) in the TAPT group. Kaplan-Meier curve showed lower incidence of cumulative MI up to 3 years in the TAPT group (Figure). Multivariate regression showed that initial loading of TAPT (hazard ratio 0.27, 95% confidence interval 0.08 to 0.84, p-value=0.025) or TAPT for at least 3 months in survivors within 30 days (hazard ratio 0.30, 95% confidence interval 0.1 to 0.97, p-value=0.045) were an independent predictor for MI at 3 years.
Conclusion: TAPT administration in pts undergoing uLM-PCI with DESs seems to be 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.

P2843 | BEDSIDE
Blood pressure reductions following catheter-based renal denervation are not related to improvements in adherence to antihypertensive drugs measured by urine/plasma toxicological analysis
S. Ewen1, M.R. Meyer2, B. Cremers3, U. Laufs1, D. Linz1, I. Kindermann1, C. Ukena1, H.H. Maurer2, M. Boehm1, F. Mahlouf3, 1Saarland University Hospital, Department of Internal Medicine III, Homburg, Germany; 2Saarland University Hospital, Institut für Experimentelle und Klinische Pharmacologie, Homburg, Germany
Background: Renal denervation can reduce blood pressure (BP) in patients with uncontrolled hypertension.
Objectives: The adherence to prescribed antihypertensive medication in patients undergoing renal denervation is unknown.
Methods: This study investigated adherence to prescribed antihypertensive treatment by liquid chromatography-high resolution-tandem mass spectrometry in plasma and urine at baseline and 6 months after renal denervation (RDN) in 100 patients with resistant hypertension, defined as baseline office systolic BP >140 mmHg despite treatment with ≥3 antihypertensive agents.
Results: Adherence to prescribed antihypertensive treatment was significantly reduced following RDN (ratio 0.30, 95% confidence interval 0.1 to 0.97, p-value=0.025) or TAPT for at least 3 months in survivors within 30 days (hazard ratio 0.30, 95% confidence interval 0.1 to 0.97, p-value=0.045) were an independent predictor for MI at 3 years.
Conclusions: 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.
turn thickness from 12.1±1.2 mm to 11.4±0.9 mm at 12 months and to 11.2±0.9 mm at 24 months (p<0.05 for all). After RDN, the number of patients with concentric LV hypertrophy (i.e. relative wall thickness >0.42 and LV mass >48 g/m²² for male and >44 g/m²² for female) decreased from 16 patients (80%) at baseline to 10 patients (50%) at 12 months, and to 7 patients (36.8%) at 24 months. Regressing diastolic function RDN caused an increase in mitral valve E/A ratio from 0.62±0.28 to 0.70±0.25 at 12 months and 0.84±0.32 at 24 months (p<0.05 for all) and a decrease in the E/E′ ratio from 14.8±6.1 to 11.8±3.7 at 12 months and to 9.7±4 at 24 months (p<0.05 for all).

Conclusions: This is the first study to show that multi-electrode RDN system results in a significant and sustained improvement of diastolic function and attenuation of LV mass index in increased cardiovascular risk resistant hypertensive patients after a follow-up of 24 months. These results suggest pleiotropic cardiovascular benefits of RDN therapy in the setting of resistant hypertension.

P2845 | BEDSIDE
Agreement between automatic and manual measurement of heart rate in patients with atrial fibrillation
T.T. Lin, C.L. Wang, C.L. Lai. National Taiwan University Hospital Hsin-Chu Branch, Internal Medicine, Hsinchu, Taiwan, ROC

Introduction: The accuracy of heart rate (HR) measurement by automatic oscillometric blood pressure (BP) monitors in patients with atrial fibrillation (AF) remains unclear. This study aimed to investigate the agreement between two automatic instruments and manual measurement of HR in patients with AF.

Methods: In 42 patients with persistent AF, HR was recorded using two automatic BP monitoring devices: Omron MS-I and Microlife BPA100 Plus. Meanwhile, manual counting of HR by stethoscope was treated as the reference. For each method, three readings were made at 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. If patients had HR above 80 bpm, the mean of HR had significant difference when using the Microlife device compared with manual counting (89.26±5.5 vs. 86.27±8.8, p=0.041) and the correlation coefficient had significant difference when using the Microlife device compared with manual counting of HR by stethoscope was treated as the reference. For each

Conclusions: There is high correlation between two devices and manually counting HR, which decreased slightly in patient with HR above 80 bpm via the Microlife device. Microlife device may over-estimate HR of AF patients.

P2846 | BEDSIDE
Quality of life after renal denervation: EuroQol 5 dimensions (EQ-5D) outcomes at 12 months in the Global SYMPlicity Registry
J. Wei¹, I. Kindermann⁰, G. Mancia³, F. Mahfoud⁴, M. Boehm⁵, on behalf of Global SYMPlicity Registry. ¹Sana Kliniken, Lübeck, Germany; ²Universitätsklinikum des Saarlandes, Homburg, Germany; ³University of Milan-Bicocca, Milan, Italy

Background: Renal denervation (RDN) has been shown to lower systolic blood pressure (SBP) in patients with uncontrolled hypertension. Less is known on its impact on quality of life. EuroQol 5 dimensions (EQ-5D) is a simple, self-administered survey that assesses health on five dimensions, including two attributes that may be related to hypertension: anxiety/depression and pain/discomfort.

Purpose: We evaluated changes in patients’ health status following RDN in the Global SYMPlicity Registry as assessed by EQ-5D.

Methods: The Global SYMPlicity Registry is a prospective, open-label, single-arm, all-comer worldwide registry that is evaluating the safety and effectiveness of treatment with the Symplity RDN system. All patients are asked to complete the Global SYMPlicity Registry SD at baseline and at follow-up. Outcomes on 497 matched patients (baseline, 6- and 12-months) are currently available.

Results: Patients with baseline office SBP >160 mmHg reported improved anxiety/depression levels; the percent of patients reporting “no problems” with anxiety/depression improved from 66% at baseline to 75% at 12 months (p<0.003); these patients also had a 12-month change in office SBP of −24.2±24.4 mmHg (p<0.001) (Table). Patients with office SBP <160 mmHg and isolated hypertension (i.e., no other comorbidities) were also less likely to report “severe problems” in terms of pain/discomfort at 12 months (8% at baseline vs. 0% at 12 months, p=0.002).

Conclusion: Patients with office SBP >160 mmHg who underwent RDN in the Global SYMPlicity Registry reported not only an improvement in SBP but also an improvement of anxiety/depression and pain/discomfort, as assessed by EQ-5D.

Acknowledgement/Funding: Medtronic, Inc. (ClinicalTrials.gov NCT01534299)

P2847 | BEDSIDE
The effect of low sodium dialysate on ambulatory blood pressure monitoring parameters in patients undergoing hemodialysis
S. Akgad¹, A. Akuyi¹, H.A. Calabrese³, A.R. Tsu², M. Askir¹, M. Yamamoto², Y. Soyora³, B. Yegin⁴, A.K. Gor⁵, H.A. Gumrukcuoglu⁶. ¹Yuzuncu Yil University Medical Faculty, Cardiology, Van, Turkey; ²Rize Kardar Government Hospital, Cardiology, Rize, Turkey; ³Mehmet Akif Ersoy Thoracic and Cardiovascular Surgery Education and Training Hospital, Cardiology, Istanbul, Turkey; ⁴Samson Education and Training Hospital, Cardiology, Samsun, Turkey; ⁵Yuzuncu Yil University Medical Faculty, Nephrology, Van, Turkey; ⁶Yuzuncu Yil University Medical Faculty, Anesthesiology and Reanimation, Van, Turkey; ⁷Yuzuncu Yil University Medical Faculty, Cardiovascular Surgery, Van, Turkey

Background: End stage renal disease (ESRD) is related with increased cardiovascular mortality and morbidity. Hypertension (HTN) is an important risk factor for cardiovascular disorder among hemodialysis (HD) patients.

Purpose: The aim of the present study was to investigate the effect of low sodium dialysate on systolic and diastolic BP levels detected by ambulatory blood pressure monitoring (ABPM) and interdiel weight gain (IDWG) in patients undergoing percutal hemodialysis treatment.

Methods: A total of 50 patients, who had creatinine clearance levels less than 1 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 enrollment, 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 night time 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). 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 night time DBP in HD patients compared with standard dialysis. We also concluded that low sodium dialysate lead to reduction in the IDWG and the number of antihypertensive medication.

P2848 | BENCH
Obstructive sleep apnea using watch-pat 200 is independently associated with an increase in the morning blood pressure surge in never-treated hypertensive patients
J.S. Cho, S.H. Her, S.H. Ihm, C.J. Kim, M.W. Park, G.M. Park, T.S. Kim. The Catholic University of Korea College of Medicine, Seoul, Korea, Republic of

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 67 patients (mean age: 55.2% male) with never-treated essential hypertension. The patients were divided into non-OSA (n=23, 49.3±12.7

Abstract P2846 – Table 1

<table>
<thead>
<tr>
<th>Baseline office systolic blood pressure</th>
<th>(N=64)</th>
<th>(N=154)</th>
<th>(N=279)</th>
<th>(N=131)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;140 mmHg</td>
<td>127.8±10.5</td>
<td>150.3±15.9</td>
<td>176.9±16.3</td>
<td>177.2±17.4</td>
</tr>
<tr>
<td>≥140 mmHg</td>
<td>127.8±10.5</td>
<td>150.3±15.9</td>
<td>176.9±16.3</td>
<td>177.2±17.4</td>
</tr>
<tr>
<td>12-month change in percent of patients reporting “no problems” in anxiety/depression</td>
<td>-1%</td>
<td>-5%</td>
<td>-9%</td>
<td>-12%</td>
</tr>
<tr>
<td>p-value</td>
<td>0.782</td>
<td>0.157</td>
<td>0.003</td>
<td>0.007</td>
</tr>
<tr>
<td>12-month change in office systolic blood pressure, mmHg</td>
<td>9.6±2.1</td>
<td>-5.5±1.8</td>
<td>-24.2±2.4</td>
<td>-25.2±2.3</td>
</tr>
</tbody>
</table>

Office systolic blood pressure presented as mean ± standard deviation.
We collected the 24-hour ambulatory BP, plasma aldosterone concentration, and plasma renin activity from all of the patients. The measured sleep-trough morning systolic blood pressure (SBP) increases were higher in the OSA group than in the non-OSA group (28.7±11.8 mmHg vs. 19.6±12.8 mmHg, P=0.008). The sleep-trough morning SBP increase was inversely correlated with the lowest O2 saturation (r=−0.272, P=0.039). OSA known to be associated with increased daytime and nocturnal sympathetic activity was associated with significantly higher sleep-trough morning SBP levels in this study.

**Acknowledgement/Funding**: The authors wish to acknowledge the financial support of the Catholic Medical Center Research Foundation.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariable</th>
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<th>Multivariable</th>
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<tr>
<td></td>
<td>Coefficient</td>
<td>SE</td>
<td>P value</td>
<td>Coefficient</td>
<td>SE</td>
<td>Partial R²</td>
<td>Model R²</td>
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<td>Age, years</td>
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<td>0.155</td>
<td>0.952</td>
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<td>Lowest SatO2 (%)</td>
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<td>0.466</td>
<td>0.001</td>
<td>0.999</td>
<td>0.499</td>
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<td>Night SBP SD</td>
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<td>e-GFR, ml/min/1.73 m²</td>
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<td>0.070</td>
<td>0.043</td>
<td>0.101</td>
<td>0.071</td>
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