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Transseptal endocardial left ventricular lead implantation after failed CRT implantation - long term results

Introduction: CRT implantation is a well established therapy in chronic heart failure patients. Transvenous left ventricular (LV) lead positioning may be challenging or in some cases impossible.

Objectives: The aim of this study was to investigate the effectiveness and safety of transseptal endocardial left ventricular lead implantation (TELIVL) in severe heart failure patients, and evaluate the long term follow-ups of the patients.

Methods: TELIVL was performed in 35 patients (30 men, 64±6 years, NYHA III-IV stage). Transseptal (TS) puncture was performed via the femoral vein. Intracardiac ultrasound was used to guide the puncture in 25 pts. The site of the puncture was dilated with a 6mm (3 pts), later with an 8 mm balloon (32 pts). After the puncture of the left subclavian vein, an electrophysiological deflatable CS catheter was introduced into the CS sheath. The CS catheter was used to reach the left atrium and the left ventricle through the dilated transseptal puncture hole. At the latest LV activation site 65 cm active fixation bipolar lead was screwed into the LV wall, at the site of the latest activation.

Results: The lead was fixed in the left ventricle in all cases with good pacing threshold (0,8±0,4 V; 0,4 ms). Puncture complication, pericardial effusion was not observed. Because of intraoperatively started anticoagulation, pocket haematoma was observed in three (9%) and needed evacuation in one case (3%). Follow-up was longer than one month in 34 patients (38 (22–49) months). Significant improvement of NYHA was observed in all but one case (97%), at the first month control LV EF was 30±9% vs 38±6%. Early lead dislocation was noticed in two cases (6%), reposition was performed using the original puncture site in one, and transvenous implantation was successfully carried out in the other case. Exploration of the system was necessary because of pocket infection in four cases (11%), in two of these cases TELIVL was carried out successfully 3 months later, in one patient 22 months later. All patients were maintained on anti-coagulation therapy with INR between 2–3. No thromboembolic complication was noticed. A total of 13 patients were lost, one of them died five years after the implantation in renal failure, the other patient died in malignant tumor 4 years after the implantation, 11 patients died due to the progression of the heart failure in average 16 months after the implantation.

Conclusions: TELIVL may be a very promising alternative technique of the surgical epicardial procedure when transvenous implantation could not be applied.

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Cardiac resynchronization therapy improves left ventricular volumes in patients with ejection fraction between 36 and 50% with left bundle branch block: MIAREF EF study
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Background: Cardiac resynchronization therapy (CRT) improves clinical status as well as left ventricular (LV) volumes in patients with QRS >120ms and left ventricular ejection fraction (LVEF) <35%. However, preliminary data suggest similar benefits might be realized in heart failure patients with EF ≥35%, and increased QRS duration. The MIAREF EF trial was designed to test this hypothesis. However, the study was stopped prematurely due to slow enrollment. Here we present LV volume data on those who qualified.

Methods: Major inclusion criteria were LVEF >35% and ≤50%, QRS >130 ms, and left bundle branch morphology. Patients were randomized 2:1 to treatment with CRT-P vs. Control (implanted, LV lead turned OFF). In addition to clinical assessments, echocardiograms were obtained at baseline and at 6 months.

Results: Twenty-six patients were successfully implanted with a CRT pacemaker and randomized (19 CRT, 7 Control). Of these patients, 10 (7 CRT, 3 Control) completed the 6-month visit with paired echocardiographic data. The median LVEF at baseline was 45% in CRT and 46% in Control. No significant increases in LVEF over time were observed. The CRT patients, however, showed reductions in median LVESV (28% decrease) and LVESVi (25% decrease). Improvement in contrast, the Control patients showed no changes in LVESVi (4% increase) or LVE SVi (8% decrease). Similar data are seen with average values. The change in LVE SVi over time was significantly different between groups (p<0.05) but the change in LVE SVi was not (p=0.11).

Conclusions: In a small sample of patients with HF symptoms, LBBB and LVEF between 36 and 50%, CRT-P appeared to reduce LV volumes compared with Control. The hypothesis that CRT can benefit selected HF patients with LVEF >35% should be tested.

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Cardiac resynchronization therapy in the elderly - is there an indication for a defibrillator?

Introduction: Cardiac resynchronization therapy (CRT) is an effective treatment option for heart failure in elderly patients, but the additional benefit of an implantable defibrillator (ICD) in these patients is not evidenced.

Purpose: To evaluate the impact of an ICD on all-cause mortality in elderly patients undergoing a CRT device implantation.

Methods: Patients at the age of >75 years who underwent implantation of either a CRT-pacemaker (CRT-P) or CRT-defibrillator (CRT-D) were identified out of hospital records. Only patients with a Class I or IIa indication for CRT and the primary prophylactic implantation of an ICD due to a severe impairment of the left ventricular ejection fraction (LVEF) were included in the analysis. Patient characteristics, procedural data and all-cause mortality were compared between the two groups.

Results: Between January 2008 and August 2014 two hundred forty-five seniors were implanted with a CRT device in our centre, whereof 80 patients with CRT-P and 97 patients with CRT-D represent the two study groups. Patients in the CRT-P group were more often females (44 vs. 25%; p<0.001), older (82±6 vs. 77±1.9 years, p<0.001), had a better LVEF (29±6 vs. 27±4%; p=0.015) and narrower QRS-complexes (150±19 vs. 158±18 ms; p=0.025). During a mean follow-up of 25±13.9 months 62 (35%) of the 177 study patients died, 28 (35%) in the CRT-P and 34 (35.1%) in the CRT-D group, respectively. The Kaplan-Meier analysis of survival probability showed no significant difference (p=0.502) between the two groups (Figure). Inadequate ICD interventions were recorded in 4 patients (4.1%) and 5 patients (5.2%) received adequate therapies in the CRT-D group.

Kaplan-Meier survival probability

Conclusion: An additional ICD has no impact on survival in elderly patients implanted with a CRT device.

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Relationship between indices of left ventricular lead electrical position in spontaneous rhythm and right ventricular pacing: implications for optimization of cardiac resynchronization therapy
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Purpose: Left ventricular (LV) electrical delay measured from the beginning of the QRS complex to the local LV lead electrogram (EGM), normalized by QRS duration (Q-LV ratio), was found to be a strong and independent predictor of short-term response to cardiac resynchronization therapy (CRT), heart failure events and mortality. We investigated relationship between Q-LV ratio and similar index obtained during right ventricular pacing (RVP-LV ratio).

Cardiac volumes

Kaplan-Meier survival probability

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Methods: We prospectively collected ECGs and EGMs in 133 consecutive patients (aged 66±10 years; 72% males; 56% nonischemic cardiomyopathy; LVEF 26±5%; 81% true-LBBB) with native non-RBBB QRS morphology undergoing CRT implant. Recordings of spontaneous rhythm and RV midseptum paced rhythm were edited, signal-averaged and measured by electronic calipers.

Results: The LV lead position was characterized by the Q-LV ratio of 0.73±0.11 and RVP-LV ratio of 0.77±0.11. Native QRS width (180±21 ms) was shortened by 14±28 ms during biventricular pacing. There was significant but weak correlation between Q-LV and RVP-LV ratios (r=0.23, p<0.0001, Figure). With a cut-off value for both Q-LV and RVP-LV ratio = 0.70, defining adequate electrical LV lead positioning, 67% of patients with suboptimal Q-LV ratio had optimal RVP-LV ratio and 13% of patients with optimal Q-LV ratio had suboptimal RVP-LV ratio.

Conclusions: While observational studies found association between Q-LV ratio and CRT outcome, this measure may not be optimal for LV lead positioning because intrinsic atrioventricular conduction is not maintained during biventricular pacing. Therefore, RVP-LV ratio may better reflect the interlead electrical distance and deserves further evaluation.

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Prognostic role of right ventricular function in patients with heart failure undergoing cardiac resynchronization therapy

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Introduction: Since 20–40% of patients undergoing CRT do not respond to therapy, the identification of potential factors predicting response to CRT is a relevant research topic. Recent evidence suggests a possible association between right ventricular function and response to CRT.

Methods: We analyzed data from the CRT MORE registry, about patients who received CRT according to current guidelines (NYHA class II-IV, optimal medical drug therapy, Left ventricular ejection fraction (LVEF) ≤35% and a QRS duration ≥120ms) from April 2013 to December 2013. Response to therapy was defined as an absolute improvement in LVEF ≥10% and as a decrease of at least 15% in left ventricular end-systolic volume (LVESV) on echocardiography at 6 months.

Results: A total of 163 patients with a baseline estimation of tricuspid annular plane systolic excursion (TAPSE) and echocardiographic examination at 6 months follow up were considered for this analysis (age 70±10 years, male gender 71%, ischemic etiology 37%, history of atrial fibrillation 27%, NYHA class II in 46% of patients, spontaneous QRS duration 160±25ms, left bundle branch block 85%). Baseline echocardiographic parameters were: LVESV 125±48 ml. On the basis of receiver operating characteristic curve analysis of TAPSE, the cutoff that maximized the sensitivity and specificity of the receiver operating characteristic curve analysis was at a value of 17mm.

Conclusions: Baseline signs of right ventricular dysfunction suggest possible remodeling after CRT. A TAPSE value of 17mm was identified as a good cutoff for predicting improvement in both LVESV and LVEF.

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Different long-term outcome depending on cardiac rhythm in heart failure patients undergoing cardiac resynchronization therapy


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Purpose: The aim of the study was to assess the prognostic impact of heart rhythm (sinus rhythm – SR; atrial fibrillation – AF) with and without low biventricular pacing percentage (CRT%) in heart failure (HF) patients undergoing cardiac resynchronization therapy (CRT).

Methods: We prospectively selected a single centre cohort of 304 consecutive patients implanted with CRT-D and subsequently monitored via remote monitoring was divided into four groups depending on rhythm type (SR – sinus rhythm vs AF – atrial fibrillation) and the mean CRT%:

- Group 1 – SR and CRT% <95% (n=132; 43.4%)
- Group 2 – SR and CRT% <95% (n=12; 3.9%)
- Group 3 – AF and CRT% <95% (n=95; 31.3%)
- Group 4 – AF and CRT% <95% (n=61; 20.1%

Results: The mean CRT% in Group 1 was 98.6%, 88.8%, 97.8%, 85.5%, respectively. Patients with SR and low CRT% had higher mortality than AF subjects with high CRT% (33.3% vs 8.4%, P<0.01). Within subgroups of patients with high or low CRT% mortality rates were similar in SR and AF subjects (9.1% for Group 1 vs 8.4% for Group 3, P=NS, 33.3% for Group 2 vs 26.2% for Group 4, P=NS). Mortality rates for both group of patients with low CRT% were higher than subjects with high CRT% (Group 2 vs Group 1: P<0.01; Group 4 vs Group 3: P<0.002).

The main cause of CRT% lost in SR group were premature ventricular contractions (81.8%).

Conclusion: Irrespective of underlying rhythm (SR, AF), high CRT% seems to be crucial to improve the prognosis in HF patients undergoing CRT. Long-term survival of patients in SR and low CRT% is worse than those with AF and high CRT%.

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Effect of apical and non-apical right ventricular lead position on cardiac resynchronization therapy outcome

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Introduction: Cardiac resynchronization therapy (CRT) has been shown to improve outcomes in patients with heart failure (HF). The optimal site of right ventricular (RV) stimulation in CRT has not been established. We aimed to conduct a meta-analysis of randomized controlled trials and observational studies comparing the mid- and long-term effects of RV apical (RVA) and non-apical (RVNA) pacing on CRT outcome.

Methods: We systematically searched the Cochrane library, EMBASE, and MEDLINE databases for studies assessing RVA versus RVNA pacing in CRT with regards to left ventricular end-systolic volume (LVESV) reduction and functional status improvement (defined as ≥1 New York Heart Association class improvement). Effect estimates [standardized mean difference (SMD) and odds ratio (OR) with 95% confidence intervals (CI)] were pooled using random-effects models. In meta-analyses, LVESV reduction and functional status improvement were similar in patients with RVA and RVNA pacing (SMD 0.13, 95% CI: −0.24 to 0.50, p=0.48; OR 1.08, 95% CI: 0.81 to 1.45, p=0.60, respectively).

Conclusion: Our meta-analysis suggests that the beneficial effect of CRT on LV remodeling and functional status is similar irrespective of RV lead location.

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Targeting the LV pacing site by means of electrical delay and LVdP/dtmax may predict the long term clinical outcome in CRT patients

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Background: Targeting the optimal LV pacing site is decisive for CRT effectiveness.

Purpose: The aim of the study was to assess the prognostic impact of heart rhythm (sinus rhythm – SR; atrial fibrillation – AF) and LVdP/dtmax was lower than those with AF and high CRT%.

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Purpose: The aim of the study is to assess the 12 months clinical response of CRT patients whose LV lead was positioned, after the systematical screening of all the available pacing sites, according to the criterion of the maximum electrical delay (Q-LV) and the highest response in LV dp/dtmax.

Methods: 58 patients (43 male, 35 with ICM, 34 with LBBB) underwent to CRT implantation. All available tributary veins of the coronary sinus were assessed, on average 3.2±0.7 different veins and 7.2±1.8 pacing sites. The Q-LV interval and the hemodynamic effects by invasive measurement of LV dp/dtmax at baseline and during pacing were evaluated at each site. In 57/58 (98%) patients the highest LV dp/dtmax coincided with the maximum Q-LV interval and the corresponding pacing site was selected as the target site.

Results: At 12 months follow up, the HF clinical composite score (Packer) was evaluated in 57 patients. 42/57 (78%) patients improved their clinical status. 6/57 (11%) unchanged, 9/57 (16%) worsened (4 died, 5 were hospitalized because of worsening of HF). Mean LV EF was 30±6% at baseline, and 40±11% at follow up (p<0.001). Mean ESVI was 73±29 mL/m² and 59±28 mL/m², at baseline and follow up respectively (p<0.001). The patients whose target site was associate with a higher Q-LV (median value 133 ms) reported better 12 months clinical response (figure).

Conclusions: In our experience, with advanced NYHA class patients, the acute optimization of LV lead target site, by means of a systematical screening of local electrical delay and LV dp/dtmax, resulted in 74% of patients who responded clinically to CRT. A subanalysis in patients with higher QLV reported 83% of responders.

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Impact of collagen turnover markers on echocardiographic response and mortality after CRT-D implantation in TRUST-CRT study population
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Introduction: Cardiac resynchronization therapy (CRT) was showed to effectively reduce mortality and provide the symptomatic relieve for subpopulation of heart failure patients with LBBB and wide QRS. However despite of continuous efforts CRT is still burdened with a relatively high proportion of unresponsiveness. The aim of present study is to assess the impact of serum level of collagen turnover (PINP and PIIINP), NT-proBNP, CRP and metalloproteinases (MMP-2, MMP-9) on echocardiographic response and clinical outcomes in population of patient of TRUST-CRT study.

Materials and methods: Study population consisted of patients enrolled into the Triple Site Versus Standard Cardiac Resynchronization (TRUST-CRT) trial. TRUST-CRT was a single-center, single-blind, parallel, randomized, clinical trial that was performed to test the hypothesis that triple-site (double-left single-right) pacing with defibrillator is superior over conventional CRT with defibrillator. Echocardiographic evaluation was performed at baseline, and after 6 months. The echocardiographic response was defined as an increase of left ventricle ejection fraction for more than 10%. Serum and plasma samples for PINP, PIIINP, MMP-2 and MMP-9 measurements were obtained on admission before CRT-D implantation and stored in –80 °C until analysis. Concentrations of PINP, PIIINP, MMP-2 and MMP-9 were determined by commercially available ELISA kits. Concentrations of hsCRP and NT-proBNP were determined with standard way in hospital laboratory.

Results: Between 2008 and 2010, 100 consecutive patients were enrolled to the TRUST CRT study. Blood samples for further analysis were collected from 74 of 100 patients before CRT-D implantation. Three years follow-up data were available for 97 of the 100 patients. PINP and PIIINP level was significantly lower in echocardiographic responders. Results of multivariate logistic regression demonstrated that among analyzed parameters only low level of PIIINP is associated with favorable echocardiographic response (P<0.011). Univariate and multivariate logistic regression showed that higher all-cause mortality is associated with higher baseline PINP (P=0.01) and NT-proBNP (P=0.02) concentrations. Survival analysis with cutoff value 9.315 ng/ml identified on the basis of ROC analysis (sensitivity ~50%, specificity~90%), revealed significant survival benefit associated with low baseline PINP (HR: 4.58; 95% CI 2.05–10.24, P=0.0002) level.

Conclusion: Results of our study indicate that low baseline level PIIINP is associated with favorable echocardiographic response and longterm survival in CRT recipients.

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Ventricular anti-arrhythmia pacing therapy in heart failure patients with cardiac resynchronization therapy defibrillator: efficacy, safety and impact on heart failure hospitalizations and mortality
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Background: Cardiac resynchronization therapy defibrillator (CRT-D) can terminate slow ventricular tachycardia (VT) and fast VT (FVT) via antitachycardia pacing (ATP).

Purpose: We evaluated efficacy and safety of ATP, and whether ATP may be associated with mortality and heart failure (HF) hospitalizations.

Methods: 1404 ICD patients (286 female,67±10 years) were prospectively followed in a multicenter observational research. Mortality and hospitalization rates were estimated in patient’s sub-groups in order to uncouple the trigger (VT/FVT or other rhythms causing inappropriate detections) from the ATP therapy.

Results: Over a median follow-up of 31 months, 2938 VT/FVT were treated with ATP in 361 patients. The adjusted ATP success rate was 63% (95% CI: 57–69%) on FVTs and 68% (CI: 62–74%) on VTs. Acceleration occurred in 55 (1.87%) and syncope in 4 (0.14%) of all ATP-treated VT/FVT episodes. The rate of death, per 100 patient-years, was 5.6 (CI: 4.3–7.5) in patients with ATP on true VT/FVT, 3.3 (CI: 2.6–4.2) in patients with no episodes and 1.5 (CI: 0.4–6.1) in patients with inappropriate ATP (p=0.045 vs. appropriate ATP patients and p=ns vs. patients with no episodes after adjusting for baseline differences between patients’ groups). The attached figure shows freedom from endpoint composed by death or HF hospitalizations for the sub-groups of 304 patients with ATP only on true VT/FVT, 833 patients with no episodes/therapies and 43 patients with only inappropriate ATP.

Conclusions: ATP was highly effective in terminating VT/FVT episodes and displayed a good safety profile. Patients with inappropriate ATP had a better prognosis than those with ATP on true VT/FVT suggesting that an adverse prognosis is related to the arrhythmia itself – a marker of disease progression – rather than to an adverse effect of ATP.

HAEMODYNAMICS IN HYPERTENSION

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The VKORC1 (-1639) G>A promoter polymorphism is associated with elevated systemic arterial blood pressure
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Background: Genetic variations in the vitamin K epoxide reductase complex subunit 1 (VKORC1) have been found to affect warfarin dose response. VKORC1 haplotypes may represent novel genetic markers for cardiovascular disease and aortic calcification. We hypothesized that genetic polymorphisms in the VKORC1 gene effect arterial blood pressure either directly or via vascular calcification thus contributing to cardiovascular diseases.

Methods and results: We analyzed two frequent VKORC1 single nucleotide polymorphisms (SNPs), (-1639)G>A promoter polymorphism and (-1404)T>C promoter polymorphism.
multplex PCR. Individuals carrying the VKORC1(−1639) A variant showed significantly elevated invasively measured systolic, diastolic and mean arterial blood pressures compared with carriers of the G allele. The (3730) SNP showed only a borderline significance for the diastolic blood pressure. No association with vascular calcification could be observed.

Conclusions: The VKORC1(−1639) A allele is associated with elevated systemic arterial blood pressure. This suggests a novel concept of blood pressure regulation through pathways involving vitamin K epoxide reductase and calcium binding proteins.

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Lack of regression of left ventricular hypertrophy and combined cardiovascular disease in essential hypertensives

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Purpose: Blood pressure (BP) reduction produces regression of left ventricular hypertrophy (LVH) which is considered to be associated with improved prognosis. We sought to investigate the prognostic role of left ventricular hypertrophy (LVH) regression regarding incidence of cardiovascular disease in essential hypertension.

Methods: We prospectively followed up for a median period of 3.8 years 1226 essential hypertensives (mean age 57.8 years, baseline office BP = 143.6/89.3mmHg). All patients visited periodically the outpatient periodically the outpatient clinic of our institution and office BP at follow up was calculated based on the measurements of the last 3 visits. Echocardiographic evaluation and determination of the metabolic profile and creatinine levels was performed at entry and at follow up. LV thickness and LV mass index were measured using speckle tracking echocardiography. LVH was defined as LVMI≥116g/m² in men and LV mass index ≥96g/m² in women. Endpoint of interest was the incidence of stroke, coronary artery disease and their composite.

Results: At the end of follow up the incidence of the composite end-point was 4.0% (17 patients with stroke, 34 with CAD, 2 with both). According to the presence of LVH at baseline (20.2%) and at the end of follow-up (15.9%) patients were divided in two groups: with normal LV mass index at both examinations or with LVH at baseline and regression of hypertrophy (n=1031, 84.1%, group 1) and with LVH at baseline and follow-up and with normal LV mass index at baseline and LVH at follow-up (n=195, group 2). Hypertensives of group 2 compared to those of group 1 were older (by 6.3 years, p<0.001), more frequently females (by 19%, p<0.001) and had at baseline greater duration of hypertension (by 2.6 years, p<0.001), increased number of anti-hypertensive drugs (by 0.6, p<0.001) office pulse pressure levels (by 5mmHg, p<0.001), increased body mass index (by 0.86kg/m², p<0.024), glucose (by 7.4 mg/dl, p<0.001) and decreased creatinine clearance (by 10.5 ml/min, p<0.001). Survival analysis revealed that hypertensives without LVH regression (group 2) compared to those of group 1 exhibited significantly higher rates of stroke (51% vs. 0.7%, log rank p<0.001) and the composite end-point (7.7% vs. 3.3%, log rank p<0.020).

Conclusions: Lack of regression of LVH is accompanied by increased incidence of stroke and combined cardiovascular disease in essential hypertensives.

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Prognostic implications of left ventricular strain and strain risk score in patients with hypertensive heart disease

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Background: Major adverse cardiovascular events (MACE) in pts with hypertensive heart disease (HHD) are associated with LV geometry, but their association with LV function is unclear. Longitudinal and circumferential strain (GLS, GCS) were measured using speckle tracking echocardiography and to develop a risk score for predicting MACE.

Methods: We studied 2.280 hypertensive patients (aged 57.7±11 years, 50% males) without history of AF episodes for a median period of 3.3 years (IQR 2.3–5 years). All subjects had at least one visit annually and at entry underwent complete echocardiographic study and additional workup for exclusion of secondary causes of resistant hypertension (RH). Four groups were identified depending on presence or absence of RH (office-based uncontrolled hypertension under at least 3 drugs including a diuretic or controlled hypertension under 4 or more drugs) at baseline and follow-up: 1.494 patients (65.7%) never having RH, 185 (8.1%) with resolved RH, 230 (10.1%) with incident RH and 365 (16.1%) with persistent RH. Endpoint of interest was new-onset AF.

Results: The incidence rate of new-onset AF over the whole follow-up period was 7.06/1000 persons-years. In the univariate analysis age (HR=1.08, p<0.001), office pulse pressure (HR=1.02, p=0.003), duration of hypertension (HR=1.03, p<0.001), left ventricular mass index (HR=1.02, p<0.001), left atrium diameter (HR=3.27, p<0.001), E/Em (HR=1.09, p<0.001), creatinine clearance (HR=0.98, p=0.002) resolved RH (HR=2.65, p=0.009) and persistent RH (HR=1.97, p=0.03) were independent predictors of new-onset AF. Multivariate Cox regression analysis revealed that age (HR 1.07, p<0.001) and LAD (HR 2.67, p<0.001) turned out to be the only independent predictors of new-onset AF while resolved RH just lost statistical significance (HR 2.00, p=0.09). Based on ROC analysis LAD≥39 mm predicted new-onset AF with sensitivity 76.5% and specificity 56.7%.

Conclusions: Hypertensives with new-onset AF are characterized by a greater prevalence of cardiorenal adaptations and a longer and unfavorable pattern of hypertension control.However, only older age and enlarged LA size turned out to predict new-onset AF in the setting of essential hypertension.

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Hypertensive left ventricular geometry and myocardial mechano-energetic efficiency: refining cardiovascular risk profile in arterial hypertension

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Background: Myocardial mechanical efficiency (MME) can be approximated by the ratio of stroke work (i.e. systolic blood pressure [SBP] times stroke volume [SV]) to a rough estimate of energy consumption, the “double product” (SBP times heart rate [HR]), which can be simplified as SV*HR). Purpose: We characterized MME in relation to LV geometry and evaluated its prognostic value.

Methods: Hypertensive participants of the Campania Salute Network (n=12,104) without prevalent coronary or cerebrovascular disease and with ejection fraction (EF) ≥50% were analysed cross-sectionally and longitudinally over a follow-up...
Results: MME was greater in women (0.35±0.08 mL/mmHg/m²) than in men (0.33±0.07 mL/mmHg/m², p<0.001) and was closely related to LVM (p<0.0001). MME was normalized for LVM (MMEm) and divided in quartiles. In logistic analysis, the lowest quartile of MMEm was associated with older age, male gender, obesity, diabetes, LV hypertrophy (LHV), concentric geometry, more use of diuretics and CCB, less use of β-blockers and higher blood pressure (all p<0.002). During follow-up, age, LVM and sex-independent risk of composite fatal and non-fatal myocardial infarction and stroke was higher in the lowest quartiles of MMEm than in the three higher quartiles (HR=1.79 [1.29–2.49], p<0.001), and was only attenuated by addition of LHV (HR=1.59, p<0.008) in the model (figure).

Conclusions: A simple estimate of low MME, expressing the amount of ejected volume per second per gram of LVM is associated with altered metabolic profile, LHV, especially concentric, and less use of β-blockers, and predicts hard CV end-points, independently of age, sex and LHV.

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Aortic stiffness and essential hypertension phenotypes
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Purpose: Since that recently normative and reference values have been published for Carotid-femoral Pulse Wave Velocity (cf-PWV), they did not take into account all phenotypic expressions of hypertension (HTN), such as isolated office (white coat) and masked HTN.

Methods: We studied 1163 consecutive subjects (383 normotensive, 780 newly HTN, free of diabetes and overt cardiovascular disease). CF-PWV was evaluated by Sphygmocor device using intersecting tangent algorithm and substracted path length method. According to age and office, home and ambulatory blood pressure monitoring participants were categorized in 8 blood pressure (BP) categories and 6 age groups.

Results: The prevalence of optimal, normal, high white, masked, HTN stage I, stage II and stage III was 3.1%, 6.5%, 12.3%, 11.2%, 3.9%, 36.9%, 18.7% and 7.4%, respectively. CF-PWV increased with age and BP category, it was significantly higher in HTN compared to normotensive subjects (8.3 vs. 7.5 m/s, p<0.001) and there were not any gender differences (8.09 in males vs. 8.06 in females, p=0.771). Importantly, normal BP category exhibited significantly higher values of PWV compared to optimal BP group (7.4 vs. 6.3, p<0.001). Moreover, white coat category had significantly higher cf-PWV compared to masked and high normal groups (8.1 vs. 7.2 vs. 7.5, p<0.004 and p=0.001, respectively) and significantly lower compared to HTN stage II and stage III (8.1 vs. 8.6 vs. 9.2, p=0.035 and p<0.001, respectively), while they did not differ regarding HTN stage I (8.11 vs. 8.15, p=0.833). In contrast, masked category had significantly higher cf-PWV compared to optimal group (7.23 vs. 6.32, p=0.008, and significantly lower compared to HTN I, II and III (7.23 vs. 8.15 vs. 8.55 vs. 9.24, p<0.001 for all, respectively), while they did not differ regarding normal and high normal groups (7.23 vs. 7.35 vs. 7.47, p=0.3 for all, respectively).

Conclusion: In a large population of normotensive and essential hypertension newly diagnosed normotensive patients, even normal levels of BP are characterized by increased cf-PWV compared to optimal levels. Contrary to widely held beliefs, white coat phenotype presents a worse aortic stiffness profile compared to masked HTN.

4872 | BEDSIDE
An increase in left ventricular wall thickness augments ejection fraction in hypertensive heart disease through changes in absolute wall thickening: a cardiac magnetic resonance imaging study
J.C.L. Rodrigues1, S. Rohan2, A. Ghosh Dastidar1, M.C.K. Hamilton1, C. Bucciarrelli-Ducci1, A.K. Nightingale1, J.R.F. Paton4, N.E. Manghati1, D.H. Macleod2,1, Bristol Heart Institute, NIHR Bristol Biomedical Research Unit, Bristol, United Kingdom; 2University of Bristol, Medical School, Bristol, United Kingdom; 3Bristol Heart Institute, Cardiology Department, Bristol, United Kingdom; 4University of Bristol, Bristol CardioVascular, School of Physiology and Pharmacology, Bristol, United Kingdom; 5Mugrosve Park Hospital, Cardiology Department, Taunton, United Kingdom

Background: Hypertensive heart disease is often associated with the paradox of impaired longitudinal strain but preserved left ventricular ejection fraction (LVEF). We explored the impact of absolute wall thickening (AWT) on LVEF in hypertensive heart disease using cardiac MRI.

Methods: CMR studies from 55 hypertensive patients (mean age: 52±12.8, 58% male) performed at 1.5T were analysed. Longitudinal fractional shortening (LFS) was estimated using a modified 6-point mean mitral annular plane systolic excursion and expressed as a percentage of end-diastolic LV length. Radial strain was defined by AWT as a percentage of EDWT. Midwall fractional shortening (mFS) was estimated using an established equation. Multivariate linear regression analysis was performed to investigate the independent influence of EDWT, LAS and mFS on LVEF with increasing EDWT.

Results: Increasing EDWT correlated with significantly reduced LAS (R=−0.62, p<0.001), radial strain (R=−0.48, p<0.001) and mFS (R=−0.68, p<0.001). However as EDWT increased, and myocardial shortening decreased, AWT was maintained. On multivariate analysis (Table 1), increasing EDWT by 1mm independently resulted in an absolute increase in LVEF of 3.43 percentage points (3.43±0.426, p<0.001), which compensated for the independent negative effects of LAS and mFS on LVEF with increasing EDWT.

Multivariate linear regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Crude ß coefficient (95% CI)</th>
<th>p-value</th>
<th>Adjusted ß coefficient (95% CI)</th>
<th>p-value</th>
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<tr>
<td>EDWT</td>
<td>0.91 (−0.01–1.82)</td>
<td>0.051</td>
<td>3.34 (2.60–4.26)</td>
<td>&lt;0.0001</td>
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<td>LAS</td>
<td>0.86 (0.06–1.66)</td>
<td>0.035</td>
<td>2.01 (1.29–2.74)</td>
<td>0.0001</td>
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<tr>
<td>mFS</td>
<td>0.91 (0.23–1.59)</td>
<td>&lt;0.01</td>
<td>1.05 (0.26–1.84)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: We show how hypertensive patients can maintain normal LVEF despite significantly impaired longitudinal, radial and circumferential myocardial shortening. We propose that an increase in EDWT augments LVEF as a consequence of a preserved AWT. LVEF and systolic function are not synonymous. LVEF should not be used in hypertensive heart disease, without correction for the degree of EDWT. Our findings have wider implications for understanding the pathophysiology of heart failure with preserved ejection fraction.

854 | Haemodynamics in hypertension
Associations of hemodynamic load with impaired myocardial flow reserve: role of sex and hypertension
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Background: Heart failure with preserved ejection fraction (HFpEF) predominately affects hypertensive women, with coronary microvascular dysfunction and rarefaction recently described as novel arterial abnormalities. To determine alterations in ventricular-arterial interactions that may predispose to HFpEF, we evaluated sex-specific associations of hemodynamic load with microvascular coronary dysfunction in subjects with preserved ejection fraction.

Methods: Subjects with a cardiac 82Rb positron-emission tomography between 2010 and 2013, ejection fraction >50%, no heart failure, dyspnea, coronary artery disease or regional perfusion defects were eligible. Left ventricular microvascular reactivity was assessed by myocardial flow reserve (MFR = peak hyperemic stress/rest myocardial blood flow). ‘Low MFR’ was defined as the lowest sex-specific quartile. Steady and pulsatile components of load were estimated by systemic vascular resistance index [SVRI = (80*mean arterial pressure/ cardiac output)/(BSA)] and indexed aortic compliance (AoCl = stroke volume/pulse pressure)/BSA, respectively. Multivariable linear and logistic regression evaluated associations of SVRI and AoCl with MFR and ‘low MFR’, adjusting for age, heart rate, hypertension, diabetes, dyslipidaemia, smoking, use of aspirin, statins and anti-hypertensives. Interaction terms for sex and hypertension with load measures were included.

Results: 297 subjects (61% women, age: 61.3±11.0 years) were eligible. Risk factors, medications and MFR did not differ, but SVRI was higher [5348±1676 vs. 4616±1514 (dyn s/cm²)] and AoCl was lower [0.40±0.00 vs. 0.52±0.28 (mL/mmHg)] in women (P<0.001). Each SD increase in SVRI and AoCl was 1.24–4.96% greater risk of coated with 2.24 [95% CI: 1.1–4.4%] and 1.95 (1.06–4.70, P<0.003) greater odds of having ‘low MFR’, respectively, in hypertensive women. SVRI and AoCl interacted in the prediction of MFR (P<0.01).

Conclusions: In subjects at highest risk for HFpEF (hypertensive women), but not in men or normotensive women, lower steady and higher pulsatile arterial load were associated with worse MFR. Since coronary perfusion is related directly to diastolic and inversely to systolic aortic pressure, a combination of lower SVR and higher aortic stiffness (lower AoCl) in hypertensive women may adversely affect the coronary microvasculature, a mechanism that could predispose to HFpEF.
Background and introduction: Although arterial stiffening is related to arterial remodeling, its prognostic role in hypertension is not fully elucidated, while augmented left ventricular mass index (LVMI) is linked to adverse outcome. 

Purpose: The aim of the present study was to compare the predictive role of arterial stiffness and LVMI for the incidence of coronary artery disease (CAD) in a cohort of essential hypertensive patients.

Methods: We followed up 1033 essential hypertensives (mean age 55.6 years, 538 males, office blood pressure (BP) ≥145/92 mmHg) free of cardiovascular disease for a mean period of 6 years. All subjects had at least one annual visit and at baseline underwent complete echocardiographic study for estimation of LVMI and blood sampling for assessment of metabolic profile. Arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV), by means of a computerized method (Complior SP) and the distribution of PWV was split by the median (8.1 m/sec) and accordingly subjects were classified into those with high (n=520) and low values (n=513). Moreover, LV hypertrophy (LVH) was defined as LVMI ≥125 g/m² in males and LVMI ≥110 g/m² in females, while CAD was defined as the history of myocardial infarction or significant coronary artery stenosis recorded by coronary angiography. Coronary revascularisation was also performed.

Results: The incidence of CAD over the follow-up period was 2.8%. Hypertensives who developed CAD (n=29) compared to those without CAD at follow-up (n=1004) had at baseline higher waist circumference (101.8±11.1 vs 97.2±11.9 cm, p=0.033), LVMI (123±22.9 vs 107±24.2 g/m², p=0.014), prevalence of LVH (46% vs 25%, p=0.027) and prevalence of high PWV levels (69% vs 48%, p=0.019). No difference was observed between hypertensives with and those without CAD at respect to baseline office BP, serum creatinine and lipid levels (p=NS for all). By univariate Cox regression analysis it was revealed that baseline PWV levels predicted CAD (hazard ratio=1.218, p=0.025). However, in multivariate Cox regression model baseline glomerular filtration rate (hazard ratio=1.020, p=0.026) and LVMI (hazard ratio=1.021, p=0.0001) but not baseline PWV were independent predictors of CAD outcomes.

Conclusions: In essential hypertensive patients LVMI predicts future development of CAD, whereas high baseline PWV exhibits no independent prognostic value. These findings support that LVMI constitutes a superior prognosticator of events than PWV and its estimation is essential in order to improve overall risk stratification in hypertension.

Electrocardiographic detection of hypertensive left ventricular hypertrophy in the presence of obesity and left ventricular remodeling: re-calibration against cardiac magnetic resonance

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Background: ECG criteria for left ventricular hypertrophy (LVH) have traditionally been validated against echocardiography. Cardiac magnetic resonance (CMR) is the non-invasive gold-standard for assessing left ventricular mass (LVM). We re-calibrated 6 ECG criteria for LVH against CMR-defined LVMI. We also investigated the impact of obesity and LV remodeling on the diagnostic performance of the ECG at detecting LVH.

Methods: Consecutive referrals for CMR (1.5T) from a tertiary hypertension clinic were identified, while the ECG sensitivity for detecting LVH was assessed, blinding to CMR findings. ECGs and trabeculations were evaluated, blinded to CMR data. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated. Area under the receiver operator curve analysis was performed. 

Results: 150 patients were reviewed, 22 were excluded due to concomitant cardiac pathology that may confound the hypertrophic response were excluded. LVMI was measured (including papillary muscles and trabeculations) from CMR, blinded to ECG data. From a 12-lead ECG, the Sokolow-Lyon voltage and product, Cornell voltage and product, Gubner-Ungerleider voltage and Romhilt-Estes score were evaluated, blinded to CMR data. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were calculated. Area under the receiver operator curve analysis was performed.

Conclusions: Among diabetes population, implementation of a large-scale cardiovascular risk reduction program in this IHS was associated with continued improvement in risk factors control rates when compared with national rates. 

Acknowledgement/Funding: Community Benefits Grant, Kaiser Permanente Northern California

Resting heart rate and measures of effort related cardiac autonomic dysfunction predicts cardiovascular events in asymptomatic type 2 diabetes

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Background: Autonomic control of the cardiovascular (CV) system can be impaired in diabetes and is associated with increased morbidity and mortality. Parameters obtained during stress testing may identify early stages of cardiac autonomic dysfunction and provide prognostic information in asymptomatic diabetics.

Methods: We performed maximal exercise treadmill testing in 954 type 2 diabetics without known coronary heart disease. Prognostic significance of parameters associated with autonomic dysfunction were assessed, including chronotropic incompetence (<80% heart rate reserve), abnormal heart rate recovery at 1 min (HRR1) <18 beats, and resting tachycardia >100 beats/min. Cox proportional hazards analysis was used to determine the association of exercise parameters with a composite event of all-cause mortality, myocardial infarction or stroke.

Results: Resting heart rate >100/min was observed in 18% of patients, chronotropic incompetence in 30% and HRR1 <18 beats in 35%. During mean
follow-up of 79±16 months, there were 72 (12%) events. Each of the 3 abnormalities was significantly associated with event risk in an adjusted multivariate analysis: chronotropic incompetence [HR 1.89, 95% CI 1.18–3.01; p=0.008], resting heart rate > 100 beats/min [HR 1.97, CI 1.19–3.26; p=0.008] and HRR1 < 18 beats [HR 1.77, CI 1.12–2.81; p=0.015]. A progressive relationship between the number of abnormal parameters and event risk was observed (P < 0.001).

Conclusions: Chronotropic incompetence, resting tachycardia and reduced heart rate recovery are independently and additively associated with long-term mortality, myocardial infarction or stroke in type 2 diabetes without known CV disease. Exercise stress test may identify early stages of cardiac autonomic dysfunction with considerable long-term prognostic significance.

4887 | BEDSIDE
Impact of stress testing for coronary artery disease screening in asymptomatic patients with diabetes mellitus: a community-based study
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Purpose: Asymptomatic patients with diabetes mellitus (DM) are at increased risk for cardiovascular events. We evaluated the impact of screening stress testing for coronary artery disease (CAD) in asymptomatic diabetic patients in a community-based cohort.

Methods: Using Rochester Epidemiology Project resources, we studied 3,146 adult patients with a new diagnosis of DM from 1992–2008 without prior history of CAD. Weighted Cox proportional hazards regression was performed with screening stress testing within 2 years of diagnosis of diabetes as a time-dependent covariate. In a landmark analysis, subjects were classified into a screened cohort and an unscreened cohort based on their experience during the 2 years following DM diagnosis. Kaplan-Meier methods were used to compare event rates. The primary outcome was all-cause mortality or myocardial infarction (MI).

Results: The age at diagnosis of diabetes was 55±13.8 years. Participants were 53% men and 97% had type 2 DM. The time-dependent variable of having a screening stress test within 2 years of DM diagnosis was associated with improved MI-free survival (HR=0.67, p=0.02), independent of other risk factors. In the landmark analysis, 294 patients received stress testing within 2 years (screened cohort) and 2246 remained at risk without stress testing (unscreened cohort). Median follow-up was 9 years (IQR: 4.1, 6.7) for the screened cohort and 9.8 years (IQR: 4.5, 9.8) in the unscreened cohort. Death or MI occurred in 455 patients [33 patients in the screened cohort and 422 in the unscreened cohort (5 year rates 2.3% and 5.3%, respectively)] (Figure).

Conclusion: Screening cardiac stress testing in asymptomatic diabetic patients in a community-based cohort was associated with improvement in long-term event-free survival.

LEFT VENTRICULAR HYPERTROPHY

4896 | BEDSIDE
Urinary albumin predicts future hypertension and increases in blood pressure in the general population
S. Murai1, H. Takase2, T. Sugira1, S. Yamashita1, N. Ohte1, Y. Doi1. 1 Nagoya City University, Graduate School of Medical Sciences, Dept of Cardio-Renal Medicine & Hypert. Nagoya, Japan; 2 Enshu Hospital, Hamamatsu, Japan

Background: Primary prevention of hypertension is an important public health aim. An intensive targeted strategy focused on identified individuals at highest risk of developing hypertension is an attractive approach for primary prevention of hypertension. The kidney plays a central role in regulating blood pressure. Indeed, glomerular filtration rate has been reported to be a novel predictor of the onset of hypertension in the general population.

Purpose: The present study sought to investigate whether increased excretion of urinary albumin within the low-grade levels (<300 mg/g creatinine) is associated with increased risk of hypertension and future elevations of blood pressure in the general population.

Methods: Normotensive subjects who visited our hospital for a physical checkup (53.4±11.4 years old, n=6,205) were enrolled in this study. A single-void, morning urine sample was used to measure urinary excretion of albumin. Urinary albumin concentrations were expressed as the ratio of concentrations of urinary albumin to urinary creatinine (mg/g Cr). After the baseline examination, subjects were followed up with the endpoint being the development of hypertension.

Results: The total follow-up period was 17,025 person-years and the median follow-up period was 1,089 days. Urinary albumin was in the normal range (<30 mg/g Cr) in most subjects (97.5%). During the follow-up, hypertension developed in 1,184 subjects (19.1%, 69.5 per 1,000 person-years). Kaplan-Meier analysis revealed that the incidence of hypertension was increased across the quartiles of urinary albumin (log-rank, P=0.0001). The hazard ratio (lowest vs highest quartile of urinary albumin, 1.14 mg/g Cr) as reference) was 1.39 (95% confidence intervals, 1.18–1.64) in the highest quartile (median urinary albumin, 8.87 mg/g Cr). Furthermore, multivariate Cox hazard analysis where urinary albumin was taken as a continuous variable identified urinary albumin as a significant predictor of hypertension (hazard ratio: 1.24, 95% CI: 1.09–1.41). Urinary albumin was also an independent predictor of future increases in systolic blood pressure (P=0.001).

Conclusions: Urinary albumin is a novel predictor of future hypertension and increases in blood pressure in the general population. The risk of developing hypertension increases even with levels of urinary albumin near the threshold defined for microalbuminuria. Thus, minor alterations in kidney function could be an important sign for managing blood pressure with the view to preventing hypertension onset.

4899 | BEDSIDE
The hypertrophic microRNAs miR-208b, miR-499 and miR-21 are differentially expressed in peripheral blood mononuclear cells of hypertensive patients in relation to left ventricular hypertrophy
J.E. Kontarak1, M.E. Markou1, E. Panahi-Kakazad1, S. Maragoudakis2, E.A. Zacharis2, G.E. Kochiadakis2, P.C. Vardas2. 1 University of Crete, Faculty of Medicine, Molecular Cardiology Laboratory, Heraklion, Greece; 2 University Hospital of Heraklion, Department of Cardiology, Heraklion, Greece

Purpose: To determine whether cardiac hypertrophy related microRNAs were differentially expressed in peripheral blood mononuclear cells of hypertensive patients in relation to left ventricular hypertrophy. Left ventricular hypertrophy is an initial compensatory mechanism in response to cardiac stress that can degenerate into heart failure and sudden cardiac death. It is one of the most recognized features of hypertensive heart disease, a marker of subclinical organ damage and strongly related to adverse cardiovascular outcomes and risk of mortality. Urinary albumin is a novel predictor of future hypertension and increases in blood pressure in the general population. The risk of developing hypertension increases even with levels of urinary albumin near the threshold defined for microalbuminuria. Thus, minor alterations in kidney function could be an important sign for managing blood pressure with the view to preventing hypertension onset.

Methods: We assessed the expression levels of the microRNAs miR-208b, miR-499 and miR-21 in 102 patients with essential hypertension (50 men, mean age 62.5±8.3 years) and 30 healthy individuals (14 men, mean age 58.8±8.3 years). All patients underwent two-dimensional echocardiography. MicroRNA expression levels in peripheral blood mononuclear cells were quantified by real-time reverse transcription polymerase chain reaction.

Results: Hypertensive patients showed significantly higher miR-208b (22.29±6.25 versus 12.95±3.98, p=0.001), miR-499 (10.06±1.05 versus 5.70±0.91, p=0.003) and miR-21 (2.75±0.15 versus 1.82±0.20, p=0.002) expression levels compared with healthy controls. In hypertensive patients, we observed significant positive correlations of miR-208b (r=0.426, p=0.033) and miR-21 (r=0.498, p=0.001) expression levels with left ventricular mass index.

Conclusions: Our data reveal that the miyomiRs miR-208b and miR-499 as well as the fibrosis related miR-21 are upregulated in hypertensive patients related to healthy individuals and they show strong positive correlations with left ventricular mass index in hypertensive patients. Thus, they may be implicated in the pathogenesis of left ventricular hypertrophy in hypertensive patients and possibly they are candidate therapeutic targets in hypertensive heart disease.
4900 | BEDSIDE
Probability of echocardiographic left ventricular hypertrophy regression during antihypertensive treatment in a real-world context: The Campania Salute Network

1University of Bergen, Department of Clinical Science, Bergen, Norway; 2Federico II University Hospital, Hypertension Research Center, Naples, Italy

Background: Regression of hypertensive left ventricular (LV) hypertrophy (LVMH) is a successful goal in clinical trials, but less in known of LVH regression in a real-world context.

Methods: We identified 2,234 hypertensive patients (mean age 57±10 years, 48% women) free of prevalent cardiovascular (CV) disease, with baseline LVM (LV mass index (LVMi) =47±2 g/m² in women and ≥50 g/m² in men) and at least 24 months follow-up (80±49 months) from the Campania Salute Registry. The characteristics associated with LVH regression was assessed, also considering number and type of antihypertensive medications.

Results: 299 patients (13%) exhibited regression of LVH during follow-up (reduction in LVMi was 13±8% vs. ≥10% in patients with stable LVH, p<0.001). Patients with LVH regression were younger, more likely to be males, less likely to have diabetes or obesity and with a shorter history of hypertension (all p<0.001). Average systolic and diastolic blood pressure (BP) during follow-up, baseline BMI, carotid IMT and LVM were lower (all p<0.01), while lipid profile, renal function and type of antihypertensive medication did not differ. In multivariate analysis, significant independent predictors of LVH regression were: younger age, male gender, lower systolic BP during follow-up and lower baseline LVMi and BMI (all p<0.001) (Table), after adjustment for duration of hypertension, diastolic BP during follow-up, fasting plasma glucose, renal function, carotid IMT, number of antihypertensive drugs and follow-up time (all p<0.01).

Conclusion: In a real-world context, LVH regression occurs in 13% of treated hypertensive patients, and is more likely in younger and male subjects, with better BP control during follow-up and more favorable CV risk profile. In particularly, obesity and more severe LVH at baseline reduce the chance of hypertensive LVH regression independent of BP control.

Table 1. Significant predictors of LVH regression in treated hypertensive subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR 95%CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.97</td>
<td>0.96–0.99</td>
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<td>Male gender</td>
<td>2.79</td>
<td>2.08–3.75</td>
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<td>Average systolic BP during follow-up (mmHg)</td>
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<td>LVMi (g/m²)</td>
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NEW ERA IN MYOCARDIAL PERFUSION IMAGING

4911 | BEDSIDE
Myocardial perfusion imaging predicts mortality in patients evaluated for kidney transplantation

S. Helve1, M. Laine2, I. Helanterä3, J. Sinisalo2, O. Lammintausta2, J. Lehtonen2, H. Hanninen3, P. Finne3, T. Nieminen4, 1University of Helsinki, Cardiology, Helsinki, Finland; 2Helsinki University Central Hospital, Cardiology, Helsinki, Finland; 3Helsinki University Central Hospital, Nephrology, Helsinki, Finland

Background: Value of myocardial perfusion imaging (MPI) in patients with severe renal disease is controversial.

Purpose: To assess the prognostics of MPI in a large evaluation population for kidney transplantation.

Methods: The local MPI data was collected in 2004–2013 and linked with the national kidney registry. All the 564 patients evaluated for transplantation were searched (94.1% with LVH). To assess the prognostics of MPI, Cox regression as well as integrated discrimination and net reclassification improvement methods were used.

Results: Of the 564 patients screened for kidney transplantation, 54 of cardiovascular (CV) causes (9.6%). In a real-world context, LVH regression occurs in 13% of treated hypertensive patients, and is more likely in younger and male subjects, with better BP control during follow-up and more favorable CV risk profile. In particularly, obesity and more severe LVH at baseline reduce the chance of hypertensive LVH regression independent of BP control.

Conclusion: Value of myocardial perfusion imaging (MPI) in patients with severe renal disease is controversial. To assess the prognostics of MPI, Cox regression as well as integrated discrimination and net reclassification improvement methods were used.

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4912 | BEDSIDE
Incremental Prognostic Value of Noninvasive Coronary Flow Reserve

M. Al-Mallah, A. Ahmed, A. Aljzeeri, I. Suleiman, National Guard Hospital, King Abdulaziz Cardiac Center (KACC), Riyadh, Saudi Arabia

Background: Impaired coronary flow reserve is considered an early manifestation of coronary artery disease, even in vessels free of angiographic stenosis. The aim of this analysis is to determine whether noninvasive CFR in patients with suspected or known coronary artery disease adds incremental prognostic significance over clinical variables.

Methods: We included 2,645 consecutive patients with known or suspected coronary artery disease (mean age 61±11 years, 42% females) who underwent rubidium-82 rest/stress emission tomography for clinical indications. The scans were interpreted for the presence of perfusion defects. Rest and stress myocardial blood flows were calculated with factor analysis and a 2-compartment kinetic model and were used to calculate coronary flow reserve (CFR). Patients were followed up for a median duration of 1.4 years (interquartile range, 0.5–1.8 years) for the incidence of cardiac death or myocardial infarction. (CD/MI)

Results: A total of 34% patients had evidence of perfusion defects while 42% had ischemia. The overall rate of CD/MI was 4.7%. In a multivariate analysis, the lowest tertile of coronary flow reserve (<1.8) was associated with a 3.7-fold increase in the risk of CD/MI (95% confidence interval, 2.2–6.6 P<0.001) compared to the highest tertile. This remained significant after adjusting for clinical variables, perfusion defect and resting ejection fraction (Hazard ratio 2.0, 95% confidence interval, 1.1–3.45; P<0.10).

Conclusion: Noninvasively measured CFR with positron emission tomography is an independent predictor of cardiac death or myocardial infarction in patients with known or suspected coronary artery disease.

4913 | BEDSIDE
Comparison of coronary flow reserve detected by positron emission tomography (PET) in patients with hypertrophic cardiomyopathy and hypertrophic cardiomyopathy with hypertension

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Background: Hypertrophic cardiomyopathy (HCM) is a common genetic cardiomyopathy and microvascular dysfunction is the major factor for clinical deterioration and cardiovascular disease–related death in HCM. Hypertension (HTN) may also lead to microvascular dysfunction which can be detectable by inadequate coronary flow during pharmacologic stress infusion in PET.

Methods: We studied 38 patients with HCM (mean age 51±12.6 years) and 38 patients with HTN (mean age 53±15.4 years). Hypertension was defined by blood pressure value was >140/90 mmHg or those who were on antihypertensive medication. All patients underwent rest and stress 13N-ammonia studies following administration of dipyridamole or regadenoson. All data was obtained using the same PET/CT scanner in list mode, with CT attenuation maps. List-mode data was resampled to create static, electrocardiographically-gated and 36-frame-dynamic images. Coronary flow reserve (CFR) was determined as the ratio of the peak myocardial blood flow to rest myocardial blood flow.

Results: The patients were comparable, there was no differences in systolic function of the patients; ejection fraction (58.5±8.7% in HCM vs 57.1±7.3% in HCM with HTN) in both groups. End-diastolic and end-systolic total LV volumes were similar in the 2 groups in echocardiographic analyses. Patients in both groups had similar septal wall thickness (1.9±0.47 cm in HCM vs 1.9±0.39 cm in HCM with HTN). Patients with HCM with HTN had decreased CFR (2.3±0.62), whereas CFR in patients with HCM was 2.8±0.9 (p<0.001).

Conclusion: In patients with both HCM and HTN, decreased CFR was detected compared to that in HCM patients using PET.
STATE OF THE ART IN INVASIVE IMAGING AND FUNCTIONAL ASSESSMENT

4930 | BEDSIDE
Wave intensity analysis reflects microcirculatory capillary density: a combined histological and intracoronary physiology study

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Background: Assessment of coronary microcirculation is hampered by the availability of markers. Wave intensity analysis (WIA) is a novel method to analyse intracoronary pressure and flow with the potential to outline specific causes of microcirculatory dysfunction. Theoretically, the magnitude of the backward decompression wave in WIA is assumed conceptually to be related to the increase in capillary density of the capillary bed, but this has never been directly verified.

Purpose: We investigated this concept in vivo using histological samples in a population of cardiac transplant patients with variable degree of capillary rarefaction resulting from allograft vasculopathy.

Methods: 15 cardiac transplant patients with unobstructed epicardial vessels underwent combined pressure (from catheter tip) and flow (from a mid-LAD Doppler guidewire) during rest and hyperemia. Offline wave intensity analysis was performed using bespoke Matlab software. Ventricular biopsies were simultaneously obtained using a 7Fr biopsy catheter. Capillaries were identified with specific antibodies against endothelium. Quantitative morphometric analysis of the histological sections was performed in dedicated workstation and the density of capillaries (capillaries per 1 mm²) was assessed.

Results: There were 445 patients (11 male) with the majority of transplantations having been undertaken for dilated cardiomyopathy (60%). Capillary density was 623±278 capillaries/mm² (range 259–1005). Resting mean coronary velocity was 17.0±8.3 and rose to 38.4±16.6 cm/s with adenosine (CFR 2.28±0.6). Mean systolic pressure was 127 and diastolic pressure 83mmHg. Resting microvascular resistance was 7.6±6.5 mmHg/cm²/s and hyperaemic microvascular resistance 3.4±3.3 mmHg/cm²/s. Coronary flow reserve was not correlated with capillary density (r=−0.41, p<0.1). A good correlation was demonstrated between capillary density and the wave intensity profile. Of the other waves a second correlation was noted with the peak (r=−0.76, p<0.01) and cumulative (r=−0.72, p=0.01) late backward compression wave (of systolic microcirculatory compression). No other correlations were noted with the wave intensity profile.

Conclusions: This study supports coronary wave intensity analysis as a potential tool in the diagnosis of myocardial capillary rarefaction in cardiac diseases associated with microcirculatory remodeling. It also provides clinical evidence supporting the theoretical explanation of the documented coronary waves of WIA.

4931 | BEDSIDE
Performance of two novel invasive indices of coronary microvascular resistance (CMVR) in invasive and non-invasive reference standards: superiority of Doppler derived hyperaemic microvascular resistance (hMR) and a thermodilution derived index of microvascular resistance (IMR), against myocardial perfusion reserve index (MPRI) using high-resolution cardiac magnetic resonance imaging (CMR).

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Purpose: Coronary microvascular resistance (CMVR) is increasingly measured after myocardial infarction, both as a prognostic marker and to compare treatments. There is currently no gold-standard invasive measurement of CMVR. We compared two novel invasive measurements of CMVR measured in the cardiac catheter laboratory: a Doppler-derived hyperaemic microvascular resistance (hMR) and a thermodilution-derived index of microvascular resistance (IMR), against myocardial perfusion reserve index (MPRI) using high-resolution cardiac magnetic resonance imaging (CMR).

Methods: 37-patients (61±10 yrs) were recruited, 63% following an ACS. Simultaneous intracoronary pressure, Doppler flow velocity and cold-bolus transit time were measured in 45 coronary arteries, using a Volcano Combowire and St Jude Pressure Wire, at rest and during intravenous adenosine hyperemia. Measurements were taken post PCI in patients with significant coronary artery stenoses (stable angina and ACS patients). When clinically feasible, a second set of measurements was taken in a normal reference vessel. We calculated, using standard definitions: mean coronary flow reserve (CFR) from thermodilution and Doppler, hMR and IMR. 3-tessa CMR perfusion scans were performed, as close as possible to invasive measurements, and MPRI calculated in the corresponding segments as previously described. In ACS patients, regional wall motion in corresponding segments and overall left ventricular ejection fraction (from cine CMR images), and infarct size (from contrast enhanced CMR images) were also calculated.

Results: hMR and IMR assessed the severity of regional hypoperfusion. hMR was the only independent predictor of regional wall motion. Moreover, hMR had superior diagnostic accuracy over IMR to predict mean CFR (area under curve 0.79 versus 0.59, p<0.01) and separately to predict MPRI (area under curve 0.97 versus 0.84, p<0.05), using DeLong receiver operating characteristic comparison analysis.

Conclusions: Accurate assessment of CMVR on the cardiac catheter laboratory table is feasible, safe and rapid. This study, for the first time, simultaneously assessed the diagnostic accuracy of two such measures of CMVR. We demonstrated Doppler-derived hMR had superior diagnostic accuracy over IMR at predicting established invasive and non-invasive reference standards of CMVR; in CFR and MPRI respectively.

4932 | BEDSIDE
Accounting for right atrial pressure in the calculation of fractional flow reserve (FFR) significantly increases the number of physiologically significant stenoses suitable for PCI.

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Background: Right atrial pressure (RAP) was included in the original validated FFR equation (FFR0), but is now omitted from clinical use with a presumed negligible consequence.

Purpose: In this real world cohort, we investigate the effects omission of right atrial pressure has on the revascularisation decisions made in everyday clinical practice.

Methods: 304 coronary stenoses underwent coronary angiography with FFR measurement. FFR was calculated using the simplified equation of distal coronary pressure/proximal aortic pressure (Pd/Pa). And also accounting for right atrial pressure (FRRap). Where not feasible, a pragmatic consideration would be to use a RAP of 0mmHg. Using a RAP of 0mmHg should be abandoned in favor of routine measurement. Using a RAP of 0mmHg significantly decreased the FFR value.

Results: Mean FFR (Pd/Pa) of the cohort was 0.83 (±0.09). The inclusion of RAP significantly decreased the FFR value. Mean FFR of the cohort decreased to 0.82 (±0.10), 0.81 (±0.11) and 0.79 (±0.11) at RAPs of 5mmHg, 10mmHg and 15mmHg respectively. The decrease reached statistical significance at RAP 7mmHg (p<0.001). In this within the published normal RAP range (-8mmHg). Decrease in FFR increased the proportion of stenoses meeting revascularisation criteria (FFR<0.80). Due to the clustering of data around FFR 0.80, small changes in FFR value led to big changes in classification. The additional stenoses fulfilling reclassification criteria were 4% (11/304), 9% (27/304) and 17% (51/304) at RAPs of 5mmHg, 10mmHg and 15mmHg respectively. These represented potentially missed cases for appropriate revascularisation. In this cohort, FFR 0.83 was the highest non-significant FFR where reclassification still occurred at normal RAP (-8mmHg). In patients with elevated RAP (15mmHg), this figure was FFR 0.85. These FFR values are well above the FFR: 0.80 cut off for revascularisation. Lastly, when RAP was included, systolic aortic blood pressure (Pa) became an important determinant of the FFR value. RAP always lowered the FFR of a stenosis more in patients with low systolic blood pressure. Therefore, the inclusion of RAP is non-linear, and its effects on FFR calculation are critically dependent on the systolic blood pressure.

Conclusions: FFR is a current form (Pd/Pa) systematically underestimates true stenosis severity, oversimplifies the relationship with systolic blood pressure and FFR and potentially denies patients the opportunity for appropriate revascularization. Using a RAP of 0mmHg should be abandoned in favor of routine measurement of RAP. Where not feasible, a pragmatic consideration would be to use a physiological RAP (8mmHg) in the automated console calculation of FFR.

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SUDDEN CARDIAC DEATH IN THE CARDIOMYOPATHIES

4959 | BEDSIDE
Clinical profile and predictors of arrhythmia-related symptoms in scandinavian arrhythmogenic right ventricular cardiomyopathy patients

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Purpose: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a genetic disease with largely unpredictable course. Prediction of prognosis and risk stratification in regard to sudden cardiac death (SCD) in patients with ARVC remains a challenging task. We aimed to assess clinical predictors of arrhythmia-related symptoms in ARVC patients enrolled in the Nordic ARVC registry.

Methods: Patients with definite ARVC by 2010 Task Force (TF2010) criteria recruited at 8 sites in Denmark, Norway and Sweden were included in the cross-sectional analysis. Patients were defined as symptomatic based on the occur-
Hypertrophic cardiomyopathy (HCM) patients are at risk of ventricular arrhythmias and sudden death. 

**Background:** Hypertrophic cardiomyopathy (HCM) is a common cause of sudden cardiac death in young adults. Global longitudinal strain (GLS) is a non-invasive imaging marker of myocardial function that is related to risk of ventricular arrhythmias and sudden death. Recent studies have shown that GLS is an independent predictor of ventricular arrhythmias and sudden death in HCM patients.

**Methods:** We included 150 HCM patients (54±14 years, 39% female) and 50 age-matched healthy individuals. GLS was measured by echocardiography and a reference value of GLS was defined as <−16%.

**Results:** In HCM patients, GLS was lower compared to healthy individuals (−15.7±3.6% vs. −21.1±1.9%, p<0.003). GLS was an independent predictor of ventricular arrhythmias and sudden death in HCM patients (OR 8.26 95% CI 1.76–38.70, p=0.007) and T-wave inversion in lead aVF (OR 0.001).

**Conclusions:** GLS is a strong and independent predictor of ventricular arrhythmias and sudden death in HCM patients and may help risk stratification of HCM.

**FLASH NEWS ON ANTITHROMBOTICS**

**4971 | BESIDOE**

**PER977 (ciraparantag) reverses edoxaban anticoagulation at steady state and has no effect on-re-anticoagulation at the next scheduled dose**

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**Background:** There is no approved reversal agent for non-vitamin K antagonist oral anticoagulants (NOACs), including edoxaban. Of the three reversal agents in clinical development, based on non-clinical data, PER977 is the only one that has been confirmed in edoxaban and exenapran clinical studies.

**Methods:** An ongoing Phase II single-blind, placebo-controlled clinical trial in healthy volunteers (n=50 completed) is evaluating escalating doses of PER977 in subjects administered 60 mg edoxaban daily to steady state. Reversal of anticoagulation was measured by whole blood clotting time (WBCT) at 3 hours post dose.

**Results:** Edoxaban increased mean WBCT by 30±2.2%. PER977 completely and statistically significantly reversed the increase in WBCT to pre-edoxaban levels within 60 minutes following administration of 100 mg PER977 (p<0.01) on Day 3 (for comparison, WBCT following reversal of anticoagulation with edoxaban was similar to that observed after the first anticoagulation and the impact of the second reversal with 100 mg PER977 on Day 4 was similar to Day 3). Reversal of anticoagulation was observed within 30 minutes at 300 mg PER977 (p<0.05) on Day 3. Electron micrographs of the clots showed restoration of normal fibrin structure indicating return to normal clotting following PER977 after the anticoagulated state achieved with edoxaban. Prothrombin time remained elevated and does not appear to be a sensitive measure of reversal of anticoagulation by PER977. Adverse events, temperature sensations at the site of injection and flushing were mild and transient.

**Conclusion:** PER977, beginning at doses of 100 mg, completely reversed anticoagulation of steady state doses of edoxaban as demonstrated by decreased return to normal clotting following PER977 after the anticoagulated state achieved with edoxaban. Prothrombin time remained elevated and does not appear to be a sensitive measure of reversal of anticoagulation by PER977. Adverse events, temperature sensations at the site of injection and flushing were mild and transient.

**Conclusion:** HCM patients had reduced LV function by GLS, despite normal function by ejection fraction. MD was a strong and the only independent predictor of VAs and was related to fibrosis and may help risk stratification of VAs in HCM.
mean WBCT to pre-edoxaban levels and return of clot formation to normal from its anticoagulated state. As noted in previous trials, a single injection of PER977 sustains reversal of edoxaban as measured by WBCT without the need for prolonged infusion and with no post-injection pro-coagulation signals.

4972 | BEDSIDE
Treatment pattern of dual antiplatelet therapy in 104,012 patients with acute coronary syndrome: a Swedish nationwide population-based cohort study

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Introduction: Dual antiplatelet therapy (DAPT) with aspirin and clopidogrel has previously become a cornerstone in treatment of acute coronary syndrome (ACS). With the introduction of prasugrel and ticagrelor, new DAPT regimens are available. ESC guidelines recommend 12 months’ DAPT after an ACS.

Purpose: To investigate DAPT patterns, changes in type and duration of DAPT, and patient characteristics associated with the various treatments in a nationwide population of all patients with ACS in Sweden over 5 years.

Methods: This observational, cohort study linked morbidity, mortality and medication data from national registries from all 104,012 patients alive after discharge from hospital with ACS during 2009–2013. Patients were categorized into two groups whether or not coronary angiography was performed.

Results: In patients investigated with angiography, treatment switch from DAPT/clopidogrel to DAPT/ticagrelor was observed in beginning of 2011. DAPT/clopidogrel remained the preferred DAPT treatment in patients not investigated with angiography. DAPT duration increased from 225 to 298 days in patients investigated with angiography, and from 155 to 208 days in patients not investigated with angiography. 10% of patients initiated on prasugrel or ticagrelor were investigated with angiography, and from 155 to 208 days in patients not investigated with angiography. DAPT duration increased from 225 to 298 days in patients investigated with angiography, and from 155 to 208 days in patients not investigated with angiography. 10% of patients initiated on prasugrel or ticagrelor were investigated with angiography, and from 155 to 208 days in patients not investigated with angiography. DAPT duration increased from 225 to 298 days in patients investigated with angiography, and from 155 to 208 days in patients not investigated with angiography.

Conclusions: Dual antiplatelet therapy (DAPT) with aspirin and clopidogrel has previously become a cornerstone in treatment of acute coronary syndrome (ACS). With the introduction of prasugrel and ticagrelor, new DAPT regimens are available. ESC guidelines recommend 12 months’ DAPT after an ACS.

**Acknowledgement/Funding:** This work was supported by Astra Zeneca.

4973 | BENCH
A new strategy to reverse the platelet inhibitory effect of ticagrelor

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Background: Platelets play a pivotal role in the pathogenesis of acute coronary syndromes (ACS). In contrast to Clopidogrel (Cl) and Prasugrel (Pr), Ticagrelor (Ti) has a different binding site from ADP with reversible blockage of the P2Y12-receptor. Like all the P2Y12-receptor antagonists Ti is bound to plasma proteins to a high extent. In case of acute bleedings or emergent surgical procedures, the platelet inhibitory effect should be reversed rapidly. There are a few cases that report bleeding complications with the impossibility to reverse the effects of Ti.

In 2014 we presented the data of our ex vivo study, in which we could show a marked difference between the possibility to reverse the effect of Ti after administration of platelet-rich-plasma (PRP) or pooled-platelets (PP). Surprisingly there was a significant lower response to PP compared to PRP measured by the PRI-VASP. Aim of the continued work was to evaluate the mechanism of poor response of Ti to PP as well as to discover a new strategy to reverse successfully the platelet inhibitory effect of Ti ex vivo.

Methods: We collected blood samples from patients with ACS after intake of Ti. On one hand, the inhibition of the P2Y12-receptor was determined by measuring the Platelet Reactivity Index (PRI-VASP) ex vivo after addition of PRP centrifugated platelets resuspended in PP-buffer solution. On the other hand we administrated pooled platelet concentrates (PP) in addition with human serum and human serum alone to take the high plasma protein binding into account.

Results: After addition of PP to Ti inhibited blood samples there was no significant increase in PRI-VASP values ($Ti \pm 11.7\% \pm 10.9\% - 18.2\% \pm 9.6\%$, $p = 0.523$). There was also no difference after addition of in buffer solution resuspended platelets received from centrifugated PRP ($Ti \pm 11.7\% \pm 10.9\% - 12.8\% \pm 9.4\%$, $p = 0.792$). In contrast a significant increase in PRI-VASP index was observed after addition of PRP alone ($Ti \pm 14.8\% \pm 12.6\% - 36.7\% \pm 13.1\%$, $p = 0.001$) or PP with human serum ($Ti \pm 11.7\% \pm 10.9\% - 61.3\% \pm 10.9\%$, $p = 0.001$). These increase of the PRI-VASP was also obvious after administration of human serum alone ($Ti \pm 11.7\% \pm 10.9\% - 54.1\% \pm 2.7\%$, $p < 0.001$).

Conclusion: The present study demonstrated a pioneer potential solution to reverse the platelet inhibitory effect of Ti in plasma, pooled platelets with human serum and human serum alone are able to reverse the effects of ticagrelor ex vivo. This approach is unique and might be a possible solution to solve the problem of reversing the effects of ticagrelor in acute bleedings or urgent surgical procedures.

4975 | BEDSIDE
Balancing the risk of ischaemic and bleeding events in ACS

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Background: Evaluation of antithrombotic treatments for acute coronary syndromes (ACS) requires balancing ischaemic and bleeding risks to assess the net benefit. However, the impact on mortality of ischaemic events and bleeding complications may differ.

Purpose: Compare the impact and relative importance of different types of bleeding and ischaemic events on mortality.

Methods: Predicted probabilities of ischaemic (MI or stroke) and bleeding events at 1 yr following randomisation were estimated for all pts included in the PLATO trial using Cox proportional hazards regression. Time-dependent Cox models assessed the association of time-dependent bleeding and ischaemic events with subsequent mortality, adjusted for baseline characteristics.

Results: Only GUSTO severe bleeding had a similar impact on mortality compared to ischaemic events (Table 1).

<table>
<thead>
<tr>
<th>HR (95% CI)</th>
<th>p-value (vs MI/Stroke)</th>
<th>HR (95% CI)</th>
<th>p-value (vs MI/Stroke)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30 days</td>
<td>&gt;30 days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI or Stroke</td>
<td>14.22 (11.54–17.53)</td>
<td>&lt;0.001</td>
<td>2.33 (1.66–3.26)</td>
</tr>
<tr>
<td>PLATO Major</td>
<td>5.59 (4.48–6.97)</td>
<td>0.001</td>
<td>1.25 (0.91–1.72)</td>
</tr>
<tr>
<td>TIMI Major</td>
<td>4.92 (3.81–6.36)</td>
<td>&lt;0.001</td>
<td>0.87 (0.57–1.35)</td>
</tr>
<tr>
<td>GUSTO Severe</td>
<td>11.73 (9.04–15.22)</td>
<td>0.201</td>
<td>2.29 (1.64–3.23)</td>
</tr>
</tbody>
</table>

Conclusion: Of 14,544 pts, 97.7% had a higher predicted ischaemic risk median (25th–75th) 6.3% (4.6%–9.2%) and might be a possible solution to solve the problem of reversing the effects of ticagrelor in acute bleedings or urgent surgical procedures.
Conclusions: When comparing ischaemic to bleeding events of similar mortality, the higher predicted risk of ischaemic events emphasise the importance of potent antithrombotic therapy in ACS.

Acknowledgement/Funding: Astra Zeneca

4976 | BEDSIDE

Rivaroxaban and vitamin K antagonists are equally effective in preventing recurrent venous thromboembolism - a Danish nationwide study

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Background: In 2012, rivaroxaban was approved as an alternative to vitamin K antagonists (VKAs) for the treatment of venous thromboembolism (VTE).

Methods: Through the Danish registries we identified all patients diagnosed with VTE from 6th of February 2012 through 31st of December 2012, and treated with either VKAs or rivaroxaban. Risk of recurrent VTE was estimated by cumulative incidence curves and multivariate Cox proportional-hazards model adjusted for sex, age, comorbidities and concomitant pharmacotherapy, both accounting for death as competing risk.

Results: A total of 3517 patients were included. Of these, 3259 (92.7%) were treated with VKAs (51.4% male; median age 67.8 years; IQR 54.0–78.2) and 258 (7.3%) were treated with rivaroxaban (50.8% male; median age 66.5 years; IQR 50.1–78.6). The two groups were similar with respect to comorbidities and concomitant pharmacotherapy. Recurrent VTE occurred in 248 (7.6%) of the patients in the VKA group and in 19 (7.3%) of the patients in the rivaroxaban group. No significant difference in the risk of recurrent VTE was found between the VKA group and the rivaroxaban group, with cumulative incidences after 180 days of 8.3% (95% CI: 0.07–0.09) and 10.9% (95% CI: 0.05–0.14) respectively (Figure 1), and an adjusted hazard ratio of 1.17 (95% CI: 0.73–1.87), P=0.51 associated with rivaroxaban treatment.

Conclusion: In patients with VTE, rivaroxaban was equally effective as VKAs in preventing recurrent VTE.

4977 | BEDSIDE

Clinical outcome of patients with venous thromboembolism under oral anticoagulation in regular medical care versus a telemedicine-based anticoagulation clinic

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Background: Venous thromboembolism (VTE) is a life-threatening disease. Oral anticoagulation is an effective treatment to prevent thromboembolic recurrence.

Purpose: We aimed to compare the clinical outcome of VTE patients under oral anticoagulation therapy (OACT) in regular medical care (RMC) and in a telemedicine-based anticoagulation clinic (CC).

Methods: ThrombEVAL is a prospective, dual-armed, multi-center study to investigate oral anticoagulation treatment (NCT01809015). Data were assessed in clinical visits, computer-assisted personal interviews, self-reported data and laboratory measurements according to standard operating procedures with detailed quality control. Information on study endpoints was validated and adjudicated by a review committee. Study monitoring was carried out by an independent institution.

Results: The sample comprised 360 patients with history of VTE from RMC and 254 patients from CC, predominantly treated with phenprocoumon (97.4%). VTE patients in RMC were older (72.0 (IQR06.0–79.0) vs. 69.0 (IQR50.0–77.0), P=0.0020) and showed a higher Charlson-Index (5.67±2.56 vs. 4.42±2.71, P=0.0011) than those of CC. Median follow-up time in both cohorts were 12.0 (11.4/12.0) and 12.9 (6.3/19.4) months. The primary study endpoint, a composite of thromboembolic events, major and clinically-relevant non-major bleeding, and death as net clinical benefit outcome, differed significantly between both cohorts. In RMC vs. CC, 4.5 events per 100 patient-years (py) were observed (CC: 3.5, 95% CI 1.8–7.3; P<0.001). Rate of thromboembolic events (RR 4.84 [1.33–26.26], P=0.012), major bleedings (RR 5.58 [1.19–52.40], P=0.024) under OAC, hospitalisations (RR 2.08 [1.52–2.97], P=0.001) and mortality (RR 3.42 [2.21–5.47], P=0.001) were higher in RMC compared to the CC. Cox re-gression analysis adjusted for age, sex, traditional cardiovascular risk factors and comorbidities, the net clinical benefit was substantially worse in RMC (HR 3.61 [1.42–9.14], P=0.0068). Mortality was still higher in RMC (HR 3.03 [1.22–7.52], P<0.017) and hospitalizations were also more frequent in RMC (HR 1.76 [1.19–2.58], P=0.0043).

Conclusions: The clinical outcome of VTE patients under treatment with VKA was distinctly better in a telemedicine-based CC than in RMC. Future studies should evaluate whether these findings can be translated into the treatment with new oral anticoagulants.

Acknowledgement/Funding: grants of state initiative health economy of ministries of health and economy, Rhineland-Palatinate Germany, federal ministry of education and resear

4978 | BENCH

Prothrombin complex concentrate or Idarucizumab in combination with dabigatran plus tranexamic acid are equally effective in a dabigatran anticoagulation experimental polytrauma model

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Aim: Trauma-induced bleeding and coagulopathy may be complicated by the direct thrombin inhibitor dabigatran. To restore hemostasis and control bleeding a multimodal approach using hemostatic agents is essential.

Methods: In this study assessed the effect of prothrombin complex concentrate (PCC) or the antibody fragment (Fab) idarucizumab in combination with tranexamic acid (TX) and fibrinogen (FG) in a porcine polytrauma model. After ethical approval dabigatran etexilate (n=6/group) was administered orally and infused prior to injury to achieve supratherapeutic plasma levels. A standardized polytrauma including bilateral femur fractures and a blunt liver injury was induced. Subsequently, animals received either placebo (control); TX (20 mg/kg)+FG (80 mg/kg, TF); PCC+TX+FG (PCC: 50 U/kg, TFP) or idarucizumab+TX+FG (Iduarcizumab 60 mg/kg, TF) according to randomization. Coagulation was assessed by coagulation parameters and diluted TT. Blood loss (BL) was measured over 240 min.

Results: Dabigatran levels were 506±113 ng/mL prior to injury and remained significantly elevated in controls, TX and TFP animals over the 240 min. Dabigatran was not measurable in TF-substituted animals. The degree of injury was similar with a BL of 798±56 mL prior to intervention. Control and TF animals had the highest BL (3583±507 mL) and 100% mortality (mean survival time 101 min). TFP (1234±215 mL) or TFI (987±168 mL) resulted in a significant reduction in BL and 100% survival. INR levels and thrombin generation were significantly elevated in the TFP group.

Conclusion: This study shows that cessation of life-threatening bleeding necessiates either substitution with a thrombin-generating drug or the neutralization of the anticoagulant effects of dabigatran. This is supported by the lack of impact on BL following monotherapy with FG plus TX. However, therapy with the Fab may be favorable since there is no overcorrection of thrombin generation of coagulation.

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4979 | BEDSIDE

Management and clinical consequences of major bleeding in high-risk patients following an acute coronary syndrome. Is aspirin the problem? Insights from the APPRAISE-2 trial

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Background: High-risk patients with a recent acute coronary syndrome (ACS) treated with antplatelet and anticoagulant agents are at risk of bleeding. Recent
data indicate that aspirin may be associated with a higher risk of bleeding than other anticoagulants in select patient populations.

**Purpose:** The aim of this study is to explore antithrombotic therapy changes and clinical events following major bleeding.

**Methods:** APPRAISE-2 was a multinational clinical trial that included 7392 high-risk patients. A recent ACS randomized to aspirin (5 mg twice daily) or placebo in addition to antiplatelet therapy, most commonly aspirin and a P2Y12 inhibitor. Antithrombotic therapy changes and clinical events during a 30-day period after an ISTH major/clinically relevant non-major (CRNM) bleed were reported and analyzed in Cox proportional hazard models during a median follow-up of 241 days. The models were adjusted for baseline characteristics, comorbidities, prior diseases, and antithrombotic therapy at baseline.

**Results:** Of the 214 (2.9%) patients who experienced an ISTH major/CRNM bleed in the 30-day period, 604 patients were randomized to aspirin (n=595; HR 70.6, 95% CI 9.5–527) or aspirin + apixaban (n=595; HR 64.7, 95% CI 6.9–614). Among patients with a high risk of subsequent myocardial infarction (MI) or ischemic stroke (HR 6.6, 95% CI 3.6–12.1, p-value <0.001) during a 30-day period following the bleeding event, Patients with ISTH major/CRNM bleeding had a higher risk of subsequent mortality, but the increase in risk differed across antithrombotic therapy status at randomization (interaction p-value = 0.021). The risk of subsequent mortality in the 30-day period after a bleeding event was higher in patients receiving aspirin alone (n=604; HR 70.6, 95% CI 9.5–527) or aspirin + apixaban (n=595; HR 64.7, 95% CI 6.9–614) compared with patients receiving a P2Y12 inhibitor alone (n=3334; HR 12.7, 95% CI 6.2–26.4).

**Conclusions:** In this cohort of high-risk post-ACS patients, bleeding was associated with a higher rate of subsequent major ischemic events and mortality. Patients receiving aspirin, irrespective of concomitant anticoagulation, had a markedly higher risk of subsequent bleeding events compared with treatments not including aspirin. The data suggest that having a bleed post-ACS, regardless of the type of bleed, was associated with a higher risk of subsequent ischemic events, which is at least in part likely related to aspirin treatment.

**Acknowledgement/Funding:** APPRAISE-2 was supported by Bristol-Myers Squibb and Pfizer.
During the first year of follow-up, the patients with pNVAF experienced 44 (20%) and the patients with NVAF experienced 86 (7%) stroke or death. The Kaplan-Meier curves (Log-rank \( p < 0.0001 \)) show that pNVAF patients with a CHA2DS2VASC score \( \geq 2 \) were at higher risk of stroke or death but not pNVAF patients with a CHA2DS2VASC score \( \leq 2 \). The adjusted Cox model showed that pNVAF and a CHA2DS2VASC score \( \geq 2 \) (adjusted HR, 10.95, 95% CI 4.29–27.95, \( p < 0.0001 \)) were predictors of risk of stroke or death.

**Conclusion:** These results suggest that a CHA2DS2VASC score \( \geq 2 \) is associated with a higher risk of stroke and death, at short-term follow-up in precipitated NVAF. The guidelines should be implemented to recommend the determination of CHA2DS2VASC stratification in all types of NVAF, including patients with a precipitating factor.

P4983 | BEDSIDE
Ablation of atrial fibrillation with uninterrupted NOAC treatment is not associated with severe peri- and postprocedural complications
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Catheter ablation of atrial fibrillation (AF) is a widely adopted therapy in patients with drug-resistant AF. Pulmonary vein (PV) isolation is the cornerstone of that procedure. Since periprocedural thromboembolic complications represent one of the most worrisome complications of catheter ablation tailored periprocedural anticoagulation is of central importance. Accumulating evidence suggests that ablation performed without stopping vitamin K antagonists is associated with lower periprocedural complications as compared to discontinuation of vitamin K antagonists and bridging with fractionated heparin. Whether the same holds true for uninterrupted treatment with the novel oral anticoagulants (NOAC) is a matter of investigation.

During the observational period (Jan 2013–Oct. 2014) a total of 549 consecutive patients were scheduled for PVI because of drug refractory AF. All patients were bridged with DOAK for 5–7 days, whereas DOAK treatment was continued throughout the procedure. No periprocedural complications such as major bleeding, neurological or non-neurological complications were noted in any of these patients. Only 1 patient suffered a transient ischemic attack (TIA) after the procedure. Of note, however even in high risk patients, further study is necessary to investigate the role of warfarin in reducing dementia in AF patients.

P4989 | BEDSIDE
Prognosis in patients with atrial fibrillation and CHA2DS2-VASc score \( \geq 1 \) in a community based cohort study
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**Objectives:** Patients with atrial fibrillation (AF) and a CHA2DS2-VASc score \( \geq 1 \) are at increased risk for ischemic stroke and major bleeding. Whether the same holds true for patients with AF characteristics similar to those of a community-based cohort is still not fully understood.

**Methods and results:** All patients with AF seen in our institution between 2000 and 2010 were identified in a database. The adverse outcomes were investigated during follow-up. Among 8962 patients with AF, 1077 (12%) had a CHA2DS2-VASc score \( \geq 1 \) in whom an oral anticoagulant was prescribed in 49%, antiplatelet therapy alone in 21%, and no antithrombotic treatment in 26%. Duration of follow-up was 958±1146 days, 71 of these patients sustained events with 29 stroke/thromboembolism (yearly rate 1.0%) and 49 deaths (yearly rate 1.7%). The lowest yearly rate of these combined events was seen in female patients (0.8%) and was higher in patients with hypertension (1.8%), vascular disease (2%), age 65–75 (2.8%), heart failure (3.2%) and diabetes (4.4%) (overall \( p < 0.004 \)). Prescribed oral anticoagulation was not associated with a better prognosis in the six individual components constituting CHA2DS2-VASc and the impact of antithrombotic management in a community based cohort of unselected AF patients with a CHA2DS2-VASc score \( \geq 1 \).

**Conclusion:** In a real life cohort study, AF patients with CHA2DS2VASC score \( \geq 1 \) had a risk of death/stroke/thromboembolism which was low in female patients and significantly higher in other patients. Oral anticoagulation was associated with a better prognosis in these patients. This supports the current expert consensus in the European guidelines for oral anticoagulation in these not so “low risk” patients when they are not female patients.

P4986 | BEDSIDE
Warfarin therapy is associated with lower risk of dementia in patients with incident atrial fibrillation in a community based cohort
**Background:** Atrial fibrillation (AF) has been associated with dementia independent of clinical stroke. This risk may be modulated by clinically silent cerebral embolism, though influence of warfarin on risk of dementia in AF is not well understood.

**Purpose:** We hypothesized that warfarin may reduce incidence of dementia in AF by reducing cerebral thromboembolism.

**Methods and results:** 1860 cases of incident AF were identified in Olmsted County, MN between 2004–2010 [mean age 71 (±15) y. 54% males, median CHA2DS2VASC score 3 (IQR 2–4)]. Warfarin was prescribed to 834 (45%) patients within the first 90 days after incident AF. Men and subjects with CHA2DS2-VASC score \( \geq 2 \) were more likely to be prescribed warfarin. CHA2DS2-VASC score \( \geq 2 \) was noted in 76% of patients not prescribed warfarin. Incident dementia identified using ICD codes occurred in 198 (11%) over mean follow-up of 4.3 y. Cox proportional hazards regression was used to identify significant predictors of dementia. After adjusting for age, sex, warfarin therapy was protective [HR 0.75 (95% CI 0.57–0.99)]. In a fully adjusted model with pre-specified potential dementia risk factors, age [1.09 (1.07–1.10) p < 0.0001], warfarin therapy [HR 0.40 (0.24–0.66) p < 0.0001] and CHA2DS2-VASC score [2.04 (1.26–3.31)] predicted dementia. Similar findings were noted when warfarin therapy was considered as a time dependent variable [HR 0.64 (0.45–0.91)].

**Conclusion:** Warfarin therapy is associated with 35% reduction in risk of dementia in a community based cohort of incident AF, even in high risk patients. Further study is necessary to investigate the role of warfarin in reducing dementia in AF patients.
the incidence of recurrent bleeding during FU including early anticoagulant therapy after LAAC was very low with only one patient suffering from major bleeding (1.2%).

Conclusion: In our real-world experience using all available occluder devices, LAAC in patients with high thrombembolic and bleeding risk proved to be safe and effective with low rates of stroke and bleeding during 2 years.

P4987 | SPOTLIGHT
Comparative cost-effectiveness of oral anticoagulants for stroke prevention in non-valvular atrial fibrillation patients in the UK
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Background: Efficiency frontier analysis is increasingly used in many parts of Europe to aid in identification of the treatments that provide most clinical value for a given investment, considering the trade-offs between costs and benefits for each alternative in the context of other relevant interventions. Limited information is available about relative value of non vitamin K antagonist (VKA) oral anticoagulants (NOACs) versus warfarin in non-valvular atrial fibrillation (NVAF) patients.

Purpose: To assess cost-effectiveness dose-adjusted warfarin, apixaban 5mg BID, dabigatran 150mg BID followed by 110mg and edoxaban 60mg OD in the UK NVAF patients using efficiency frontier analysis.

Methods: A lifetime Markov model was developed to evaluate the health and economic impact of NOACs and warfarin from the UK NHS perspective. Clinical events comprised ischemic stroke, intracranial hemorrhage, other major bleed, clinically relevant non-major bleed, myocardial infarction, cardiovascular hospitalization and treatment discontinuations. Key input data sources were as follows: clinical and indirect treatment comparison data derived from ARISTOTLE, AVERROES, RELY, ROCKET-AF and ENGAGE-AF; UK life tables; published literature and NHS reference costs. Medical costs were estimated in 2012 GBP and discounted at 3.5% per year. Comparative cost-effectiveness of various anticoagulants was assessed by establishing efficiency frontier using total costs on horizontal axis and QALYs gained on vertical axis.

Conclusions: Warfarin, dabigatran and apixaban were the optimal treatment strategies with apixaban producing the highest QALY gain. Apixaban appears to be a more effective treatment alternative to other two drugs at an economically accepted cost.

ACUTE PHASE OF STEMI

P4988 | BEDSIDE
Impact of ESC guidelines system delays on myocardial salvage in STEMI
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Background: According to current ESC STEMI guidelines, primary PCI is recommended if performed within 120 min of first medical contact (FMC). However, it is preferred to achieve shorter FMC to PCI delays, that is, a FMC to PCI delay <90 min and ≤60 min for patients initially presenting to a PCI-capable centre or patients within 120 min of symptoms onset.

Purpose: To quantify myocardial salvage provided by fulfillment of more restrictive PCI recommendations as compared to accepted system delays according to ESC 2012 guidelines.

Methods: The BARI score was adapted to quantify the angiographic myocardial area at risk in 333 patients (80% men, 46% anterior) with first STEMI admitted or referred to a tertiary hospital for primary PCI. A myocardial salvage index (MSI) was computed as the percentage of the area at risk that spared infarction by late gadolinium enhancement magnetic resonance. MSI was compared between subjects who fulfilled or not current ESC recommendations regarding FMC-to-PCI delays.

Results: MSI decreased with increasing ischemic time, but only up to 4 hours (Fig.1A). Achieving FMC-to-PCI ≤120 min (53% of cases) did not confer a significant increase in MSI (40±32% vs 35±28.7%, p=NS). However, MSI was higher among the 83 (25%) patients who met the more restricted and preferred FMC-to-PCI delays (43±33.0% vs 36±29.7%, p<0.05). This difference was mainly observed among patients with an initial TIMI flow 0–1 (Fig 1B).

Conclusion: Adherence to preferred shorter FMC-to-PCI delays (≤60 or ≤90 min) confers a benefit in myocardial salvage, compared to more relaxed and acceptable delays (≤120 min). The difference was mainly seen in subjects with an occluded artery and those reperfused within the first 4 hours from symptoms onset.

P4989 | BEDSIDE
High mortality in patients with ST elevations undergoing emergency coronary angiography not treated with primary PCI or CABG
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Background: Immediate coronary angiography is recommended in every patient presenting with acute chest pain and ST segment elevations suggestive for ST elevation myocardial infarction. Little is known about the fate of patients with ST elevations not treated with primary percutaneous coronary intervention (PCI).

Methods: We evaluated the diagnosis and in-hospital outcomes of patients undergoing emergency angiography for presumed STEMI within 24 hours after symptom onset in the ALKK-registry. We divided patients into groups

Results: Between 2009 and 2013 a total of 22429 patients underwent angiography for presumed STEMI – 24 hrs. Of these 2040 were treated with primary PCI, 635 underwent coronary artery bypass graft surgery and 1817 were treated conservatively. The in-hospital mortality in patients with PCI was 7.1%, with CABG 6.3% and 6.8% in the conservative group. We then further subdivided the conservative group in patients with significant coronary artery disease (STEMI treated conservatively) (n=555), without significant coronary artery disease (n=877) and with other cardiac diseases (n=350); diolated cardiomyopathy 43%, hypertensive heart disease (12%), valve disease 3%, aortic aneurysm 0.5%, other 43%. The corresponding in-hospital mortality rates were 12.3%, 4.4% and 5.2%, respectively.

Conclusion: Patients undergoing angiography for STEMI having significant coronary artery disease but treated conservatively have a high mortality. Unexpectedly the mortality in patients with presumed STEMI without significant coronary artery disease or other cardiac diseases is around 5%. These patients deserve further research to improve outcome in this so far neglected patient group.

P4990 | BEDSIDE
Cerebral and renal impact in 5,040 patients with acute myocardial infarction with cardiogenic shock combined coronary revascularization and intra-aortic balloon pump support: implications from popular
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Objective: Prior studies have suggested intraaortic balloon pump (IABP) have a neutral effect on acute myocardial infarction (AMI) patients with cardiogenic shock (CS). However the effects of IABP on patients with profound CS remain unclear.

Purpose: We therefore investigated cerebral and renal outcomes between low-dose dopamine+IABP and high-dose dopamine in AMI patients with profound CS undergoing coronary revascularization.

Methods: The present study enrolled 5,040 adult patients with acute myocardial infarction with cardiogenic shock (MI and profound CS who underwent coronary revascularization) and divided them into the IABP+low dose dopamine group (n=2520) and the high-dose dopamine group (n=2520) after propensity score matching to equalize confounding variables. Primary outcomes included MI, stroke or cardiovascular death. In-hospital events, including dialysis, pneumonia and sepsis, were secondary outcomes. We used propensity score matching to reduce selection bias and to balance baseline characteristics and clinical variables that could potentially affect outcomes.

Results: The MI recurrence rate was higher (HR=1.3, p<0.007) and cardiovascular death was much higher in the IABP+low dose dopamine group (HR=1.61, p<0.001). However, the incidence of stroke was similar between the two groups (HR=0.94, p=0.65). Interestingly, the IABP group had lower incidence of dialysis (HR=0.29, P<0.001), pneumonia (HR=0.43, P<0.001) and sepsis (HR=0.56, P<0.001) during hospitalization than the Nonuser group.

Conclusion: In AMI combined cardiogenic shock and PCI, IABP with low-dose
dopamine had worse cardiovascular outcome but it reduced incidence of acute renal failure and dialysis. They had neutral neuroprotective effects between two groups.

### P4991 | BEDSIDE

**Gender differences in cardiogenic shock after acute myocardial infarction. The FAST-MI programme**

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**Rationale:** Cardiogenic shock (CS) complicating acute myocardial infarction (AMI) occurs more frequently in women, but little is known about its potential specificities according to gender.

**Methods:** We analysed the incidence, management, and one-year mortality of CS according to gender in 4 nationwide French surveys carried out 5 years apart from 1995 to 2010, including consecutive STEMI and NSTEMI patients over one month periods, and with one-year follow-up available.

**Results:** Among the 10,610 patients included in the surveys, the prevalence of CS was 4.8% in men and 8.2% in women (p < 0.001). Absolute prevalence of CS decreased from 1995 to 2010 in both genders (5.4% to 3.0% in men, 10.5% to 6.5% in women). In men, the prevalence significantly decreased after adjusting for baseline characteristics (OR for 2010 vs 1995: 0.54, 0.39–0.75, p < 0.001), but the decrease was not significant in women (OR 0.86, 0.58–1.29, p=0.47). In particular, in STEMI patients, the prevalence of CS decreased in men (OR 0.52, 0.35–0.77) but remained stable in women (OR 1.09, 0.69–1.71).

Mean age in patients with CS tended to decrease in men (from 72±12 to 69±13 years, p=0.09) and to increase in women (from 76±10 to 80±9 years, P=0.18). Use of PCI was 3 days of admission increased for both men (from 24% to 68%, P=0.01) and women (from 11% to 56%, P=0.001). Occurrence of atrial fibrillation and ventricular fibrillation remained constant for both men and women. Atri- ventricular block decreased in men (from 25% to 10%) and women (from 23% to 15%). One-year mortality significantly decreased in men (from 70% in 1995 to 48% in 2010) and women (from 81% to 54%). By Cox multivariate analysis, female sex was not an independent correlate of one-year mortality (HR 0.98, 0.78–1.22). In men, only age, history of stroke, and study period (HR for 2010 vs 1995 0.41, 0.26–0.65) were associated with one-year death, while early use of PCI was associated with a non-significant trend (HR 0.85, 0.61–1.19); in women, NSTEMI (HR 0.49, 0.32–0.75), early use of PCI (HR 0.55, 0.37–0.81) and study period (0.54, 0.33–0.89) were independent predictors of one-year death.

**Conclusion:** The prevalence of CS is higher in women. In STEMI patients, the prevalence of CS has decreased in men, but not in women. One-year mortality, however, has significantly decreased for both men and women, and the role of early PCI as a potential mediator of decreased mortality seems greater in women than in men. Better understanding of the pathogenesis and specificities of cardiogenic shock in women is still needed.

### P4992 | BEDSIDE

**30 day clinical outcomes of bivalirudin vs heparin in the elderly patients with ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention, a pooled analysis**

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**Background:** Large randomized trials have demonstrated that bivalirudin administration in patients presenting with ST elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (pPCI) improved 30 day clinical outcomes (in particular less bleeding and thrombocytopenia) when compared with heparin with or without a glycoprotein inhibitor (GPI), although at the cost of greater stent thrombosis (ST). Since older age is a strong predictor of not only bleeding but also of thrombotic adverse events, understanding the effect of bivalirudin in the elderly is important.

**Methods:** We performed a patient level pooled analysis (n=5800) of two large randomized trials (EUROMAX and HORIZONS-AMI). A total of 2149 elderly patients (≥65 years of age) with STEMI were enrolled and randomly assigned to either bivalirudin or heparin with or without a GPI (control group) before pPCI. 30-day clinical outcomes were analyzed.

**Results:** Stroke (1.3% vs 0.4%, p=0.01), protocol-defined non-CABG major bleeding (8.8% vs 4.3%, p<0.001) and death (5.5% vs 1.1%, p<0.01) occurred significantly more often in elderly than in younger patients. Conversely, event rates of myocardial infarction (MI) and stent thrombosis (ST) were comparable in both age groups. In the elderly, bivalirudin significantly reduced 30-day non-CABG major bleeding (7.1% vs 10.4%; relative risk [RR], 0.68; 95% confidence interval [CI], 0.51 to 0.90; p<0.01), subacute ST (0.4% vs 1.5%; RR 0.25; CI 0.05 to 0.73; p<0.01) and the composite endpoint of death, myocardial infarction, non-CABG major bleeding, stroke or ischemia-driven revascularization (13.7% vs 17.2%; RR 0.80; 95% CI, 0.65 to 0.98; p<0.03) with non-significantly different rates of acute ST (0.7% vs 3.3% RR, 2.5; 95% CI, 0.65 to 9.56; p=0.17), MI (1.5% vs 1.6%; RR 0.95; CI 0.49 to 0.1.84; p=0.87) and death (4.9% vs 6.1%; RR 0.80; 95% CI, 0.56 to 1.14; p=0.21) when compared with heparin ± GPI.

**Conclusion:** In elderly patients enrolled in the EUROMAX and HORIZONS-AMI trials, bivalirudin significantly reduced 30 day non-CABG major bleeding and sub-acute ST with comparable rates of acute ST, MI and death, when compared with heparin with or without GPI.

### P4993 | BEDSIDE

**Revascularization strategies in patients with ST-segment elevation myocardial infarction and multivessel disease in a real world population**


**Rationale:** The ideal revascularization (Rv) strategy in patients (P) with ST-segment elevation myocardial infarction (STEMI) and multivessel coronary disease is controversial.

**Purpose:** Identify in a real world population the factors that had been influencing our Rv strategies choices in P with STEMI and multivessel coronary disease.

**Methods:** Retrospective, unicentric study based on 1142 P admitted with STEMI over 5 years and during a minimal 6 months (6m) follow-up. P with multivessel coronary disease who undergone successful 1ª PCI were included (n=409). P were ineligible if they had: history of surgical myocardial revascularization (n=83); stem of ostial left anterior descending artery (LAD) disease (n=22); cardiogenic shock (n=21) or died during admission (n=30). The following Rv strategies were compared: 1) culprit artery 1ª PCI only (Rv1); 2) staged complete Rv (Rv2) and 3) ischemia guided Rv (Rv3). The primary endpoint studied was a composite of 6m mortality, nonfatal myocardial infarction and repeated revascularization.

**Results:** The most common Rv strategy performed was Rv1 (59.8%) followed by Rv2 (29.3%). P managed with Rv1 were older (66±13 vs 60±11 years, p<0.001) and had more chronic renal failure (3.9% vs 0%, p=0.01). They had more often bifurcation (6% vs 5% vs 5.2%, p=0.07) and long (8.6% vs 5.2% vs 6.2%, p=0.07) coronary stenosis, in smaller branches (30.1% vs 8% vs 17%, p<0.001) and distal coronary segments (29.4% vs 15.6% vs 14.2%, p<0.001). P who underwent Rv1 had more often LAD non culprit lesions (31% vs 51% vs 40%, p=0.005) and more severe stenosis (76±11% vs 85±12% vs 83±9%, p<0.04). P managed with Rv3 had lower mean ejection fraction values (44±9% vs 47±3% vs 42±8%, p=0.04). After multivariate analysis, stenosis severity, presence of LAD non culprit lesions and renal dysfunction persisted as independent variables that had been influencing Rv strategy choice. The incidence of primary endpoint was higher in P managed with Rv1 (34.9% vs 10.5% vs 28.6%, p<0.003). After multivariate analysis, this strategy persisted as an independent predictor of the clinical event studied (HR 1.9; CI 95% p<0.02).

**Conclusion:** In P with STEMI and multivessel coronary disease the Rv of culprit artery only had a poorer 6m outcome when compared with complete staged or ischemia guided Rv. Stenosis severity, the presence of LAD non culprit lesions and renal dysfunction were the main determinants of Rv strategy choice in a real world population.
Background and purpose: Coronary CT angiography (CTA) reliably detects coronary artery disease (CAD), but its diagnostic accuracy is reduced in patients with highly calcified or previously stent-implanted vessels. In this study we investigate the feasibility and diagnostic accuracy of subtraction CTA using a recently developed software, on a series of patients with these features, as compared to invasive coronary angiography (ICA).

Methods: Selected were 23 patients with calcified or stented CAD shown at a previous ICA. CTA exams were performed using 320-row CT with an acquisition protocol that includes 2 studies (non-contrast and contrast) obtained during the same breath-hold. The non-contrast CT is subtracted from the contrast CT to provide image subtraction. Subtraction CTA significantly improved in comparison with conventional CTA by subtraction CTA significantly improved in comparison with conventional CTA (AUC 0.91 vs. 0.83; p=0.05).

Results: A total of 129 coronary artery segments were analyzed. There was significant improvement in image quality in subtraction compared to conventional CTA (3.3±0.9 vs 2.7±0.9; p<0.01), although in those segments with motion artefact it was not significant (2.7±1.2 vs 2.4±1.2; p=0.23). Metal subtraction from stented segments led to significantly improved image quality (3.3±0.9 vs 2.7±0.9; p<0.01), while in those stents >3 mm of diameter this was not significant (2.7±0.9 vs 2.1±0.8; p=0.17). Diagnostic accuracy to detect stenosis >50% by subtraction CTA significantly improved in comparison with conventional CTA (AUC 0.91 vs. 0.83; p<0.05).

Conclusion: Subtraction CTA is a promising tool to overcome limitations of conventional CTA due to calcium/metal artefacts, which significantly improves the CTA diagnostic accuracy, particularly when no motion artefact are present.
ily calcified plaques may preclude high-quality images and diagnostic accuracy. Recently, a new CT technology that combines dual-energy CT (DECT) with rapid peak kilovoltage (kVp) switching (gemstone spectral imaging, GSI) and allows to reconstruct material decomposed images (MDI) was introduced in clinical prac-

tice.

Objectives: To evaluate the diagnostic accuracy of coronary CT angiography us-
ing DECT with monochromatic images and calcium removal by MDI vs. simulated conventional polychromatic image evaluation as standard of reference (sSTD).

Methods: We enrolled 75 patients referred for clinically indicated invasive coro-
nary angiography who had a coronary calcium score (CCS) >400 and under-
went coronary CT angiography with prospective ECG-triggering without padding. In all patients, 77 keV mono-chromatic images used to simulate a conventional 120 kVp poly-chromatic images (sSTD) and the corresponding MDI (iodine minus calcified plaque) were reconstructed from a GSI Cardiac exam. Two independent cardiac imaging experienced readers interpreted all studies for both STD and GSI reconstructions.

Results: The mean CCS was 606±253. Twenty patients had a 1-vessel disease (>50% stenosis), 26 patients had a 2-vessel disease, 5 patients had a 3-vessel disease. Coronary evaluability (number of coronary segments evaluable/total number of coronary segments), in a segment-based model, was significantly higher with MDI vs. sSTD (98% vs. 95%, p<0.001). A significantly lower number (6 vs. 46, p<0.001) of beam-hardening artifacts (large coronary calcifications impairing accurate evaluation of the lumen) was observed with MDI vs. sSTD. In a segment-based analysis, specificity, positive predictive value and accuracy for >50% coronary stenosis identification were significantly higher with MDI vs. sSTD (99%, 94% and 99% vs. 96%, 96% and 96%, respectively, p<0.001). The sensi-
tivity was 100% in both groups. Similarly, in a patient-based analysis, specificity, negative predictive value, positive predictive value and accuracy were significantly higher with MDI vs. sSTD (89%, 100%, 94% and 96% vs. 11%, 50%, 65% and 64%, respectively, p<0.001).

Conclusions: DECT with MDI improves coronary CT angiography evaluability and diagnostic accuracy in patients with suspected CAD and high CCS.

P4998 | BEDSIDE

Relationship between adverse coronary plaque characteristics, coronary CT angiography and fractional flow reserve: comparison of proximal and total vessel based analyses

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Background: An association between adverse plaque characteristics (APC) as assessed by coronary CT angiography (CTA) and ischemia by fractional flow reserve (FFR) sensor has recently been demonstrated. This association has only been evaluated for APC proximal to the FFR sensor. However, it may be difficult in prac-
tice to determine a priori the exact vessel location in which APC are “proximal-toFFR”.

Objective: To evaluate a “proximal-to-FFR” versus “total” vessel based model to a standard coronary CTA stenosis assessment in discriminating lesion-specific ischemia. CTA vs. CTA was the preferred plaque analysis strategy.

Methods: In 254 patients (mean age 64±10 years, 64% males) suspected of coronary artery disease, coronary CTA and FFR were performed in 484 ves-
sels in a prospective multicenter trial. Coronary CTA lumen reduction >50% was considered as lesion-specific ischemia. Independent predictors of FFR <0.80 were quantified non-calcified plaque (NCP), low-density NCP (LD-NCP), calcified (CP) and total (TP) plaque volumes, remodeling index (RI), lesion length (LL) and contras-
t density difference (CDD, maximum percent attenuation difference/proximal cross-section) by semi-automated software (AutoPlaq); spotty calcification (SC) was visually assessed from standard CTA images. Plaque analyses were per-
formed in a “proximal-to-FFR” (proximal to FFR sensor located 10–20 mm distal to lesion) and “total” vessel (entire vessel) fashion. Univariate and multi-
variate analyses of APC for prediction of ischemia were performed. Models com-
bining coronary CTA stenosis and APC independently predictive of ischemia from multivariate analyses were created. Receiver operating curve (AUC) for coronary CTA were compared to coronary CTA + “proximal-to-FFR” or coronary CTA + “total” vessel APC model.

Results: In 80 patients (100 vessels) FFR <0.80. In univariate analyses, “proximal-to-FFR” and “total” vessel NCP, L-DNCP, TP volumes, RI (only for total), LL and CDD were predictors of FFR <0.80 (all, p<0.02); however in multi-
variate analyses, only “proximal-to-FFR” and “total” vessel L-DNCP and CDD (all, p<0.001) remained independent predictors of FFR <0.80. The AUC for coronary CTA + “total” vessel APC had higher discrimination for ischemia than coronary CTA + “proximal-to-FFR” (AUC 0.85 [0.81–0.90] vs. 0.83 [0.78–0.88], p=0.03), both models superior to coronary CTA (AUC 0.79 [0.74–0.85], both, p<0.003).

Conclusions: Coronary CTA and “total” vessel APC provided the highest discrim-
ation of lesion-specific ischemia, incremental to coronary CTA and “proximal-to-
FFR” APC model, and to coronary CTA alone. “Total” vessel APC thus should be the preferred plaque analysis strategy.

P5000 | BEDSIDE

Epicardial adipose tissue expansion and differentiation status predict myocardial redox state and coronary calcification

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Background: Epicardial adipose tissue (EAT) is an endocrine organ that secretes paracrine adipokines, which affect the myocardial redox state and coronary calcification. Recently, a new CT technology that combines dual-energy CT (DECT) with rapid peak kilovoltage (kVp) switching (gemstone spectral imaging, GSI) and allows to reconstruct material decomposed images (MDI) was introduced in clinical prac-
tice, affecting major biological processes in the myocardium and the coronary arteries.

Purpose: To explore the role of EAT expansion in the regulation of myocardial redox state and coronary calcification.

Methods: In 220 patients undergoing coronary CT angiography (CTA), the volume of EAT and thoracic (THAT) adipose tissue were measured. In 18 additional patients undergoing cardiac surgery, CTA was used to calculate EAT and THAT volume, and arterial stiffness was measured fluoroscopically.

Results: Men had significantly smaller CSA (404±73 vs. 506±112 mm², Perim [71.8±7.6 vs. 80.1±8.6 mm], STJ [27.3±29.4 mm], and SOV [32.5±3.7 vs. 35.6±4.6 mm] versus men; P<0.001 for all, even after adjustment of the small Body surface area in women. The EI was comparable between women and men (1.24±0.12 vs. 1.25±0.12, P=0.7), and the mean left and right coronary artery ostia height were lower in women versus men (12.4±2.7 vs. 13.9±3.1 mm, P<0.001; 14.8±2.6 vs. 17.2±2.2 mm, P<0.001). AVE was borderline lower in women versus men (124±7 cm² vs. 143±9 cm², P=0.1). Conclusion: In this large severe AS population, women had smaller annulus, shallow SOV and STJ, and lower-lying coronary ostia, even after indexing for their smaller body size. The aortic annulus shape was similar in women and men and the valvular calcification in women had a trend towards lower value compared to men.

Conclusions: Increased EAT expansion is associated with increased NAPOD oxide and TNF-alpha levels in the myocardium and the coronary arteries.
Cardiac Computed Tomography permits coronary artery visualization to identify coronary calcium and to detect and rule out coronary artery stenoses. It further allows anatomic and functional imaging of the heart. Data concerning indications, acquisition parameters, results and clinical consequences of cardiac computed tomography are not available on a large scale.

Methods: The German Cardiac CT Registry includes 13 experienced clinical sites using at least 64-slice computed tomography systems. Between 2009 and 2014, 7061 consecutive cardiac CT examinations were included in the registry. Patient parameters and procedural data, results and clinical consequences of the test result were recorded in a systematic fashion.

Results: Mean patient age was 61±12 years, 63% were male. 63% of cases were performed on outpatient basis, 37% in inpatients. 91% were scheduled electively and 9% as an emergency. In 9% of cases, only coronary calcium imaging was performed (n=630), in 17% (n=1163) only coronary CTA, and in 57% (n=4043) coronary calcium and coronary CTA. Other cardiac CT examinations were performed on 16.5% of patients (n=1162). Specific indications are listed in table 1.

Conclusion: The majority of cardiac CT examinations are performed to rule out or detect coronary artery stenoses. With a low average radiation dose, further diagnostic testing – including invasive coronary angiography – can be avoided in a high percentage of patients.

CARDIOVASCULAR DYSFUNCTION AND REPAIR – ROLES OF INFLAMMATION AND IMMUNE CELLS

P5002 | BENCH
Sphingosine-mono-phosphate (S1P) induces the migration of Muse cells but not non-Muse cells toward the rabbit post-infarct heart and contributes to the improvement of cardiac function and remodeling

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Background: It has been reported that the S1P-S1PR receptor is a critical mediator of smooth muscle cell migration. We then examined whether S1P-S1PR2 directly mediates migration of Muse cells toward the serum and cardiac tissue of the AMI rabbit compared to those of non-Muse cells. Muse cells migrated positively toward the S1PR2 agonist, while non-Muse cells did not.

Conclusions: The post-infarction administration of Muse cells reduces the myocardial infarct size and improves cardiac remodeling and functioning. S1P-S1PR2 is one of the relevant axis enabling Muse cells to actively migrate toward the AMI heart.

P5003 | BENCH
Perivascular accumulation of M1 macrophages elicits the development of immature vascular formation

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Background: The formation of immature vascular structure underlies the development of cardiovascular diseases including atherosclerosis and tumor progression. However, the mechanism of immature angiogenesis, however, is still unclear. Hematopoietic cells such as macrophages are believed to play a key role in vascular remodeling. Recently, macrophages can be broadly classified into two subpopulations, pro-inflammatory M1 macrophages and anti-inflammatory M2 macrophages. The aim of this study is to elucidate the roles of each macrophage subpopulation in vascular remodeling.

Methods: We established murine Lewis Lung Carcinoma Cells (LL/2) xenograft model as an immature angiogenesis model and characterized M1 and M2 macrophage surface markers by Flow cytometry (FACS) analysis. We also performed pimodindazole FACS analysis, and investigated the intratmural localization of macrophages, perivascular (pimo low) and intratumoral (pimo high).

Results: We examined the surface markers of the macrophage subpopulations in tumor tissue, and classified M1 macrophages as Ly6c high, and M2 as Ly6c low. Ly6c high macrophages expressed CCR2 and inducible nitric oxide synthase, whereas Ly6c low cells express arginase1 and CD206. FACS analysis using pimoindazol showed that M1 macrophages accumulate in perivascular area (pimo low), whereas M2 macrophages intratumoral (pimo high). Importantly, perivascular M1 macrophages expressed higher level of VEGF-A expression, one of the most potent angiogenic factors. To explore the role of M1 macrophages in vascular remodeling, we searched for a chemokine receptor which expressed exclusively in M1 macrophages. Among the chemokines, we found that Fli-1 expressed in M1, but not in M2 macrophages. We subsequently generated myeloid cell specific Fli-1 deficient (Lys/M-Fli-1 flox) mice. Intriguingly, M1 macrophages accumulation was strikingly attenuated in Lys/M-Fli-1 flox mice, whereas M2 macrophages recruitment unchanged. Histological study showed that tumor vasculature in Lys/M-Fli-1 flox mice were less tortuous and greater pericyte coverage. Tumor xenograft in Lys/M-Fli-1 flox mice grew faster, which were consistent with the vascular normalization in myeloid cell specific VEGF-A deficient mice.

Conclusion: Collectively, we showed that the accumulation of VEGF-A expressing M1 macrophages to the perivascular area underlies the development of immature vascular formation. We also identified that Fli-1 plays a key role in M1 macrophage recruitment. These data suggest that targeting Fli-1 signaling can be a therapeutic target to reestablish well organized vasculature.
juvenile beagles (12 weeks old; weight ca. 3 kg). After 3-month transplantation all biotubes were patent without any stenosis or aneurysm formations, and vascular reconstruction including endothelialization was achieved. In this period, angiographic observation revealed that the diameter of the host arteries was gradually dilated from 2 to 3 mm, in tandem with body growth. However, little change was observed in the diameter of the transplanted biotubes. Thereafter, monthly angiographic evaluation revealed that the biotubes were continuously expanded in diameter, similarly to the growth of the native arteries with little size-mismatching in all cases. At 5 months of transplantation (weight ca. 8 kg) both vascular diameters reached 4 mm.

Conclusion: After vascular reconstruction within several months of transplantation, biotubes could be dilated according to the growth of native arteries. This is the first study to confirm the growth adaptation of biotubes in an animal experimental model. Based on our results, biotubes have a high potential usefulness in pediatric surgery.

P5005 | BENCH

Chronic cardiac allograft rejection after heterotopic rat heart transplantation: effects of antibody-based targeted delivery of interleukin-10 in a preventive and a therapeutic approach

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Methods: A heterotopic rat heart transplantation model was used to induce chronic rejection within 70 days. For therapeutic interventions, F8-humanIL10 (F8-huIL10), F8-ratIL10, KSF-humanIL10 (KSF-huIL10, control) and PBS (control) were used. Treatment was performed every week (1 mg/animal) for 10 weeks (F8-huIL10) or 10 days starting at day 7 (preventive approach) or day 70 (therapeutic approach) after transplantation.

Results: In the preventive approach, treatment with F8-huIL10 or F8-ratIL10 revealed a significant increase in allograft weights, rejection score, alpha-smooth muscle actin (α-SMA) expression, immune cell infiltration (CD4+, CD8+ and CD68+ cells) and serum brain natriuretic peptide (BNP) levels compared to control groups. In the therapeutic approach, administration of F8-IL10 was neither capable to stop progression of chronic rejection nor to reverse its tissue manifestations.

Conclusion: This is the first study focusing on the antibody-based targeted delivery of IL-10 in an animal model of chronic cardiac rejection. All observed interventions, including F8-specific to ED-A+ Fn, may serve as a vehicle for targeted delivery of bioactive payloads like interleukin-10 (IL-10), an anti-inflammatory cytokine, which might reduce chronic rejection.

Purpose: The aim of this study was to investigate the preventive and therapeutic effects of F8-interleukin-10 (F8-IL10) administration in a rat model of chronic cardiac rejection.

Background: The occurrence of silent bacteraemia from periodontal pockets is associated with cardiovascular diseases.

Methods: Experimental sepsis was induced using endotoxin injection (LPS) or Cacl2, increased diastolic LV diameter (LVdd). AM groups presented with preserved EF, CO and LVd, compared with SC; this was accompanied by ~50% mortality reduction. Experimental sepsis in SC groups induced downregulation of SOCS1, myocardial cytokine upregulation, reduced apoptosis and adhesion protein expression as well as pro-inflammatory transcription factor activation, all of which were attenuated AM.

Conclusions: Pharmacological inhibition of miR-155 attenuated sepsis-induced cardiac dysfunction, blunted pro-inflammatory activation and reduced mortality. This suggests miR-155 as a potential target in human sepsis-associated cardiac dysfunction.

P5007 | BENCH

Whole blood omega-3 fatty acid content predicts recurrent venous thromboembolism and death in elderly patients with acute venous thromboembolism


Background: Venous thromboembolism (VTE) is a leading cause of cardiovascular disease (CVD) and death. Omega-3 fatty acids (n-3 FA) have been shown to reduce the risk of CVD as well as mortality due to their antiinflammatory and anti-thrombotic properties. Inflammation, activation of platelets and coagulation are key mechanisms of VTE. Elderly patients with previous VTE are at particular risk for recurrent VTE due to their frequent proinflammatory and prothrombotic co-morbidities. We therefore hypothesized that increased n-3 FA are associated with a lower risk of recurrent VTE and death in this elderly population with previous VTE.

Methods: We determined baseline whole blood fatty acid composition by gas chromatography in 826 patient samples from The Swiss Cohort of Elderly Patients with VTE (SWITCO65+), a prospective multicenter cohort study of in- and outpatient aged ≥65 years with acute VTE. We categorized n-3 FA into low, medium, and high levels based on the 25th and 75th percentile (low: 2.7–4.9%, medium: 4.9–6.6%, high: 6.6–11.6%). Associations between n-3 FA and the primary composite endpoint of recurrent VTE or death and the secondary endpoint of major and non-major bleeding within six months were assessed by ordinary Cox regression analysis. Risk factors of VTE, VTE prevention, and recent bleeding were used as covariates. Cumulative incidences of recurrent VTE or death and bleedings were estimated by the Kaplan-Meier method and compared using the logrank test. Recurrent VTE or death was adjusted for age, gender, overt PE, cancer, heart failure, chronic lung disease, BMI, history of aspirin and antiplatelet therapy and periods of anticoagulation.

Results: The cumulative incidence of recurrent VTE or death was significantly different among levels of n-3 FA (p < 0.001). A high level of n-3 FA was significantly associated with a reduced risk of VTE recurrence or death after six months. Adjusted HR for high versus low level: 0.36 (95% confidence interval 0.20–0.67, p < 0.001). In contrast, n-3 FA were not associated with major and non-major bleedings.

Conclusion: Our findings demonstrate that increased levels of whole blood omega-3 fatty acids are strongly associated with a reduced risk of recurrent VTE or death from any cause in patients with previous VTE. Anti-inflammatory and anti-coagulant mechanisms may mediate this effect. Total n-3 FA was not associated with risk of major and non-major bleedings.

P5008 | BENCH

Periodontal bacteria promote systemic immune responses and persistence of intramural hematoma in experimental abdominal aortic dissection/aneurysm


The occurrence of silent bacteraemia from periodontal pockets is associated with abdominal aortic aneurysm (AAA) in patients but the putative pathogenic link remains to be elucidated. The occurrence of silent bacteraemia from Porphyromonas gingivalis (Pg), a usual periodontal bacteria, in the circulating blood could affect the immune response involved in the physiopathology of AAA. Twenty-seven week-old male apolipoprotein E knockout mice were submitted to...
chronic angiotensin II infusion, a common model of aortic wall dissection followed by AAA formation. The presence of AAA was validated by Doppler tissue echography and mice were thereafter randomly assigned to the intravenous weekly injection of Pg (n=13, 1.108 CFU) or of the vehicle (n=14), for 4 weeks. Plasma, spleen and aortic wall samples were collected at the end of the study.

The intramural hematoma was partially resolved in 4 out of 13 Pg-injected mice vs 10 out of 14 control mice (χ², p=0.01). Total as well as Pg-specific IgM, IgG plasma concentrations were consistently increased in Pg-injected mice. Flow-cytometry analysis of the spleen leukocytes revealed an enrichment of CD19+CD95highIgMlow germinal center B cells and CD69+ activated CD4+CD8+ T cells. These findings were consistent with the enhanced levels of plasma CC19 and CXCL13 chemokines. Finally, IL-2, IL-10, IL-12 and IFN-γ were also found enriched in the plasma of Pg-injected mice. This study is the first of a systemic activation of the immune system triggered by Pg bacteriaemia, which could be involved in the pathological processes leading to the persistence of intramural hematoma AAA.

OUTCOMES AFTER TAVI

P5009 | BEDSIDE

Aortic stiffening is a strong determinant of heart failure after transcatheter aortic valve replacement

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Background: In the presence of aortic stenosis, left ventricular afterload involves not only a valvular load but also a vascular load. After transcatheter aortic valve replacement (TAVR), the vascular load becomes the prevailing feature and may prolong the impairment of cardiac function leading to heart failure (HF) On the other hand, the principal objective of this study was to examine the impact of aortic stiffening on the risk of HF after TAVR; two indices were used: ascending aorta calcifications (AAC) and pulse pressure (PP). They were compared to the non-CO group (1.53 vs 1.30, p=0.038). By using a receiver-operating characteristic analysis with the area under curve (AUC) as a measurement of accuracy, the ratio had moderate accuracy in predicting the incidence of CO (AUC=0.786, p=0.009) among S/XT cases. The frequency of CO tended to be lower in recipients of the CoreValve compared with the S/XT (0.4% vs 1.6%, p=0.260). Furthermore, the frequency of CO significantly decreased in S3 cases compared to S/XT (0% vs 1.6%, p=0.022). Percutaneous coronary intervention was attempted in 5 (62%) patients, 3 of whom underwent successful revascularization, but 2 patients required emergency cardiac surgery. The 30-day mortality was very high in the CO group (11.2±1.7 vs 13.4±2.5, p=0.009) among S/XT cases. The frequency of CO tended to be higher in recipients of the S/XT valve compared with the CoreValve. The preliminary data showing that CO has not yet been reported in patients receiving the S3 despite the increased height need further confirmation.

Conclusions: CO tended to occur more frequently in women at the ostium of LCA. The frequency of CO tended to be higher in recipients of the S/XT valve compared with the CoreValve. The preliminary data showing that CO has not yet been reported in patients receiving the S3 despite the increased height need further confirmation.

P5010 | BEDSIDE

Pre- and postprocedural mitral regurgitation and mortality following transcatheter aortic valve replacement for severe aortic stenosis - an interaction with aortic regurgitation (POL-TAVI registry)

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Methods: In 141 patients treated by TAVR, AAC was measured by computed tomography and expressed either as a crude variable or corrected for Aortic Volume (AV). PWV was measured before TAVR in a subset of patients. The primary outcome was a composite of deaths and hospitalizations related to HF.

Results: The survival rates in the two highest AAC tertiles were lower than that in the first tertile (p[log-rank]=0.031). A similar trend was observed according to AAC/AV albeit not significant (p[log-rank]=0.259). PP did not change across AAC tertiles and was not predictive of HF in univariate analysis (hazard ratio; 1.01 [0.99–1.03], p=0.39). In multivariable Cox regression models adjusted for major confounders including EuroSCORE, AAC remained predictive of the primary outcome (tertiles 2 and 3 vs. 1 hazard ratio: 2.42; 95% CI: 1.16 to 5.06; p=0.019). Total as well as Pg-specific IgM, IgE plasma concentrations were consistently increased in Pg-injected patients (n=13, 1.108 CFU) or of the vehicle (n=14), for 4 weeks. Plasma,

P0510 | BEDSIDE

Type of atrial fibrillation and clinical outcomes in patients undergoing transcatheter aortic valve implantation

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Background: Atrial fibrillation (AF) is a major risk factor for stroke and death after transcatheter aortic valve implantation (TAVI). However, there is paucity of data regarding the association between AF clinical type, anticoagulation therapy, and clinical outcomes after TAVI.

Methods: We analyzed data from a single center TAVI registry, including 325 consecutive patients with severe aortic stenosis. Patients were divided into 3 groups based on their history of AF type: sinus rhythm (SR), paroxysmal AF (PAF) or non-paroxysmal AF (NPAF, including persistent AF and permanent AF). We also analyzed the effects of oral anticoagulation (OAC) treatment on outcome in these groups. The primary endpoint was stroke or death.

Results: There were 215 (66%), 57 (18%), and 53 (16%) patients in the SR, PAF and NPAF groups, respectively. The cumulative risk for stroke or death at 2 years was highest among patients with NPAF (38%), but similarly low in PAF (15%) and SR patients (17%, p=0.001, Figure). By multivariate analysis, patients...
with NPAF demonstrated a significantly higher risk of stroke or death (HR=2.36, 95% CI 1.35–4.13, p=0.003), as compared with SR. By contrast, patients with PAF compared with SR had a similar risk of stroke or death (HR=0.69, p=0.306). Patients with NPAF not treated with OAC demonstrated an 8-fold (HR=8.19, 95% CI 3.32–20.17, p=0.001) increased risk of stroke or death, whereas patients with PAF not treated with OAC had a similar risk of stroke or death compared with the SR group (HR=1.07, p=0.875).

Conclusions: History of NPAF, but not PAF, is associated with a significant increased risk of stroke or death compared with sinus rhythm in patients undergoing TAVI. This finding may be helpful to estimate the risk-benefit of anticoagulation therapy in patients undergoing TAVI.

P5014 | BEDSIDE
Seven-year outcome after TAVI
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Finally, in the 116 survivors, 70% were in NYHA class I-II at last follow-up. In 32 patients frequent after TAVI (29% of cases in this series) and may often lead to pace-


diary, only post-TAVI arrhythmias (supraventricular in 32 patients and PAP (p=0.02) and arrhythmias (p=0.02). Whereas conduction disorders are more common after TAVI.

In conclusion, we report the seven-year outcome after TAVI including predictive factors of late mortality. Multivariate analysis: cancer (p<0.001), diabetes under insulin therapy (p=0.02), NYHA class III-IV (p=0.03), atrial fibrillation (p=0.04), higher creatinine level (p=0.0001) and 2 post-procedural predictors, PAP (p=0.02) and arrhythmias (p=0.02). Whereas conduction disorders are more frequent after TAVI (29% of cases in this series) and may often lead to pacemaker implantation, only post-TAVI arrhythmias (supraventricular in 32 patients or ventricular in 4) were predictive of late mortality. Finally, in the 116 survivors, 70% were in NYHA class I-II at last follow-up.

Conclusions: At 7-year follow-up after TAVI, the survival rate was 27% and most patients have few or no symptoms. The predictive factors of late mortality emphasized the weight of comorbidities. Particular awareness is needed toward the occurrence of post-TAVI arrhythmias which identifies high-risk patients.

P5015 | BEDSIDE
Changes in the pacemaker rate after transition from Edwards Sapien XT to Sapien 3 transcatheter aortic valve implantation are primarily related to the implantation height
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Background: The introduction of the Edwards Sapien-3 valve (S-3) for transcatheter aortic valve implantation (TAVI) has led to a marked reduction of paravalvular regurgitation. However, it remains unclear whether the increase in stent length and the additional seal may result in a higher risk of conduction abnormalities (CA) and pacemaker (PM) requirement. The aims of this study were to compare the PM rate after TAVI using S-3 versus Sapien XT valves (XT), and to explore risk factors for the development of CA for D-3 after TAVI, considering in particular the implantation height (IH).

Patients and methods: The first 206 patients treated in our institution with S-3 were compared to 371 preceding patients treated with XT. After exclusion of patients with a previously implanted PM or ICD, transapical and valve-in-valve procedures, 162 S-3 patients (age 82±6 yrs., 38% male) and 287 XT patients (age 82±6 yrs., 37% male) were analyzed. All patients were monitored for 7 days \(\geq 40\) and \(\leq 40\). Main outcome measures were cardiovascular mortality and nonfatal myocardial infarction.

Conclusions: The incidence of PM implantation after TAVI is higher with Sapien 3 than with Sapien XT and is independently associated with the implantation height. This increase in PM rate can apparently be eliminated by optimizing the implantation height with keeping the extension of the stent into the left ventricular outflow tract short.

ADVANCING THE CLINICAL APPLICATION OF BIOMARKERS

P5016 | BENCH
Prognostic value of circulating MicroRNAs in patients with coronary artery disease - results from the AtheroGene study
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Introduction: Stratification for subsequent coronary events among patients with coronary artery disease (CAD) is of considerable interest because of the potential to guide secondary preventive therapies. MicroRNAs (miRNAs) are a class of small noncoding RNAs found to be involved in cardiovascular pathophysiology. In a previous study -using a three-phase approach of (i) miRNA profiling in patients with unstable angina pectoris and controls groups; (ii) replication of significant miRNAs in an independent patient cohort, (iii) validation of a multi-miRNA panel for clinical application, we identified eight miRNAs facilitating diagnosis of acute coronary syndrome (ACS). This study aimed to evaluate the potential role of the identified miRNAs as prognostic biomarkers for cardiovascular disease.

Methods: Plasma levels of eight candidate miRNAs - miR-19a, miR-19b, miR-122, miR-142-3p, miR-142-5p, miR-150, miR-210, and miR-210 were measured by real-time quantitative polymerase chain reaction (RT-qPCR) at baseline in a cohort of 1,112 patients with documented CAD including 430 ACS patients and 682 patients with stable angina pectoris (SAP). Cycle threshold (Ct) values were normalized to cel-miR-39 using the formula 2^(-

\text{\Delta}Ct)\) for Ct \(<40\) and \(>40\) in the case Ct \(>40\). Main outcome measures were cardiovascular mortality and nonfatal myocardial infarction.

Results: Spearman analyses yielded a strong positive correlation of all miRNAs among each other (all \(r>0.5\)). During a median follow-up of 4.0 years, we observed a significant higher risk of stroke or death compared with sinus rhythm in patients undergoing TAVI.

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Circulating aldosterone predicts future cardiorenal and metabolic disease in the general community
Mayo Clinic, Rochester, United States

Purpose: To investigate the relationship between hs-TnI and coronary artery calcification (CAC) in a healthy background population.

Methods: 1257 randomly selected subjects, 50 or 60 years old, underwent a clinical examination as well as a non-contrast cardiac-CAT scan for determination of CAC. The magnitude of CAC was measured using Agatston score. Cardiac tropinin I was detected using a high-sensitivity assay. Subjects with known CVD were excluded. The relationship between hs-TnI and CAC was assessed using multivariate regression analyses adjusted for cardiovascular risk factors including age, sex, diabetes, family history of CVD, BMI, hypercholesterolemia, hypertension and smoking. Receiver operating characteristic curves were plotted and the area under curve (AUC) was calculated.

Results: A total of 1173 subjects were included in this study, 52% were female and 48% were 50 years old. Concentrations of hs-TnI above the limit of detection (1.9 ng/L) were measured in 87% of all subjects, 80% in women and 95% in men. Hs-TnI above the 99th percentile of 24 ng/L was detected in 25 subjects (2.1%). Presence of CAC (Agatston score >0) was detected in 29% in the lowest hs-TnI quartile compared with 55% in the highest, with a stepwise increase over the quartiles. In fully adjusted regressions with dichotomous CAC outcomes, hs-TnI was associated with presence of CAC of OR: 1.25, 95% CI: 1.03–1.51, p=0.03 and an Agatston score >100 (OR: 1.36, 95% CI: 1.08–1.71, p=0.01). Subjects in the fourth hs-TnI quartile had an increased risk for presence of CAC (OR: 1.56, 95% CI: 1.19–2.03) and for an Agatston score >100 (OR: 1.39, 95% CI: 1.04–1.82, p=0.04), compared with the lowest quartile. When stratified by gender, hs-TnI was associated with presence of CAC in men (OR: 1.48, 95% CI: 1.10–2.00, p=0.01) but not in women (OR: 1.11, 95% CI: 0.85–1.45, p=0.46).

Conclusions: Presence of hs-TnI predicted future CAC independent of classical CVD risk factors. hs-TnI may improve risk prediction in both BRHS and MIDSPAN, but evidence of improvement is not clear whether current efforts to lower thresholds for statin prescription might impact utility of these biomarkers across the age ranges relevant for screening.

P5019 | BEDSIDE
Cardiac biomarkers and the prediction of primary CVD events in two cohort studies: results from the BRHS and MIDSPAN family study
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Background: High-sensitive cardiac troponin I (hs-TnI) is clinically used to diagnose myocardial infarction (AMI). Hs-TnI is also an important individual risk marker for prediction of future cardiovascular disease (CVD) in the general population. The development of an AMI is most often precipitated by atherosclerotic plaques in the coronary arteries.

Purpose: To investigate the relationship between hs-TnI and coronary artery calcium (CAC) in a healthy background population.

Methods: 1257 randomly selected subjects, 50 or 60 years old, underwent a clinical examination as well as a non-contrast cardiac-CAT scan for determination of CAC. The magnitude of CAC was measured using Agatston score. Cardiac tropinin I was detected using a high-sensitivity assay. Subjects with known CVD were excluded. The relationship between hs-TnI and CAC was assessed using multivariate regression analyses adjusted for cardiovascular risk factors including age, sex, diabetes, family history of CVD, BMI, hypercholesterolemia, hypertension and smoking. Receiver operating characteristic curves were plotted and the area under curve (AUC) was calculated.

Results: A total of 1173 subjects were included in this study, 52% were female and 48% were 50 years old. Concentrations of hs-TnI above the limit of detection (1.9 ng/L) were measured in 87% of all subjects, 80% in women and 95% in men. Hs-TnI above the 99th percentile of 24 ng/L was detected in 25 subjects (2.1%). Presence of CAC (Agatston score >0) was detected in 29% in the lowest hs-TnI quartile compared with 55% in the highest, with a stepwise increase over the quartiles. In fully adjusted regressions with dichotomous CAC outcomes, hs-TnI was associated with presence of CAC of OR: 1.25, 95% CI: 1.03–1.51, p=0.03 and an Agatston score >100 (OR: 1.36, 95% CI: 1.08–1.71, p=0.01). Subjects in the fourth hs-TnI quartile had an increased risk for presence of CAC (OR: 1.56, 95% CI: 1.19–2.03) and for an Agatston score >100 (OR: 1.39, 95% CI: 1.04–1.82, p=0.04), compared with the lowest quartile. When stratified by gender, hs-TnI was associated with presence of CAC in men (OR: 1.48, 95% CI: 1.10–2.00, p=0.01) but not in women (OR: 1.11, 95% CI: 0.85–1.45, p=0.46).

Conclusions: Presence of hs-TnI predicted future CAC independent of classical CVD risk factors. hs-TnI may improve risk prediction in both BRHS and MIDSPAN, but evidence of improvement is not clear whether current efforts to lower thresholds for statin prescription might impact utility of these biomarkers across the age ranges relevant for screening.

P5020 | BENCH
Effects of combined cognitive and physical training on telomere length in patients with mild cognitive impairment
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Background: There is increasing evidence to support the benefits of regular physical activity and training on the vascular impairment in Mild Cognitive Impairment (MCI), but the molecular mechanisms underlying these benefits remain unknown.

Purpose: To evaluate the efficacy of combined cognitive and physical training on leukocyte telomere length (LTL), a consolidated biomarker of vascular and cellular aging.

Methods: Within the open-label clinical trial called “Train the Brain”, 94 MCI patients with mild cognitive impairment were randomized into a control group and an experimental group. The experimental group underwent a 12-week intervention consisting of combined cognitive and physical training, while the control group received usual care. LTL was assessed at baseline and at the end of the intervention. The main outcome was the change in LTL from baseline to follow-up.

Results: After 4 years, log-transformed aldosterone at V1 predicted new onset of obesity (p=0.0113, OR=1.36, CI: 1.07–1.73); HTN (p=0.0012, OR=1.38, CI: 1.13–1.63) and use of antilipemic drugs (p=0.0119, OR=1.25, CI: 1.05–1.48) at V2. Aldosterone levels in the 3rd tertile at V1 predicted new onset of type 2 diabetes (T2DM) (p=0.0392, OR=1.96, CI: 1.03–3.70), use of antilipemic therapy (p=0.0159, OR=1.59, CI: 1.09–2.31) and HTN (p=0.0034, OR 1.44, CI: 1.00–2.08) at V2. We also observed that an increase in aldosterone between V1 and V2 predicted new HTN at V2. In addition, we found that aldosterone levels at V1, even within the normal range, remained associated with HTN, obesity and CKD, whereas treated as log-transformed aldosterone and with both hs-TnI and LTL.

Conclusions: In the general community, aldosterone predicts new onset HTN, central obesity, T2DM and use of antilipemic therapy in a 4-year follow-up. Importantly, the increase of aldosterone between V1 and V2 also predicts new onset HTN. Finally, we replicated our findings from V1 and V2 observations and found that sustained associations between aldosterone at V2 with HTN, obesity and CKD as observed at V1. This study strongly advances the use of measuring aldosterone to identify high-risk subjects in the general community who may develop future cardiovascular and metabolic disease, as well as it provides support for the use of therapeutic agents targeting aldosterone to delay disease onset and progression.

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Conclusions: LTL is shortened in patients with MCI, but telomere shortening is attenuated by environmental enrichment therapy, consisting of cognitive and physical training.

P5021 | BEDSIDE
Associations of estradiol, sex hormone-binding globulin and testosterone with circulating levels of amino-terminal pro-B-type natriuretic peptide in postmenopausal women: The Rotterdam Study
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Background: Amino-terminal pro-B-type natriuretic peptide (NT-proBNP) has a well-documented prognostic value for cardiovascular disease and sex-hormones are suggested to modulate NT-proBNP levels. However, little data is available on the association of sex-hormones with NT-proBNP in postmenopausal women. Furthermore, age and years since menopause may play a role in these associations, but have not yet been investigated.

Objectives: To assess the relationships between sex-hormones and NT-proBNP in postmenopausal women and whether these associations differ by age and years since menopause.

Methods: We measured estradiol, total testosterone (TT), sex hormone-binding globulin (SHBG) and NT-proBNP in 3139 postmenopausal women (free of cardiovascular disease) participating in the prospective population-based Rotterdam Study. Free androgen index (FAI) was calculated as ratio of TT to SHBG concentration. TT, SHBG, FAI and NT-proBNP were natural log transformed. Regression coefficients and 95% Confidence Intervals (CI) were calculated using multivariable linear regression models adjusting for confounders.

Results: After adjustment for age, body mass index, years since menopause, serum total cholesterol, hypertension, alcohol intake, physical activity, smoking and prevalent diabetes, higher levels of estradiol (per SD increase, \(\beta=0.04\); 95% CI: 0.01 to 0.07) and SHBG (per SD increase, \(\beta=0.17\); 95% CI: 0.13 to 0.20) were positively associated with NT-proBNP concentrations. In contrast, TT (per SD increase, \(\beta=-0.06\); 95% CI: -0.08 to -0.03) and FAI (per SD increase, \(\beta=-0.13\); 95% CI: -0.16 to -0.10) were inversely associated with circulating NT-proBNP (both \(p<0.001\)). These associations were independent of insulin resistance, C-reactive protein or fatty liver. However, significant interactions were found between estradiol, age (interaction=0.002) and years since menopause (interaction=0.01). After stratification by median-age (68.5 years), the positive association between estradiol and NT-proBNP was present in women 68.5 years or older (per SD increase, \(\beta=0.10\); 95% CI: 0.04 to 0.16) whereas no association was observed in women younger than 68.5. Similarly, the stratification analysis by years since menopause (median) revealed that the positive association between estradiol and NT-proBNP was significant only in women 20 years or further from menopause (per SD increase, \(\beta=0.06\); 95% CI: 0.01 to 0.11).

Conclusions: These findings suggest an association between estradiol, SHBG, and testosterone with circulating NT-proBNP levels among postmenopausal women. This association seems to be modified by age and years since menopause.
were recorded by flat panel systems. The lumen of the interrogated vessel segments from the origin of the target vessel to the pressure sensor was reconstructed in 3D using a dedicated 3D QCA software package.

**Results:** Significant tight correlation was found between the calculated vFAI and the measured FFR values (r=0.81, p<0.0001). The cut off value of the vFAI of 0.92 provided a good sensitivity (95%) with 71% specificity to predict the diagnostic FFR ≤0.8 values. The area under the curve was calculated to be 0.86 according to the ROC analysis.

**Conclusions:** The vFAI demonstrates comprehensively the pathophysiological correlation of the coronary artery lesions. The level of correlation between the vFAI values and the measured FFR values calculated using the simple approach developed by our team matches the performance of the previously described method that uses dedicated software and time-consuming fluid dynamic computations.

**P5024 | BEDSIDE**

Change in characteristics of the population receiving angiography in an era with decreasing cardiovascular incidence and mortality


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**Background:** Over the past 40 years, cardiovascular mortality in Northern Norway has decreased from 8%, among the highest in Europe, to 1.7% - among the lowest. This is due to a large decrease in incidence, but lately also to >50% reduction in mortality.

**Purpose:** Our aim is to describe how decreasing incidence and case fatality is reflected in the population receiving angiography in the last decade.

**Methods:** From 2005–2012, a total of 27,218 angiographies were performed by a sole provider of angiography for 479,000 people. Patient characteristics were entered into a clinical registry. Changes in trends were analysed by age-adjusted logistic regression analyses. Gender differences were tested with interaction terms. All the reported differences below had p<0.05.

**Results:** 19,933 patients (66% men and 34% women) had 25,232 admissions for angiography. Men were 64 years old and women were 67 at admission, of whom 62% vs 75% did not have former revascularisation. 25% of men were admitted more than once vs only 20% of women. 51% of men and 45% of women were admitted as acute coronary syndrome (ACS). In both genders, the total number of acute admissions increased by 1.5% per year vs 3.8% per year for elective admissions. Age of the admitted population increased 1 year from 2005 to 2012. ST-elevation myocardial infarction (STEMI) decreased from 24% to 18%, and prevalence of obstruction in either left main stem, proximal LAD or 3 vessels decreased from 22% to 20%. The number of ACS cases resulting in revascularisation decreased from 77% to 65% among those without former revascularisation vs from 63% to 51% among those with revascularisation. In the elective population, proportion with stable angina as referral cause decreased from 91% to 85%. The proportion resulting in revascularisation decreased from 62% to 36% among those without former revascularisation vs from 49% to 40% among those with either former percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). 63% of first diagnosis of obstructive coronary heart disease did not receive acute admission in both genders.

**Conclusions:** The dramatic drop in cardiovascular mortality in Norway was reflected in less obstructive pathology detected both in emergency and elective settings and with less severe pathology. Despite a high and increasing rate of coronary plaque burden and composition in statin-treated patients with stable coronary artery disease, Acute myocardial infarction is triggered by inflammatory bursts that may precipitate plaque progression. The association between inflammatory markers and changes of coronary plaque burden and composition in patients with ST-elevation myocardial infarction (STEMI) is unknown. **Objectives:** To assess volumetric and compositional changes of coronary artery plaque in relation to serum markers of inflammation.

**Methods:** In the IBIS-4 study 82 patients with acute STEMI underwent serial intravascular ultrasound (IVUS) and radiofrequency (RF) IVUS of the two non-target and adjacent epicardial arteries following successful primary percutaneous coronary intervention and repeated imaging after 13 months of treatment with rosvastatin 40mg. All patients recruited at Bern University (n=44) with serial hsCRP measurement are included in the present analysis.

At 13 months, LDL-C decreased by 38% to 77mg/dl. HDL increased by 13% to 48 mg/dl and hsCRP decreased by 58% to 0.70 mg/L. Regression of percent atheroma volume (−0.99%, 95% CI −1.84 to −0.14, p=0.024) did not correlate with levels of hsCRP and was accompanied by reduction of fibro-fatty tissue (p=0.005), increase of dense calcium (p=0.016) and no significant change of necrotic core tissue (p=0.22). Changes of RF-IVUS-defined components did not correlate with LDL-C or HDL-C levels. In contrast, on-treatment hsCRP correlated with the change of necrotic core tissue, which decreased in patients with the lowest hsCRP tertile (−0.13mm², −0.23 to 0.04) and increased in patients across higher hsCRP tertiles (p=0.002). A per-lesion analysis showed highest on-treatment hsCRP levels for thin-cap fibroatheromas (TCFAs) at baseline that progressed to non-TCFA lesions (0.03, 0.02 to 0.19 mg/L) and highest hsCRP levels for non-TCFA lesions that progressed to TCFAs at follow-up (1.75, 0.75 to 2.87 mg/L). Last but not the least, the strongest correlation was between the calculated vFAI and CMR (r=0.92, p≤0.001) and the relative plaque content of Dense calcium increased (4.6±4.3 to 6.8±4.9%, p<0.01).

**Conclusion:** In this observational study of STEMI patients treated with high-intensity statin therapy, elevated on-treatment levels of hsCRP, but not of LDL-C, associated with serial increase of RF-IVUS-defined necrotic core. Increased lev- els of inflammatory indices with on-treatment hsCRP were associated with high-risk indices of coronary plaque composition despite aggressive statin therapy. Larger studies are needed to determine potential prognostic implications of these associations.

**P5027 | BEDSIDE**

Contrast medium induced Pa/dPa ratio (CMR) versus FFR and adenosine-free indexes in the evaluation of intermediate coronary stenosis


**Aims:** The need for adenosine administration to achieve maximal hyperemia limits the widespread application of fractional flow reserve (FFR) in the real world. With the recently introduced coronary flow reserve (CFR) determined by continuous wave Doppler ultrasound, a non-invasive hyperemia induced by conventional non-ionic radiographic contrast material (contrast medium induced Pa/dPa ratio: CMR) can be sufficient for the assessment of physiological severity of stenosis in the vast majority of cases. In this study we aimed to test the accuracy of CMR in predicting an FFR ≤0.80 in comparison with other adenosine-free indexes, such as basal Pa/dPa and instantaneous wave-free ratio (IFR).

**Methods and results:** 323 patients with 373 intermediate coronary stenoses were prospectively and consecutively enrolled. FFR was measured after administration of adenosine and measured FFR and CMR were obtained after intracoronary injection of 6 ml of radiographic contrast medium, while Pa/dPa and IFR were measured at rest. Pa/dPa was measured in all 373 lesions, while CMR in 279 and IFR in 64. Although we found a significant correlation between FFR and all measured indexes, the strongest correlation was between FFR and CMR (r=0.92, p<0.001; r=0.77, p<0.001 for correlation between FFR and Pa/dPa; r=0.76, p<0.001 for correlation between FFR and IFR). ROC curve analysis confirmed these data, showing an excellent accuracy of CMR cut-off of ≤0.83 in predicting a positive FFR (AUC 0.98).
changes in PCI procedure more than half of the cases. Thus, OCT guidance is needed to determine the mechanism of MI and ensure accurate detection and quantification of BVS malapposition, underexpansion, tissue prolapse, edge dissection, stent fracture and thrombus. These issues may be associated with increased post-procedural mobility and mortality.

Objectives: To evaluate the influence of OCT during PCI and its impact on stent procedure during bioreabsorbable scaffold implantation.

Methods: Consecutive patients undergoing PCI with OCT-guided scaffold implantation from April 2012 to October 2014 were reviewed. Angiography and OCT images —were analysed, when available, before and after BVS implantation with respect to a change in PCI strategy.

Results: A total of 162 procedures were included. The median age of the patients was 62 (35–89) years, and 72.2% of patients were male. Indication for PCI was stable angina in 74.6%, STEMI in 9.8%, NSTEMI in 5.3%, unstable angina in 6.2% of the cases. OCT was performed in 87% (n=141) before deployment of the BVS. In 13.5% (n=19) it was decided against BVS implantation after OCT analysis due to heavy calcification (6.4%) or inadequate sizing (7.1%). In 19.7% (n=24) the pre-implantation OCT-analysis influenced the further strategy. This included the additional use of scoring devices (4.9%). In 10.7% the lesion length was underestimated. OCT analysis after BVS implantation, performed in 128 (79%) of the patients, led to additional interventions in 33.6% (n=43) of the procedures. Specifically, further BVS implantation was performed in 11.7% (edge dissection 10.9%, BVS fracture 0.8%). Additional balloon dilatation was needed in 20.3% of the patients, led to additional interventions in 33.6% (n=43) of the procedures.

Conclusion: OCT during BVS implantation was associated with changes in PCI procedure more than half of the cases. Thus, OCT guidance may minimise the presence and impact of procedural issues during BVS implantation and potentially improve clinical outcome.


P5029 | BEDSIDE

Usefulness of optical coherence tomography in determining the mechanisms of myocardial infarction in patients without angiographically demonstrable coronary artery disease

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Background: Coronary angiography (CAG) generally allows us to identify culprit lesions in patients with myocardial infarction (MI) by a number of characteristic findings (e.g. obstruction, narrowing, and haziness). However, a substantial proportion of patients with MI have no angiographically demonstrable coronary artery disease (CAD), and it is occasionally difficult to determine the mechanism of MI in such patients.

Purpose: The aim of this study was to clarify the usefulness of optical coherence tomography (OCT) for determining the mechanism of MI in these patients.

Methods: We studied 441 consecutive patients with MI, diagnosed according to the third universal definition of MI, admitted to our hospital (mean age, 68.0±13.3 years; men, 78.8%). The culprit lesion morphologies by OCT were classified as follows: plaque rupture, OCT-calculated nodule, OCT erosion, and others. The patients were divided into two groups according to the presence or absence of angio graphic criteria consistent with CAD.

Results: Twenty-four patients (5.4%) had no angiographically demonstrable CAD (non-CAD group). Patients in the non-CAD group tended to be younger (63.0±16.3 vs. 68.0±13.3 years, P=0.055) and to have lower prevalence rates of diabetes mellitus and dyslipidemia (20.8% vs. 38.6%, P=0.08 and 37.5% vs. 56.3%, P=0.07, respectively) compared to those for patients in the CAD group. In the pre-intervention Thrombolysis in Myocardial Infarction (TIMI) flow grade classification, patients in the non-CAD group had a significantly higher frequency of TIMI 3 flow grade compared to that for patients in the CAD group (58.3% vs. 8.7%, P<0.01), although the rate of ST-segment elevation MI was similar between the groups (66.7% vs. 75.2%, P=0.40). Eighteen patients in the non-CAD group underwent OCT imaging. The incidences of plaque rupture, OCT-calculated nodule, OCT-erosion, and others were 22.2%, 5.6%, 27.8%, and 38.9%, respectively. The proportion of MI in patients classified as “others” by OCT included in-stent restenosis, spasm, thromboembolism caused by atrial fibrillation, and thrombus formation triggered by dehydration or hypotension in the intact coronary artery.

Conclusion: The incidence of no angiographically demonstrable CAD in patients with MI is relatively high. If the culprit lesions were located or what the mechanisms of MI were using only CAG in these patients, we could confirm the mechanisms of MI by using OCT. Hence, OCT appears to be a useful modality for determining the mechanism of MI, especially in patients without angiographically demonstrable CAD.

OMINOUS SIGNS IN HEART FAILURE

P5030 | BENCH

Overexpression of phosphodiesterase-2 in mice reduces CaMKII-dependent enhancement of late sodium current through impaired beta-adrenergic response

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In heart failure, late Na current (late If) is increased and this has been shown to lead to arrhythmias and contractile dysfunction. Chronic β-AR stimulation promotes heart failure. CaMKII, which can be activated by β-AR stimulation (via CAM-P-Epac), increases late If via phosphorylation. We hypothesized that overexpression of phosphodiesterase-2 (PDE2), which hydrolyses cAMP can abolish activation of CaMKII, thereby reducing phosphorylation of CaMKII targets (such as late If), even in the presence of β-AR stimulation. To evaluate this hypothesis we investigated ventricular cardiomyocytes isolated from PDE2-overexpression transgenic (TG) vs wild-type (WT) littermates. Late If current was measured using whole-cell patch clamp technique. CaMKII was activated upon external application of either isoproterenol (100 μmol/L, ISO) or direct Epac activator 8-(4-chlorophenylthio)-2-O-methyladenosine-3',-5'-cyclic monophosphate (5 μmol/L, 8-CPT). In WT myocytes, both ISO and 8-CPT resulted in significant and comparable increases in late If (control: −27.9±3.1 vs ISO: −18.5±4.7 vs 8-CPT: −78.6±6.3 A*ms*F−1, n=15 vs 16 vs 14; P<0.001 vs control). However, in myocytes from TG mice the ISO-dependent increase in late If was completely abolished (control: −24.6±3.2 vs ISO: −28.0±3.6 A*ms*F−1, n=16 vs 17), while direct Epac activation by 8-CPT (−74±4.5 A*ms*F−1, n=12, P<0.001) led to enhancement of late If. As hypothesized, preincubation with CaMKII peptide inhibitor AIP (1 μmol/L, 10 min) significantly reversed the ISO- and 8-CPT-dependent enhancement in late If in WT myocytes (−28.7±3.4 and −24.7±3.7 A*ms*F−1, respectively) as well as in the PDE2- deficient mice (−30.5±4.5 A*ms*F−1, n=17). Additionally, using confocal microscopy (Fluo3 AM), we studied the diastolic SR Ca-leak, which is known to be induced by CaMKII-dependent phosphorylation of ryadne-receptor. Preliminary results show that the low-frequency Ca2+ sparks in late If current in late If in TG mice (−30.5±4.5 A*ms*F−1, n=17), Additionally, using confocal microscopy (Fluo3 AM), we studied the diastolic SR Ca-leak, which is known to be induced by CaMKII-dependent phosphorylation of ryadne-receptor. Preliminary results show that the low-frequency Ca2+ sparks in late If current in TG mice (−30.5±4.5 A*ms*F−1, n=17), Additionally, using confocal microscopy (Fluo3 AM), we studied the diastolic SR Ca-leak, which is known to be induced by CaMKII-dependent phosphorylation of ryadne-receptor. Preliminary results show that the low-frequency Ca2+ sparks in late If current in TG mice (−30.5±4.5 A*ms*F−1, n=17), Additionally, using confocal microscopy (Fluo3 AM), we studied the diastolic SR Ca-leak, which is known to be induced by CaMKII-dependent phosphorylation of ryadne-receptor. Preliminary results show that the low-frequency Ca2+ sparks in late If current in TG mice (−30.5±4.5 A*ms*F−1, n=17), Additionally, using confocal microscopy (Fluo3 AM), we studied the diastolic SR Ca-leak, which is known to be induced by CaMKII-dependent phosphorylation of ryadne-receptor. Preliminary results show that the low-frequency Ca2+ sparks in late If current in TG mice (−30.5±4.5 A*ms*F−1, n=17), Additionally, using confocal microscopy (Fluo3 AM), we studied the diastolic SR Ca-leak, which is known to be induced by CaMKII-dependent phosphorylation of ryadne-receptor. Preliminary results show that the low-frequency Ca2+ sparks in late If current in TG mice (−30.5±4.5 A*ms*F−1, n=17), Additionally, using confocal microscopy (Fluo3 AM), we studied the diastolic SR Ca-leak, which is known to be induced by CaMKII-dependent phosphorylation of ryadne-receptor. Preliminary results show that the low-frequency Ca2+ sparks in late If current in TG mice (−30.5±4.5 A*ms*F−1, n=17). Thus, the low-frequency Ca2+ sparks in late If current in TG mice (−30.5±4.5 A*ms*F−1, n=17) and the high-frequency Ca2+ sparks in late If current in WT myocytes (−28.7±3.4 and −24.7±3.7 A*ms*F−1, respectively) as well as in PDE2- deficient mice (−30.5±4.5 A*ms*F−1, n=17) and the high-frequency Ca2+ sparks in late If current in WT myocytes (−28.7±3.4 and −24.7±3.7 A*ms*F−1, respectively).
Comparison of ARNI with ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF).

Methods: We examined clinical outcomes in 8399 patients during a median follow-up of 27 months according to history of diabetes and glycaemic status in the remainder, according to baseline hemoglobin A1c (HbA1c): normoglycaemia = <6.0%; pre-diabetes = 6.0–6.4% and diabetes ≥ 6.5%. Cox regression models were used to adjust for known predictors of risk: age, sex, race, HF duration, NYHA class, LVEF, heart rate, KCCQ score, BMI, eGFR, NTproBNP, ischemic etiologies, prior MI, stroke, and AF.

Results: At baseline, 2907 patients (35% of the total) had a history of diabetes, an additional 1106 patients (13%) had undiagnosed diabetes, and 2103 (25%) had pre-diabetes. Compared to the 2158 patients (26%) with normoglycaemia, the adjusted hazard ratio (HR) for the primary composite outcome of CV mortality or HF hospitalization (CV/HF) was: 1.61 (95% CI 1.41–1.83) for known pre-diabetes. Compared to the 2158 patients (26%) with normoglycaemia, an additional 1106 patients (13%) had undiagnosed diabetes, and 2103 (25%) had diabetes ≥ 6.5%. Cox regression models were used to adjust for known predictors of risk: age, sex, race, HF duration, NYHA class, LVEF, heart rate, KCCQ score, BMI, eGFR, NTproBNP, ischemic etiologies, prior MI, stroke, and AF.

Conclusion: In patients with H-REF, dysglycaemia is very common and compared to normoglycaemia, pre-diabetes, as well as diabetes, is associated with a higher risk of adverse cardiovascular outcomes. LCZ696 was similarly effective across the glycaemic spectrum.

P5032 | BEDSIDE
Respiratory syncytial virus infection is associated with acute decompensated heart in adult patients with congestive heart failure

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Respiratory syncytial virus (RSV) has been documented as an increased case of severe respiratory infections in adults. Few studies have examined RSV infections in adults with chronic heart diseases.

The aim of this study was to evaluate the occurrence of RSV infection among chronic heart disease patients, their clinical characteristics and outcomes. During RSV season we assessed RSV respiratory illnesses in prospective cohorts of adults patients presenting with congestive heart failure (CHF). RSV infection was confirmed by Real-Time PCR technique performed on respiratory samples of outpatients and those who were hospitalized because acute decompensated heart failure.

A total of 99 patients, median age 57 years, were enrolled in a prospective surveillance including 45 outpatients recruited from the CHF ambulatory, and 52 inpatients, with a history of exacerbation of underlying heart disease without an episode of acute heart failure. RSV infection was identified in 15 (15.2%) patients, with two-thirds having ID and half anaemia. Importantly, ID, in particular AbsID, with two-thirds having ID and half anaemia. Importantly, ID, in particular AbsID, or ferritin 100–300mcg/l with a Tsat <30% were more frequent in hospitalised patients than in outpatients (77.7% vs 36.8%). In addition, RSV viral load analysis was significantly higher in hospitalized patients samples (2.8 log10 copies/mL) when compared to outpatients infections (1.9 log10 copies/mL). The results of this pilot study suggest that RSV is a very frequent cause of infection in adult patients with heart disease. RSV can cause more severe disease among CHF patients and those with higher viral load are at higher risk of acute decompensated heart failure and hospitalization.

RSV infection surveillance should be intensified among CHF patients during seasonality. High-risk patients for hospitalization should be evaluated by RSV test. An effective RSV vaccine or antiviral may offer benefits for these patients.

P5034 | BEDSIDE
High prevalence of iron deficiency in heart failure with preserved ejection fraction

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Introduction: Anaemia and iron deficiency (ID) are common comorbidities present in patients with heart failure with reduced ejection fraction (HF-REF) and treatment with iron replacement for those with ID has shown to improve survival, quality of life, and symptoms of HF. The present study aimed to determine the prevalence of ID and iron status in a large cohort of adults with chronic heart failure (CHF).

Methods: A total of 774 patients, 492 (64%) had HF-REF and 282 (36%) had HF-PEF. Patients with HF-PEF were older and more likely to be female those with HF-REF: 73.8yrs vs 66.7yrs respectively (p<0.001), 45% vs 22% female (p<0.001). Overall, 440 patients (57%) had ID, of whom 265 (34%) had AbsID and 175 (23%) RelID. Patients with HF-PEF had a higher prevalence of ID compared to those with HF-REF: 64% vs 53% respectively (p<0.003). Among patients with HF-PEF 41% had AbsID compared with 30% of those with HF-REF (p<0.004). There were similar proportions of patients with ReID in the two groups (HF-PEF 23% and HF-REF 22%, p=0.83).

Conclusions: ID and anaemia are highly prevalent among patients with HF-PEF with two-thirds having ID and half anaemia. Importantly, ID, in particular AbsID, of ID and iron status in a large cohort of adults with chronic heart failure (CHF).
was commonly present even in the absence of anaemia, in both groups of patients with HF. Treatment of ID has been shown to improve morbidity in patients with HF-REF, whether this also applies for patients with HF-PEF needs urgent evaluation.

P5035 | BEDSIDE
Time-related cumulative incidence of congestive heart failure after childhood cancer treatment: a DCOG LATER study
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Introduction: Cardiac events (heart failure (HF), cardiac ischemia, valvular disease, pericarditis and arrhythmia) are among the most serious late effects after childhood cancer treatment. HF is the most common cardiac event that develops even decades after treatment. Known cardiotoxic treatments are anticholinergic and radiation where the heart was in the field.

Purpose: To determine the incidence of and associated risk factors of HF after childhood cancer treatment, we performed a large nationwide cohort study in childhood cancer survivors.

Methods: In our nationwide cohort (n=6,168) of 5-year childhood cancer survivors, in the Netherlands (diagnosed between 1963 and 2002), questionnaires were sent to identify patients with HF and medical records were used to further define HF. The outcome of HF was classified as symptomatic HF needing medication, cardiac device implant, heart transplant or fatal HF. We used a competing risk analysis to calculate the cumulative incidence of HF (death due to other causes was a competing risk) and a multivariable Cox regression model for the risk factors analysis.

Results: We collected cardiac information of 5,307 (86.0%) 5-year survivors (of which 611 (9.9%) were deceased). Of the other survivors, 521 (8.4%) refused participation and 340 (5.5%) were lost to follow-up. After a median follow-up of 20.3 years (5–50.4) and at a median attained age of 27.9 years (6.8–65.2), 106 survivors developed HF (2.0%); of these HF patients, 11 survivors needed a cardiac device, 8 survivors needed a heart transplant and 22 survivors died due to HF.

The cumulative incidence of HF in all survivors at the age of 20 years was 0.7% (95% CI: 0.69%–0.70%), at the age of 30 was 2.0% (99.9%-2.01%), at the age of 40 was 3.6% (3.5%-3.62%) and at the age of 50 was 5.9% (5.85%-6.03%). Contributing risk factors for the development of HF were treatment with anthracyclines (Hazard Ratio (HR): 11.6; 95% CI: 6.3–21.7), mitoxantrone (4.1; 2.0–8.3), high dose cyclophosphamide (> 10,000 mg/m²) (2.0; 1.2–3.3) and radiation to the heart (1.6; 1.0–2.5).

Conclusion: Survivors of childhood cancer have increasing risk of developing HF with time, starting even from young age. Especially those survivors treated with anticholinergic, mitoxantrone, cyclophosphamide and radiation to the heart. Our study has a high percentage of follow-up, and there for a low risk of bias.

Health care professionals need to be aware of these findings, and recognize the risk of developing HF in young people, even years after their childhood cancer treatment.

HYPERTENSION AND COMORBIDITIES: A CHALLENGE OF TREATMENT

P5037 | BEDSIDE
Effect of Diosmin treatment on left ventricular systolic function in hypertensive patients with chronic venous insufficiency
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Introduction: Diosmin (D) has a demonstrated activity as venotonic agent. Although flavonoids have been studied for more than 50 years, there is no data explaining the effect on left ventricular function. No study has identified so far the role of D treatment over the left ventricular systolic function in patients with chronic venous insufficiency (CVI) and arterial hypertension.

Purpose: The aim of the study was to determine whether Diosmin treatment recommended for CVI influence left ventricular ejection fraction (EF) in patients with arterial hypertension.

Methods: Our 4-year study included 501 patients, aged 40–80, admitted to our cardiology department. They were all diagnosed with essential arterial hypertension and divided according to CEAP classification. We assessed by echocardiography the left ventricular mass index (LVMI) and EF. The LVMI threshold was 95 g/m² in women and 115 g/m² in men. We divided the patients into two groups: one group with normal left ventricular mass index (LVMI) (n=124) and one group with pathologic left ventricular mass index (LVMI) (n=377). Each group was divided into two subgroups according to initiation of D treatment (500 mg twice per day): 1) LVMI - D (n=78); 2) LVMI - D + n=46); 3) LVMI - D - (n=250); 4) LVMI + D (n=127). The groups were homogeneous according to age (62±10, 64±9, 63±9, 62±10 years) and body mass index (34±4.6, 35±4.5, 35±7.5 kg/m²) and in those without (log rank, p=0.001). The unadjusted and adjusted * ORs (95% CI) of mortality were 1.61 (1.51–1.71) and 1.64 (1.51–1.78).

Conclusion: These data support that diabetes remains as a strong independent predictor of mortality in patients with systolic heart failure despite the lack of a difference in EF. Ischemic heart disease was highly prevalent in heart failure patients with diabetes, but only 50% of them were revascularised.

* Adjusted for diabetes, gender, age, duration of heart failure, weight, blood pressure, ischemic heart disease, co-morbidities, revascularisation, eGFR class, Hb class, pharmacological treatments.

P5038 | SPOTLIGHT
Sitagliptin and risk of hypertension in patients with type 2 diabetes mellitus: meta-analysis of randomized trials
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Background: Recent reports of sitagliptin use have raised questions about whether the sitagliptin have beneficial effect on blood pressure of type 2 diabetes mellitus (T2DM) patients. The aim of this meta-analysis was to evaluate the effect of sitagliptin on hypertension.

Methods: We searched PubMed, MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, and product information sheets for randomized controlled trials, systematic reviews, and meta-analyses published through December 2012. Studies were included if they were randomized controlled trials of sitagliptin vs placebo or active comparator for T2DM patients also monitored hypertension. Relative risks of hypertension events were estimated using a fixed-effects meta-analysis.

Results: We analyzed 8 randomized controlled trials. Compared with placebo therapy and control therapy, sitagliptin had no significant increase in risk of hy-
Results: as isoprostanes and paraoxonase-1 (PON-1).

We also evaluated some markers of oxidative stress such as soluble vascular adhesion protein-1 (sVCAM-1), soluble intercellular adhesion molecule-1 (sICAM-1). We also evaluated some markers of oxidative stress such as high-sensitivity C-reactive protein (Hs-CRP), tumor necrosis factor-alfa (TNF-alfa), metalloproteinase-2 (MMP-2) and -9 (MMP-9), dothelial damage such as.

We enrolled 151 hypertensive patients with mild systolic blood pressure (SBP) ≥ 140 and < 180 mmHg and diastolic blood pressure (DBP) > 90 and < 105 mmHg, type 2 diabetes mellitus, normocholesterolemia. Patients were ran- domised to losartan/placebo or to losartan/barnidipine, 20 mg/day, both in addition to losartan, 100 mg/day, for 6 months. We assessed BP monthly, in addition, pa- tients underwent ambulatory blood pressure monitoring (ABPM) at baseline, and at the end of the study. We also collected blood sample to assess: fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), some adipocytokines linked to endothelial damage and oxidative stress in diabetic and hypertensive patients.

To evaluate the effects of barnidipine or lercanidipine, in addition to
corticosteroids in patients with hypertension and diabetes mellitus: a systematic review and meta-analyses

The effect of mineralocorticoid receptor antagonists in patients with hypertension and diabetes mellitus: a systematic review and meta-analyses

Results: We identified 9 eligible studies for analysis, involving a total of 486 pa- tients and consisting of 5 randomized placebo-controlled trials, 3 randomized active-drug-controlled trials, and 1 single-arm observational study. In placebo- controlled trials, the mean difference between patients receiving MRA and the place- bo group in office systolic and diastolic BP was −9.4 (95% confidence inter- val [CI], −12.9 to −5.9) and −3.8 (95% CI, −5.5 to −2.2) mmHg, respectively. Subgroup analyses, considering study type, age, baseline office SBP, and length of follow-up, did not show any difference from the main analysis in the SBP-lowering effects of MRA between the groups. In terms of safety, MRA demonstrated a mild increase in serum potassium (0.4 mEq/L; 95% CI, 0.3 to 0.5 mEq/L).

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In our study, the SBP reduction with barnidipine + losartan was significant (p < 0.01) when compared to losartan alone (−9.4±1.5 mmHg vs −4.8±1.7 mmHg, respectively), and the difference was statistically significant (p = 0.019).

P5040 | BEDSIDE

Barnidipine compared to lercanidipine in addition to losartan on endothelial damage and oxidative stress parameters in patients with hypertension and type 2 diabetes mellitus

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Background: Hypertension causes endothelial damage revealed by higher levels of inflammatory markers.

Purpose: To evaluate the effects of barnidipine or lercanidipine, in addition to losartan, on some markers linked to endothelial damage and oxidative stress in patients with hypertension and type 2 diabetes mellitus.

Methods: We enrolled 151 hypertensive patients with mild systolic blood pres- sure (SBP) > 140 and < 180 mmHg and diastolic blood pressure (DBP) > 90 and < 105 mmHg, type 2 diabetes mellitus, normocholesterolemia. Patients were ran- domised to losartan/placebo or to losartan/barnidipine, 20 mg/day, both in addition to losartan, 100 mg/day, for 6 months. We assessed BP monthly, in addition, pa- tients underwent ambulatory blood pressure monitoring (ABPM) at baseline, and at the end of the study. We also collected blood sample to assess: fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), some adipocytokines linked to end- thelial damage such as high-sensitivity C-reactive protein (hs-CRP), tumor necrosis factor-alpha (TNF-alfa), metalloproteinase-2 (MMP-2) and -9 (MMP-9), soluble vascular adhesion protein-1 (sVCAM-1), soluble intercellular adhesion protein-1 (sICAM-1). We also evaluated some markers of oxidative stress such as isoprostanes and paraoxonase-1 (PON-1).

Results: One hundred and forty-three patients completed the study. Both barni- dipine and lercanidipine resulted in a significant reduction in SBP and DBP, even if the blood pressure reduction obtained with barnidipine + losartan was greater than that obtained with lercanidipine + losartan (p < 0.05). Data recorded with ABPM showed a similar trend. Barnidipine + losartan reduced the levels of Hs-CRP and TNF-alfa (p < 0.05 vs baseline and vs lercanidipine + losartan). There were no significant differences between the two treatments on the levels of MMP-2 and -9. Barnidipine + losartan significantly reduced the levels of sVCAM-1 and sICAM-1, both compared to baseline and to lercanidipine + losartan (p < 0.05 for both). The levels of isoprostanes were reduced by barnidipine + losartan (p < 0.05 vs baseline and vs lercanidipine + losartan), while the levels of PON-1 remained unchanged.

Conclusions: Other than giving a greater reduction of blood pressure, barnidip- ine + losartan gave an improvement of some parameters linked to endothelial damage and oxidative stress in diabetic and hypertensive patients.
Results: For primary prevention (38 trials, 283529 patients), all antihypertensive agents, except alpha-blocker, outperformed placebo in preventing any stroke events. By using probability ranking for mixed treatment comparisons, angiotensin receptor blocker may be the most preferred agent for primary prevention of stroke. For secondary prevention (10 trials, 40496 patients), only diuretics significantly decreased the 0.12 absolute risk reduction of (95% confidence interval 0.061–0.170; p=0.00012) for any stroke.

Conclusions: Evidence from randomized controlled trials supports the use of antihypertensive agents in lowering blood pressure for the primary prevention of stroke and secondary prevention of vascular events in patients with previous stroke. Although angiotensin receptor antagonist and diuretics may be preferred strategies for primary and secondary prevention, respectively, the final achieved BP may be the key element in the effective risk reduction for primary prevention of stroke.

P507 | BEDSIDE
Impact of a custom-made mandibular repositioning device (MRD) on blood pressure in obstructive sleep apnea (OSA) patients noncompliant with continuous positive airway pressure (CPAP)
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Background: Prevalence of arterial hypertension (HTN) is high in pts with Obstructive Sleep Apnea (OSA). Laboratory , Nice; 9 University Hospital of Poitiers, Poitiers, France

Purpose:

Prevalence of HTN is high in pts with OSA and noncompliance with CPAP. The MRD may improve blood pressure in OSA pts with HTN.

Methods: We randomized n=12 SHRs in 3 groups: group 1 received MANP 300 pmol/kg/min, group 2 MANP 100 pmol/kg/min and group 3 received vehicle (saline 0.9%). We infused MANP/vehicle for 75 in anesthetize rats. At the end of the protocol we collected blood and urine. We measured BP using inraventricular catheter, and glomerular filtration rate (GFR) using the clearance of inulin. Non-parametric one-way analysis of variance (ANOVA) was used for comparison.

Results: MANP significantly reduced BP through GC-A activation as demonstrated by the marked increase in urinary cGMP excretion (UcGMPV). Importantly, despite the reduction in BP, MANP increased GFR and showed a trend for increase in natriuresis (UNaV) with a reduction of distal fractional sodium reabsorption (DFFRNa) in the treated group. These results support MANP as BP lowering and renaling enhancig peptide. Further studies are needed to evaluate the long-term effects of MANP in hypertension.
5078 | BEDSIDE

Lack of evidence that frailty modifies the positive impact of antihypertensive treatment in very elderly people

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Background: Treatment of hypertension with antihypertensive medication has been shown to reduce stroke, cardiovascular events and mortality in those aged 80 and over, but there is concern that such treatment may not be appropriate in frail elderly individuals. To investigate whether there is an interaction between the effect of treatment for hypertension and frailty in older adults, we calculated a frailty index for all available participants from the Hypertension in the Very Elderly trial (HYVET) study, a double-blind, placebo controlled study of antihypertensives in people with hypertension aged 80 and over, and obtained frailty adjusted estimates of the effect of treatment with antihypertensive medication on risk of stroke, cardiovascular events and mortality.

Methods and findings: Participants in HYVET were randomly assigned 1:1:1 to active treatment with indapamide sustained release (SR) 1.5 mg 2 instead of placebo 2-4 mg or matching placebo. The FI was calculated at entry, based on fifty seven potential contributors. The distribution of FI was similar to that seen in population studies of adults age 80 years and over (median FI=0.11; IQR 0.09-0.24). Cox regression was used to assess the impact of FI at entry on the study on subsequent risk of stroke, total mortality and cardiovascular events. Models were stratified by region of recruitment. Two models were adjusted for age at entry. All-cause mortality was the outcome and the frailty index was included as a term for a possible interaction between treatment for hypertension and frailty. Cox regression was used to compare the A15% and A25% outcomes on baseline and follow-up with bilateral Wilcoxon test on matched pairs.

Conclusions: There is no evidence of an interaction between effect of treatment for hypertension and frailty as measured by the FI in HYVET participants. The FI provided a formula for the treatment effect as a function of FI. For all three outcomes, the effect of treatment for hypertension and frailty in older adults, we calculated a frailty index for all available participants from the HYVET study, a double-blind, placebo controlled study of antihypertensives in people with hypertension aged 80 and over, and obtained frailty adjusted estimates of the effect of treatment with antihypertensive medication on risk of stroke, cardiovascular events and mortality.

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ever, it is unknown what type of drugs can effectively delay the enlargement of smAAA. Preclinical studies suggest that angiotensin II induces aortic aneurysm formation that is inhibited by angiotensin II receptor blocker (ARB). In a small cohort study, ARB slowed the rate of aortic-root dilation in young patients with Marfan’s syndrome. Thus, ARB may be useful to slow down the enlargement of smAAA. We, thus, examined the effects of ARB, candesartan, on the growth rate of smAAA in comparison with a common anti-hypertensive drug, amiodipine, a calcium channel blocker.

Methods: In this randomized, multicenter and prospective study (UMIN #2216), patients with presurgical smAAA (n=128) and inoperative AAs (n=4) (mean AAA diameter, 3.9±0.7 mm) were assigned to either candesartan (n=67, CAN) or amiodipine (n=64, AML) group with 5 minimization factors (statin use, smoking, age, gender, renal function). Primary endpoint was the % changes in AAA diameter at 24 mo of the follow-up measured by plain multislice computed tomography and its difference between the two groups was evaluated based on the mixed-effect model repeated measure. Secondary endpoint was the incidence of time to surgical repair that was compared using multivariate Cox regression analysis by intention to treat.

Results: There was no statistical difference in the blood pressure time course between the CAN and AML (p=0.800) groups. The % change at 24 mo of AAA diameter did not differ between the CAN and AML groups (8.4% for CAN (95% CI, 6.23 to 10.59%) and 6.5% for AML (95% CI, 3.65 to 9.43%)) and the difference of 1.87% (95% CI, -1.13% to 5.87%) was not significant. In the AML group, the use of b-blocker had no additional effects on smAAA growth and incidence of surgery.

Conclusion: Candesartan and amiodipine had comparable efficacies on both blood pressure and the growth rate of AAA size.

5082 | BENCH

Chronic treatment with orally active angiotensin-(1-7) formulation decrease oxidative damage and improve hemodynamic parameters in spontaneously hypertensive rats

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Background: Renin-angiotensin (RAS) system has been implicated in the pathogenesis of cardiovascular diseases. The cardioprotective Angiotensin-(1–7)/Mas receptor axis has an important role in cardiovascular regulation once that Ang-(1–7) exerts beneficial effects mainly due to antihypertensive and antioxidative properties.

Purpose: To assess the effect of a chronic treatment with orally active formulation of Angiotensin-(1–7) (HPc/CD/Ang-(1–7)) in cardiac oxidative stress and hemodynamic parameters in SHR.

Methods: Male spontaneously hypertensive rats (SHR) (15 weeks) treated by gavage with tap water (C) or HPc/CD/Ang-(1–7) (A) (30 µg/kg), once a day for 10 weeks (n=8/group). After treatment systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), and heart rate (HR) were recorded from a femural catheter (WinDaq/2Hz). At the end of hemodynamic measurements, heart cells were collected for biochemical assays: cardiac lipid peroxidation by chemiluminescence (CL) initiated by t-BOOH, superoxide dismutase (SOD) antioxidant enzyme activity analysis and superoxide anion (O2-) analysis.

Results: Chronic treatment with the orally active Ang-(1–7) reduces SAP, DAP, MAP. HR in treated group (in C and A respectively; SAP=216.2±5.09 and 205.4±4.15, DAP= 147±1.90 and 134.6±3.17, MAP=180.2±3.48, and 170.4±2.55). In SHR compared to Ang-(1–7) chronic treatment (SOD=19,29±0,67 and 18,33±1,42 U/mg protein; p<0.05), we revealed the increase of its levels in both groups, but just in telmisartan subgroup oxidative changes were statistically reliable (Δ=+3,47±1,94 ng/ml, p<0.005 and Δ=+3,47±1,94 ng/ml, p<0.005 for telmisartan and amiodipine, respectively). IR-HOMA2 that was significantly increased in both subgroups at baseline also reliably decreased after treatment only in the first subgroup (Δ IR-HOMA2 = -1.07±0.44, p<0.001).

Conclusions: The antihypertensive treatment with telmisartan leads to IR-HOMA2 decrease and serum adiponectin level increase that can demonstrate the pathological effects of telmisartan in MS, while amiodipine doesn’t influence significantly those parameters.
60% of patients versus 38% with 2h ADP (p CI 99.4–100% p=ns). Regarding efficacy, 1h-algorithm +LOD allowed rule-out in patients. The safety was very high and comparable with both algorithms (LOD+1h-algorithm advantage of allowing rule-out after 1h and without the need of TIMI Score allowing the rule out of more than double of patients and has the obvious ad-

However the combination of LOD+1h-algorithm has a significantly higher efficacy ST -elevation MI (STEMI) has been excluded by the initial ECG, STEMI patients
dent from the hs-cTn assay used. As both strategies should only be applied once
Conclusion:
Both investigated rule-out strategies allow a safe rule-out of AMI.

In-hospital mortality rate was in the overall cohort 8.2% (STEMI: 9.1%, NSTEMI: 7.3%) and they were more likely to be female (41.3% vs. 31.6%). More fre-

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, selec-
tions and choices 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) T at presenta-
tion) in combination with hs-cTnT 1h-algorithm versus 2h-ADP rule-out strategy (0.0–1h levels ≤99th percentile, no significant ECG changes and TIMI Score of <1).

Methods: In a prospective international multicentre study design enrolling 1697 patients presenting with suspected AMI to the emergency department, the final diagnosis of AMI was adjudicated by two independent cardiologists using all available clinical information including serial hs-cTnT concentrations. Safety was quantified as the negative predictive value (NPV) for AMI in the rule-out zone of the respective rule-out strategies. Efficacy was quantified as the per-
centage 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 says (hs-cTnT Roche: LOD ≤5ng/l; 1 algorithm: 0.0–12ng/l and 0.0–1h–3ng/l and 99th percentile ≤14ng/l; hs-cTnT Abbott: LOD ≤2ng/l; 1h algorithm 0.0 ≤5ng/l and 0.0–1h–2ng/l; 99th percentile ≤26.2ng/l) to ensure that findings are indepen-
dent from the hs-cTn assay used. As both strategies should only be applied once S2 TElevation (TIMI) has been established by the initial ECG, STEMI patients were excluded from the analysis.

Results: Acute myocardial infarction was the final diagnosis in 16% of pa-
tients. The safety was very high and comparable with both algorithms (LOD+1h- Algorithm NPV 99.9%, 95% CI 99.5–100% versus 2h ADP: NPV 100%, 95% CI 99.4–100% p=ns). Regarding efficacy, 1h-algorithm +LOD allowed rule-out in 60% of patients versus 38% with 2h ADP (p <0.001). Using hs-cTnT, the safety was ven-

Results: During the follow-up period, 31 participants (5.5%) died from cardiovas-
cular events. In analyses adjusting for conventional risk markers, NT-proBNP, H-
FABP levels, and GRACE score were significantly associated with the incidence of cardiovascular death (odds ratio [OR]; 2.23, 95% confidence interval [C.I.], 1.24 to 4.03; OR; 2.92, C.I.: 1.44 to 5.90, and OR; 1.02, C.I.: 1.01 to 1.02 p<0.01, respectively). The AUC of NT-proBNP, H-FABP levels, and GRACE score were 0.76 (0.66–0.88), 0.73 (0.62–0.85) and 0.79 (0.68–0.90), respectively. The combi-
nation of NT-proBNP and H-FABP improved the AUC to 0.80 (0.67–0.83). Adding NT-proBNP and H-FABP to GRACE improved the area under the curve from 0.80 to 0.84 (p<0.01).

Conclusions: For assessing risk in ACS patients, the GRACE score is still a useful risk score for ACS patients even in the drug eluting stent era. Measur-
ing NT-proBNP and H-FABP provides useful prognostic information equal to the GRACE risk score. Biomarkers result in a high risk classification rate in the ACS cohort, demonstrating the benefit of prognostic value.

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808 | BEDSIDE
Kinetics of high-sensitive cardiac troponin T and I differ in patients with ST-segment elevation myocardial infarction treated by primary coronary intervention
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Purpose: Cardiac biomarkers including troponins are the cornerstone of the bi-

ological definition of acute myocardial infarction (AMI). New high-sensitive cardiac troponin T (hs-cTnT) as well as I (hs-cTnI) raises concerns because of their un-

erstanding of the test results following the presentation of their 2019 research.

Aims: This study aims to compare kinetics of creatine kinases (CK), hs-cTnT and hs-cTnI in patients with AMI treated by percutaneous coronary intervention (PCI). We prospectively studied 106 consecutive patients admitted in our institution for AMI and treated with PCI. We evaluated for all the patients si-

tant release of CK, hs-cTnT and hs-cTnI (Abbott and Siemens). Modelling of kinetics was realized using mixed effects with cubic splines.

Results: Kinetics of markers showed a first peak at 10.7h (8.0–12.0) for CK, 11.8h (10.4–13.1) for hs-cTnT (Roche) and two different hs-cTnI (Abbott and Siemens). Modelling of kinetics was realized using mixed effects with cubic splines.

Conclusions: Kinetics of hs-cTnT and hs-cTnI differ significantly with a linear de-
crease regarding the hs-cTnI contrasting with a biphasic shape curve for hs-cTnT.
Epidemiology of cardiogenic shock in French reanimations: incidence, etiologies, outcome and evolution on 15 years (a report from the CubRea database)

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Rationale: Most of data reporting epidemiology of CS concern patients with acute myocardial infarction admitted in intensive care unit of cardiology (ICUC). However, CS patients managed in Reanimation have often multiforman origin and seem to have different characteristics and outcome.

Aim: The aim of study is to analyse incidence, etiologies, outcome and evolution on 15 years of CS managed in reanimation in the French hospital setting.


Among 303 314 hospital stays, 17 494 (5.8%) were CS. The patients were managed in 60% of cases in university centers. Mean age of patients was 64±17.0. Men accounted for 11047 (63.1%) hospital stays. Mean IGS II was 62.0±24.3. Among CS, only 535 (3.06%) were acute myocardial infarctions whereas 2685 (15.3%) were cardiac arrests and 858 (4.9%) were drug intoxications.

Mechanical ventilation was required in 12967 (74.1%) of cases, inotropic drugs in 62.0±24.3. Among CS, only 535 (3.06%) were acute myocardial infarctions whereas 2685 (15.3%) were cardiac arrests and 858 (4.9%) were drug intoxications.

Conclusion: It is the first study reporting the prevalence, determinants and prognostic factors of cardiogenic shock patients managed in reanimation. The etiologies of these patients are different from those of ICUC patients. These patients are very critically ill, need often hemodynamic and ventilator supports and their mortality is high. However over the 15-year period, even if these patients are more and more critically ill, early mortality decreased.

Blood hyperosmolality and mortality in patients after an acute coronary syndrome: how does dehydration affect prognosis?

S. Fernandez Santos1, M. Pascual Izco1, S. Briongos Figueroa2, T. Segura De La Caí3, G. Alonso Salinas1, A. Camino Lopez1, M. Jimenez Mena1, M. Sammartin Fernandez1, J.L. Zamorano Gomez1, 1University Hospital Ramon y Cajal, Department of Cardiology, Madrid, Spain; 2University Hospital Infanta Leonor, Madrid, Spain

Background: Electrolyte and osmolality disturbances are common in patients admitted for acute coronary syndrome (ACS). Blood hyperosmolality development and its influence on the prognosis of these patients has not yet been studied. The aim of the study was to assess how dehydration affects outcomes of patients after ACS.

Methods: We created a registry of consecutive patients admitted due to ACS in Cardiac Care Unit (ACU) of our hospital for 18 months. Peak blood osmolality value during hospitalization was retrospectively obtained in these patients.

Results: Of a total of 397 patients with ACS, third suffered ST-elevation ACS. The mean age was 65.2 years, 77.1% were men, 56.8% and 12.3% of patients were diagnosed with previous kidney failure. During long term follow up 88 patients died (22%). Total population was divided into two strata according to peak osmolality during hospitalization: peak osmolality <290mM/l (94%) (normal range 250–290mM/l) and >290mM/l (6%). In-hospital mortality, all-cause mortality and cardiovascular (CV) mortality after a follow-up of 52±24 months, were significantly higher in patients with peak osmolality> 290mM/l (p<0.001). In an univariate analysis it was strongly associated with diuretic use and development of renal failure. After adjusting for potential confounders (age, sex, history of renal insufficiency, renal failure development, diuretic therapy or need for renal replacement therapy), blood hyperosmolality during hospitalization (>290mM/l) remained an independent predictor of all-cause, CV and in-hospital mortality at short and long term.

Conclusions: Increasing CI levels were associated with increased short-term mortality in CS complicating acute myocardial infarction. Rise of CI at day 3 is associated with bleeding, acute kidney injury and myocardial injury.

Iron metabolism in acute myocardial infarction complicated by cardiogenic shock - a biomarker subsyndrome of the IABP-SHOCK II-trial


Background: Cardiac dysfunction in acute myocardial infarction complicated by cardiogenic shock may be caused by reactive oxygen species (ROS) with further deleterious vascular effects. In acute coronary syndromes (ACS) no data exists on the prognostic impact of CI and further iron metabolism.

Methods: In 185 patients, blood samples collected at baseline and after two days were analyzed. Immediately after sample drawing, the blood was centrifuged and the serum frozen (−87°C). CI levels were measured using a modified bleomycin detectable iron assay. Furthermore levels of free hemoglobin (fHb), total serum iron (SI), ferritin and transferrin saturation (TS) were assessed.

Results: As shown in table 1 significant different levels between survivors and non-survivors at 30 days for CI, TF and TS were observed. Patients with CI levels in the highest quartile had a worse outcome in Kaplan-Meier-analysis (Day 1: HR 1.91 [1.11–3.31], p=0.005; Day 3: HR 2.15 [1.06–4.34], p=0.01). After multivariable adjustment baseline CI remained an independent predictor of 30-day mortality (HR per 10LQG 1.25 [1.25–3.47], p=0.005) together with age, development of acute kidney injury and bleeding events on days 1 and 2. Predictors of CI levels on day 3 were baseline CI, bleeding events, acute kidney injury and baseline troponin T.

Conclusions: Increasing CI levels were associated with increased short-term mortality in CS complicating acute myocardial infarction. Rise of CI at day 3 is associated with bleeding, acute kidney injury and myocardial injury.

Blood hyperosmolality and mortality in patients after an acute coronary syndrome: how does dehydration affect prognosis?

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Conclusions: Increasing CI levels were associated with increased short-term mortality in CS complicating acute myocardial infarction. Rise of CI at day 3 is associated with bleeding, acute kidney injury and myocardial injury.
5092 | BEDSIDE
Urinary output predicts survival in patients undergoing extracorporeal membrane oxygenation following cardiovascular surgery
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Background: An optimized risk evaluation in patients undergoing extracorporeal membrane oxygenation (ECMO) support may have important implications both for evaluating further therapeutic options and for clinical judgment of prognosis. We therefore analyzed the prognostic significance of urinary output (UO) within 24-hour after ECMO initiation on mortality in adult patients undergoing venoarterial ECMO support following cardiovascular surgery. We further aimed to refine established risk prediction models by implementation of UO.

Methods: We prospectively included 240 patients undergoing veno-arterial ECMO therapy following cardiovascular surgery at a university-affiliated tertiary care center into our registry.

Results: In the univariable Cox regression analysis 24-hour urinary output was the strongest predictor of outcome among renal function parameters with a HR per 1-SD of 0.55 (95% CI 1.04-0.71; P=0.001) for 30-day mortality and for long-term mortality with a HR per 1-SD of 0.63 (95% CI 0.53-0.76; P<0.001). UO lead to a substantial improvement in the C-statistic of the SAPS3 score for 30 day mortality (SAPS3: 0.52 vs. SAPS3 & UO: 0.64; P=0.003) and for long-term mortality (SAPS3: 0.54 vs. SAPS3 & UO: 0.63; P=0.01). An improvement in individual risk stratification with combined assessment of SAPS3 score and UO was shown to lead to a substantial improvement in the C-statistic of the SAPS3 score for 30 day mortality (SAPS3: 0.52 vs. SAPS3 & UO: 0.64; P=0.003) and for long-term mortality (P<0.001).

Conclusion: We identified UO as a strong and easily available predictor of mortality in patients undergoing ECMO therapy following cardiovascular surgery.

5093 | BEDSIDE
Clinical impact of delirium and antipsychotic therapy on patients admitted to the coronary care unit
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Purpose: The impact of delirium on patients admitted to the coronary care unit (CCU) has not been well characterized. Moreover, the safety of short-term antipsychotic therapy remains controversial. This study aimed to evaluate (1) the association between delirium and mortality (2) the association between antipsychotic therapy and a prolonged QTc interval and ventricular arrhythmia.

Methods: A pre-study Confusion Assessment Method (CAM)–ICU criteria was implemented in screening 11,097 consecutive patients admitted to a referral CCU from 2004 to 2013. Death status was prospectively ascertainment.

Results: The incidence of delirium was 8.5%. Delirium increased the risk of in-hospital (adjusted OR 1.45, 95% CI 1.06–2.01; P=0.02) and 1-year mortality (adjusted HR 1.46, 95% CI 1.31–1.61; P<0.001), SAPS II (44.49 vs. 41.49; P=0.001), and for long-term mortality (SAPS3: 0.54 vs. SAPS3 & UO: 0.63; P=0.01). An improvement in individual risk stratification with combined assessment of SAPS3 score and UO was confirmed by a significant improvement of the NRI with 44% for 30-day mortality (P=0.001) and 46% for long-term mortality (P=0.001) compared with the SAPS3 score alone.

Conclusion: We identified UO as a strong and easily available predictor of mortality in patients undergoing ECMO therapy following cardiovascular surgery.

5094 | BEDSIDE
The impact of multidisciplinary team approach with critical care specialist and cardiologist co-management on the clinical outcomes of cardiac intensive care unit patients
Z. Fanari1, A. Barekatian1, R. Kerzner3, S. Hammami1, W.S. Weintraub1, V. Maheshwarir1, 2Christiana Hospital, Section of Cardiology, Newark, United States of America; 3Christiana Hospital, Section of Pulmonary & Critical Care Medicine, Newark, United States of America

Background: There is increased complexity of patients’ care in intensive care units that has motivated the involvement of critical care trained physicians as a part of multidisciplinary approach in medical, surgical and neurological ICUs. Multidisciplinary care has been less common in cardiac care units (CCUs), however, no evidence-based multidisciplinary team approach with a critical care specialists and cardiologist co-management style will impact the clinical outcomes of CCU patients.

Methods: A formal protocol was implemented starting July 2012 in a hospital where a multidisciplinary team approach with critical care specialist and cardiologist co-management style will impact the clinical outcomes of CCU patients.

Results: 2475 patients were included with 916 patients admitted in the 12 months before and 1516 admitted in the 12 months after intervention. Patients admitted after the intervention had a higher mortality rate expressed by a higher mean APACHE III (56.26 vs. 53.87; P<0.001), SAPS II (44.49 vs. 41.49; P=0.001).

Conclusion: The implementation of a multidisciplinary team approach with an intensivist, cardiologist and a pharmacist to manage the critical care of CCU patients is associated with reduced ICU and in-hospital mortality, ICU and in-hospital LOS and duration of mechanical ventilation.

5123 | BENCH
Fresh fruit consumption in relation to mortality and incidence of vascular events among 26,000 individuals with diabetes: a 7-year prospective study
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Purpose: Although consumption of fruit is generally recommended in various health guidelines for patients with diabetes, concerns persist among both patients and healthcare professionals about the potential health risk posed by the relatively high levels of sugar contained in fruit. To date, there is little direct evidence about the associations of fresh fruit consumption with mortality and incidence of macro- and micro-vascular complications among people diabetes.

Methods: We analysed prospective data of 26,162 individuals with diabetes (about a half each for self-reported and screen-detected), but free of cardiovascular disease and cancer, who were enrolled through China Kadoshian Diabetes (CKD) Study from 10 diverse locations across China. During -7 years of follow-up, there were 2453 deaths, 7291 incident vascular events, and 956 microvascular complications (i.e retinopathy, neuropathy and nephropathy) identified through linkages with mortality and morbidity registries as well as with hospital records. Covariate-adjusted hazard ratios were calculated using Cox proportional hazard models.

Results: Overall mean age of study participants was 57 years and 28% were women. Total fruit consumption was divided into tertiles (<100g/d, 100-299g/d, >299g/d). Consumption of all fruits was associated with reduced all-cause mortality (P=0.0001), cardiovascular mortality (P=0.0001), and risk of vascular events (P=0.0001), adjusting for potential confounders including anti-diabetic treatment.

Conclusion: The overall mean age of study participants was 57 years and 28% were women. Total fruit consumption was divided into tertiles (<100g/d, 100-299g/d, >299g/d). Consumption of all fruits was associated with reduced all-cause mortality (P=0.0001), cardiovascular mortality (P=0.0001), and risk of vascular events (P=0.0001), adjusting for potential confounders including anti-diabetic treatment.

5094 | BEDSIDE
Diabetes Management: The Way to Control Atherosclerosis

Z. Fanari1, A. Barekatian1, R. Kerzner3, S. Hammami1, W.S. Weintraub1, V. Maheshwarir1, 2Christiana Hospital, Section of Cardiology, Newark, United States of America; 3Christiana Hospital, Section of Pulmonary & Critical Care Medicine, Newark, United States of America

Background: There is increased complexity of patients’ care in intensive care units that has motivated the involvement of critical care trained physicians as a part of multidisciplinary approach in medical, surgical and neurological ICUs. Multidisciplinary care has been less common in cardiac care units (CCUs), however, no evidence-based multidisciplinary team approach with a critical care specialists and cardiologist co-management style will impact the clinical outcomes of CCU patients.

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Conclusion: The implementation of a multidisciplinary team approach with an intensivist, cardiologist and a pharmacist to manage the critical care of CCU patients is associated with reduced ICU and in-hospital mortality, ICU and in-hospital LOS and duration of mechanical ventilation.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/36/suppl_1/849/434480 by guest on 07 February 2019
Conclusion: In Chinese adults with diabetes, higher consumption of fresh fruit lead extraction (15/1049=1.1%) than RVA (4/1405=0.3%).

Major transvenous lead extraction complications - occurrence and outcomes. An analysis of 1767 procedures
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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. Immediate cardio-surgical (C-S) intervention may solve the problem. The aim of our study was to evaluate the incidence of occurrence and management effect of major TLE complications (MC). Retrospective analysis of our 8-year TLE data-base.

Methods: Using conventional mechanical systems we have extracted 2963 leads in 1767 pts. Mean dwell implant time was 85.1 months. In 28 (1.6%) MC were noted. Results are presented in the table.

Cardiac tamponade determined 70% of MC. Other MC were less frequent. Pericardiocentesis with drainage was effective in 40% cases only. In 60% C-S intervention was necessary. Positive outcome was achieved in every TLE procedure. Delayed intervention resulted in 60% peri-procedural mortality. Cardiac tamponade appeared more frequently during RAA lead extraction (15/1049=1.1%) than RVA (4/1405=0.3%).

Conclusions: 1. Cardiac tamponade is the most frequent major TLE complication. 2. TLE is much more safe if performed in cardiac surgery operating theatre with trained cardiac surgeon presence. 3. Old RAA leads seem to generate higher risk of tamponade than RVA leads. 4. Use of conventional mechanical systems determines lower frequency of vascular tears comparing with other reports.

Diabetes management: the way to control atherosclerosis / Leads extraction
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Purpose: In the last few years upgrading and revision procedures became increasingly frequent and challenging procedures due probably to a dramatic increase in pacemaker and implantable cardioverter defibrillator (ICD) implantation. Some degree of venous stenosis is relatively frequent and may represent a major concern. The aim of this study was the analysis of occurrence and management effect of venous stenosis in patients undergoing major transvenous lead extraction (TLE) procedures.

Methods: We considered 177 consecutive patients admitted for system revision at our institution from January 2004 and July 2014. All patients underwent ipsilateral contrast venography. Venous obstruction was classified as significant stenosis (>75%), sub-occlusion or total occlusion, and non-significant stenosis (<75%).

Results: Venous obstruction was found in 38 (21.4%) patients: 7.9% as complete occlusion, 7.3% as near occlusion and 6.2% as significant stenosis (>75%). We found as predictors of venous stenosis the number of existing lead, in particular 3 (p=0.04) and 4 (p=0.03) existing leads, a previous cardiac resynchronization therapy with defibrillator (CRT-D) system (p=0.004) implanted and a previous cardiac surgery. All procedures were successful. Different techniques were performed to obtain venous access: 8 percutaneous transluminal vein angioplasty, 19 distal venous puncture, far from the stenosis and one lead extraction with laser technology. In 10 cases there weren’t any difficulties to advance cardiac leads across the stenosis with standard methods. Transluminal vein angioplasty was performed both in complete and near occlusion, with a 6x40 mm balloon, inflated at 8–10 atm for 5–10 minutes; no complications occurred during procedures and electrical parameters of existing leads remained stable after procedure and during follow up-period.

Conclusions: Venous obstruction is a relatively frequent finding during cardiac device revision; the number of existing leads, devices complexity and previous cardiac surgery have emerged as predictors of stenosis. Percutaneous techniques, like transluminal vein angioplasty and distal venous puncture, are safe and effective approach, allowing ipsilateral transvenous lead placement.
5147 | BEDSIDE
Cardiac device infections- survival after transvenous leads extractions procedure
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Background: Cardiac device infections (CDI) are divided into infections of the generator pocket (PI) and lead-dependent infective endocarditis (LDIE). Transvenous leads extraction (TLE) is a key procedure in patients with CDI. Survival after TLE in this population was rarely analyzed up to now.

Methods: Comparative analysis of clinical data of 1426 patients underwent TLE in single Center in years 2006–2013 due to CDI (619 pts) and noninfectious indications (NI-807pts) was conducted. Mean five years survival after TLE was assessed.

Results: Patients with CDI were older (67.3±14.2 vs 62.3±17.4 p=0.001), with higher number of the leads (mean 2.1±0.8 vs 1.9±0.8 p=0.001), especially inactive leads (mean 0.3±0.7 vs 0.2±0.5 p=0.001), loops of the leads (20.9% vs 17.1% p=0.04) more frequent previous procedures prior to TLE (mean 2.1±1.3 vs 1.7±1.1 p=0.001) and abrasion of the leads (30.4% vs 20.6% p=0.001). Leads dwell time was longer in NI patients (88.3±65.6 vs 79.4±59.5 p=0.008). Procedural success and clinical success were comparable (respectively: 93.7% vs 91.7% p=0.28; 98.4% vs 97.7% p=0.33).

Conclusions: Patients underwent TLE due to CDI represented more potential procedural risk factors (older age, higher number of the leads especially inactive leads and loops of the leads). Nevertheless the full procedural and clinical success of TLE was high and comparable to NI group- probably younger age of the leads in CDI patients decided on efficacy of procedures in this patients. Despite the very successful early effect of TLE, the long term five years mortality of CDI patients is very high: 45% for LDIE and 35% for PI in comparison of 20% for NI patients (p<0.001).

Figure 1. Survival after TLE CDI/PI, LDIE vs NI

WHAT IS NEW IN MITRAL VALVE DISEASE
5211 | BEDSIDE
The pan-inflammatory process may cause mitral valve deterioration in systemic autoimmune disorder patients: a transhoracic echocardiography study
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Background: Pericardial effusion (PE) occurs frequently in patients with systemic autoimmune disorder (SAD), and suggests a pan-inflammatory process.

Purpose: We evaluated the relationship between deterioration of the mitral valve and PE in SAD patients using transhorans thoracic echocardiogram (TTE).

Methods: Seventy-five SAD patients (53 female; mean age, 53±11 years; systemic lupus erythematosus, 23%; vasculitis, 23%; scleroderma, 12%; polymyositis/dermatomyositis complex 10%, mixed connective tissue disease 9%, rheumatoid arthritis 3%, and polyarteritis nodosa 1%) underwent TTE (Vivid E9, GE Healthcare or IE33, Philips). We analyzed mitral leaflet motion and leaflet thickening by measuring the height of doming and anterior mitral leaflet (AML) thickness in addition to presence of significant PE. Furthermore, we qualitatively evaluated mitral valve calcification and sub-valvular thickening. AML thickness index was calculated as the ratio of AML thickness to that of the posterior aortic wall.

Results: Seventeen patients (23%) had PE. Four patients (5%) had moderate mitral regurgitation (MR) (2 with PE and 2 without PE). Patients with PE showed significantly greater height of doming of the AML (1.33±1.49 mm vs. −0.003±0.96 mm, p=0.002), AML thickness index (1.47±0.42 vs. 1.13±0.35, p=0.002), and frequency of sub-valvular thickening (29% vs. 7%, p=0.024) than patients without PE. There were no significant differences in the frequency of MR and serum creatinine level in patients with or without PE.

Conclusions: Mitral valve and sub-valvular deterioration were frequently detected in SAD patients with PE. The pan-inflammatory process may affect mitral valve and sub-valvular deterioration simultaneously, and careful follow up of these findings using TTE should be considered.
Surgery and that correction of MR should be proposed before the onset of these triggers. Conclusion: In patients with severe degenerative MR, long-term survival is less favourable in patients without all these triggers: Symptoms (84% vs 55%, p < 0.001); PHT (80% vs 54%, p < 0.001) and LV dysfunction, 74% vs 60%, p < 0.0357). Sensitivity analysis of baseline MR severity, 211 had moderate or greater MR. Within this group, 50, 50, 62, and 49 patients underwent CABG, CABG+MVS, CABG+SVR, and CABG+SVR+MVS respectively. MR severity was numerically graded (0=trivial MR, 1=mild, 2=moderate, 3=severe, 4=severe). Cox model survival analyses were performed to assess the impact of MVS, adjusted for prognostic clinical variables and factors related to whether MVS was performed. Patients who underwent only CABG had a better 4-year mortality rate of 46%, compared with 23% in CABG+MVS patients (adjusted hazard ratio [HR] 0.48, 95% confidence interval [CI] 0.15–1.58). Results: Follow-up of 43±25 months in 164 consecutive HFrEF pts (LVEF < 40%) from the HF outpatient clinic between 2007 and 2014. Severe FMR was defined as MR grade ≥ 4–5 based on a validated integrative method. Both patients received maximal tolerable HF medication. Major adverse cardiac event (MACE) was defined as a composite of cardiac death, need for heart transplantation or hospitalisation for heart failure and/or malignant arrhythmia’s. Results: A total of 57 (35%) pts showed severe MR and had a baseline risk profile comparable to HF pts without severe MR except for slightly worse EF (27% vs 30%, p=0.05). During follow-up, 46% of the severe FMR pts showed improvement to non-severe FMR (MR grade <3) whereas 14% of non-severe FMR pts developed severe FMR despite optimal HF treatment. Deterioration of FMR was associated with a poor outcome comparable with the outcome of pts with sustained severe FMR (MACE 86% vs 77%, adjusted HR 1.2 [95% CI 0.5–2.7]) whereas outcome of improved FMR was as good as with sustained non-severe FMR. (50% vs 45%, adjusted HR 1.4 [95% CI 0.7–2.7]).

Conclusion: Severe FMR is present in more than one third of patients with HFpEF and can be successfully treated with medication in almost 50%. However, severe FMR despite optimal HF treatment is associated with a dramatic prognosis and may need a more invasive approach.

Differential impact of mitral valve surgery on outcome of coronary artery bypass grafting without or surgical ventricular reconstruction in the surgical treatment for ischemic heart failure trial

MR evolution and prognosis

Conclusion: Severe FMR is present in more than one third of patients with HFpEF and can be successfully treated with medication in almost 50%. However, severe FMR despite optimal HF treatment is associated with a dramatic prognosis and may need a more invasive approach.

Background: Functional mitral regurgitation (FMR) in heart failure patients (pts) with reduced ejection fraction (HFpEF) is associated with a worse prognosis. It is uncertain to what extent medical management may alter the severity of FMR and its prognosis.

Methods: The extent of FMR was assessed at baseline and during an average follow-up of 43±25 months in 164 consecutive HFpEF pts (UEF <40%) from the HF outpatient clinic between 2007 and 2014. Severe FMR was defined as MR grade ≥4–5 based on a validated integrative method. Both patients received maximal tolerable HF medication. Major adverse cardiac event (MACE) was defined as a composite of cardiac death, need for heart transplantation or hospitalisation for heart failure and/or malignant arrhythmia’s. Results: A total of 57 (35%) pts showed severe MR and had a baseline risk profile comparable to HF pts without severe MR except for slightly worse EF (27% vs 30%, p=0.05). During follow-up, 46% of the severe FMR pts showed improvement to non-severe FMR (MR grade <3) whereas 14% of non-severe FMR pts developed severe FMR despite optimal HF treatment. Deterioration of FMR was associated with a poor outcome comparable with the outcome of pts with sustained severe FMR (MACE 86% vs 77%, adjusted HR 1.2 [95% CI 0.5–2.7]) whereas outcome of improved FMR was as good as with sustained non-severe FMR. (50% vs 45%, adjusted HR 1.4 [95% CI 0.7–2.7]).

Conclusion: Severe FMR is present in more than one third of patients with HFpEF and can be successfully treated with medication in almost 50%. However, severe FMR despite optimal HF treatment is associated with a dramatic prognosis and may need a more invasive approach.

Surgical reconstruction in the surgical treatment for ischemic heart failure trial

MR evolution and prognosis

Conclusion: Severe FMR is present in more than one third of patients with HFpEF and can be successfully treated with medication in almost 50%. However, severe FMR despite optimal HF treatment is associated with a dramatic prognosis and may need a more invasive approach.
At last, among survivors, 21 patients were in NYHA I-II, and only 1 in NYHA III. These patients were 77±11% (Figure).

During hospitalization, 3 patients died (1 rupture of inferior vena cava, 1 infective gurgitation, and 1 infective endocarditis). The mean transmitral gradient after TVMI was 4.2±0.7 mmHg and mild mitral regurgitation occurred in 2 patients (33.3%) and was related to the presence of subvalvular apparatus had a significant obstruction of left ventricular outflow tract with a mean gradient of 45 mmHg.

**Results:** The mean age was 66±13 years. Patients had severe comorbidities leading to a mean EuroSCORE II of 7.8±4.6. All patients were in NYHA functional class III or IV. An Edwards Sapien XT and Sapien 3 valve were used in 5 (83%) and 1 patient (17%), respectively and one-half of patients received a 29-mm valve. One prosthesis was implanted in good position in all patients. Two patients required a second prostheses implantation due to a malpositioning of the first one. At 30-day, one patient had died due to acute infectious endocarditis and another one required percutaneous closure of a residual atrial septal defect. In 2 patients, the procedure was performed in high-risk patients and provides good mid-term results.

**Conclusions:** Fully percutaneous TMVI is feasible in inoperable patients with severe mitral valve disease and MAC and may provide clinical benefits and hemodynamic improvement. However, the risk of peri-procedural complications remains a concern.

**Purpose:** We determined the natural history of moderate MS, focused on embolic events and all-cause death, and analyzed the association among patient's characteristics.

**Methods:** We conducted a retrospective study by screening for isolated moderate mitral regurgitation and high surgical risk. Regarding patient selection actual guidelines are recommended by the implantation criteria of the EVEREST II trial or the newer consensus recommendations of the focus group of the German Society of Cardiology (DGK recommendations). This study aimed to investigate the appropriability of these criteria in a real world scenario to predict the acute implantation success and the long-term outcome in order to select patients more precise for PC procedure.

**Methods and results:** Consecutive 251 symptomatic patients with moderate to severe or mitral regurgitation (MR) and high surgical risk received MR implantation in our heart center. Mitral valve morphology was evaluated by transthoracic and transesophageal echocardiography based on the EVEREST II criteria and DGK recommendations. At least one exclusion criteria of EVEREST II was met in 86% of patients: mostly LVEF <25% and/or LVEDS <55 mm. According to DGK recommendations, in 28% of patients unsuitable valve morphology was considered. Carpentier IIIa morphology was the main reason for unfavorable surgery in 20% of all patients. Nevertheless, implantation success rate was high (98%, 245 of 251 patients) and procedure success (residual MR grade <2+) with successful clip implantation was 90% (227 patients). The EVEREST II criterion, mitral valve orifice area (MVOA) ≤4.0cm² (11.6%, 29/251 patients) was the significant predictor of post-procedural mitral stenosis (transmitral mean pressure gradient >5mmHg) (OR 3.41, 95% confidence interval 1.53–7.57, P=0.003). In DGK recommendations, severe calcification in the grasping area (8.4%, 21/251) was the significant predictor of residual MR-grade >2+ (OR 3.47, 95% confidence interval 1.15–10.5, P=0.028) and had a predictive power of worse 2-year outcome (HR 2.90, 95% confidence interval 1.55–5.42, P=0.001).

**Conclusion:** Beside exclusion criteria in the EVEREST II criteria or unsuitable valve morphology in DGK recommendations, MC was successfully implanted in 98% of patients and 90% of patients were successfully treated. We have to pay special attention to patients with MVOA <4.0cm² or severe calcification in the grasping area to avoid MS or residual MR after procedure. We believe that this report may help people to select the eligible patients beyond the criteria or recommendations.

**Background:** Redo mitral surgery may be high risk or contraindicated. We evaluated mid-term results of transfemoral transcatheter mitral valve implantation (TMVI) in failed bioprostheses (BP) and ring annuloplasties (RA).

**Methods:** Transfemoral implantation of Edwards Sapien XT prosthesis was performed in 31 patients with degenerated mitral BP (n=13) or previous RA (n=18) between 2011 and 2015. Mean age was 61±24 years, all patients were in NYHA class ≥II, with a high surgical risk (EuroSCORE 38±26%). The cause of mitral failure was regurgitation in 14 patients, stenosis in 14 and both in 3.

**Results:** Procedure was unsuccessful in 5 patients (16%); 1 procedural death and 1 TVMI migration during rescue procedures on patients with ECDM, 1 conversion to surgery, 1 need for a second prosthesis and 1 moderate paraprosthetic regurgitation. In the 17 patients with stenotic BP or RA, mean gradient decreased from 14±5mmHg to 8±3mmHg (p=0.0001), whereas all but 1 patient had mitral regurgitation ≤2/4 after the procedure. During hospitalization, 3 patients died (1 rupture of inferior vena cava, 1 infective endocarditis and 1 urgent surgery for perforation of the aorta). Among the 28 patients discharged alive, 6 died during a mean FU of 13 months, mostly from cardiac cause (3 sudden death, 2 heart failure); The 18-months survival rate in these patients was 77±11% (Figure).

At last FU among survivors, 21 patients were in NYHA II-III, and only 1 in NYHA III due to a periprosthesis MR 3/4. This inoperable patient benefited from a successful valve-in-valve-in-valve 38 months after the first THV implantation.
studies are needed.

Conclusions: In moderate MS, systemic embolism occurred commonly and was associated with sinus rhythm and those who did not (45.2 vs. 44.1 cm, p=0.69). The incidence of embolic events and all-cause death was similar between patients with AF and warfarin use tended to have lower incidence (HR 0.56, 95% CI 0.2–1.3; p=0.06). Embolic events were associated with mortality (HR 2.3, 95% CI 1.2–4.6; p=0.03).

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BEST POSTERS 6
BEST POSTERS IN RESYNCHRONISATION THERAPY

P5221 | BEDSIDE
Differentiating the electromechanical substrate responsive to cardiac resynchronisation therapy from non-electrical dysynchrony substrates by computer-assisted regional strain analysis
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Background: Heterogeneous regional timing of left ventricular (LV) deformation, or electromechanical dysynchrony, is often observed in heart failure (HF) patients regardless of QRS duration.

Purpose: We hypothesized that myocardial substrates for contraction heterogeneity may exist due to electromechanical activation delay, regional differences in contractility, or regional scar, and that we could differentiate the electromechanical substrates that are responsive to cardiac resynchronization therapy (CRT) from non-electrical substrates unresponsive to CRT.

Methods: We first used CircAdapt computer simulations of LV radial strain to differentiate electromechanical from non-electrical hypocontractility and scar substrates of mechanical dysynchrony. This analysis led to definition of the novel systolic stretch index (SSI), as the sum of posterolateral systolic pre-stretch and septal systolic rebound stretch. SSI was prospectively quantified by automated echocardiographic radial strain analysis in 191 HF patients (QRS=120ms) treated with CRT.

Results: Patients with baseline SSI>2.9% had significantly fewer HF hospitalizations or deaths over 2 years (figure) (p<0.001, hazard ratio [HR]=3.15, 95% confidence interval [CI]=1.90–5.23), and fewer deaths, transplants or LVADs (p<0.001, HR=3.48, CI=1.83–6.62), even after adjustment for potential covariates of age, gender and ischemic disease (p<0.05 for both endpoints). SSI was more closely associated with clinical outcome than peak-to-peak radial strain delay or interventricular mechanical delay.

Conclusions: SSI specifically characterized electromechanical substrates responsive to CRT. SSI performed better than currently used dysynchrony indices at identifying patients with electromechanical substrates who benefited more favourably from CRT.

P5222 | BEDSIDE
Anatomical and electrical interlead distance predict outcome in cardiac resynchronization therapy patients
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Introduction: Approximately one third of CRT recipients do not respond to the therapy. The presence of a heart block in a patient may play a pivotal role in obtaining CRT response.

Methods: From the CRT MORE, 216 patients with left bundle branch block and sinus rhythm who received CRT, were included in analysis. At implantation the electrical inter-lead distance (EID), defined as the time interval between spontaneous peak R-waves of the same QRS complex detected at the RV and LV pacing sites, was measured. The anatomical distance between the RV and LV lead was determined on chest X-rays in postero-anterior and lateral views. A positive clinical response was defined as Improved Clinical Composite Score at the 6-month follow-up. A positive echocardiographic response was defined as a decrease of at least 15% in left ventricular end-systolic volume (LVESV) at the 6-month follow-up visit in comparison with the baseline visit.

Results: The mean EID was 74±41mm and the mean horizontal corrected inter-lead distance (HCID) was 125±73mm. After 12 months, 138 (64%) patients were classified as responders according to the echocardiographic criteria and 87 (40%) were classified as non-responders. To investigate the ability of EID and HCID to predict clinical response, receiving operating characteristic curves analysis was performed. Optimal sensitivity and specificity were obtained at a cut off level of 84ms for EID (53% and 87%, respectively) and 90mm for HCID (48% and 48%, respectively). In a multivariable model, only baseline IED and HCID above best cut-off values were independently associated with the occurrence of cardiovascular hospitalization or death (HR [CI] 0.26 [0.11, 0.62], p<0.05 for EID=84ms, HR [CI] 0.33 [0.17, 0.62], p<0.05 for HCID=90mm). At 24 months, the rate of freedom from events was 94% in patients fulfilling both conditions, 88% in patients fulfilling one condition and 71% in patients with both variables below the stated cut off values.

Conclusion: Both anatomical and electrical RV-LV interlead distance are predictors of CRT response. Positioning the LV lead at a site that results in EID>84ms and HCID>90mm seems associated with a very good outcome.
PS224 | BEDSIDE
Metabolic scintigraphy with radiolabeled fatty acid in prognosis of cardiac resynchronization therapy in patients with dilated cardiomyopathy
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Purpose: of the study was to study perfusion and metabolism of the left ventricular (LV) myocardium in patients with idiopathic dilated cardiomyopathy (DCMP) and to identify the scintigraphic predictors of the efficacy of cardiac resynchronization therapy (CRT).
Methods: The study comprised 63 patients with DCMP and NYHA class III-IV chronic heart failure. Before CRT, all patients received scintigraphy with 99mTc-MIBI and with 123I-BMIPP for evaluation of myocardial perfusion and metabolism, respectively. Before CRT and twelve months after, all patients underwent echo-cardiography study to estimate intracardiac hemodynamics.
Results: Patients were divided into two groups 6 months after CRT: (1) responders - LV ESV decreased by ≥15% (n=39); (2) non-responders - LV ESV decreased by ≤15% (n=24). Before CRT, LV pumping function didn’t significantly differ between groups. Significant differences were found in the following preoperative scintigraphic parameters: myocardial perfusion defect size (9,22±5,06% and 12,5±4,2%, p=0,01) and metabolic defect size (9,21±5,42% and 11,27±5,39%, p=0,01). Correlation analysis demonstrated the presence of significant association (r=0.37, p<0.05) between the sizes of metabolic defect and changes in the values of LV ESV after 12 months the implantation of CRT device. Metabolic scintigraphy showed higher diagnostic efficacy in determination of indications for CRT compared with perfusion scintigraphy (AUC 0.722 and AUC 0.612, respectively). The best metabolic defect size threshold value of 7.35% predicted CRT efficacy with the sensitivity and specificity of 77.8% and 66.7%, respectively. We also made an analytical review of methods for obtaining of radiopharmaceuticals that are based on 99mTc-labeled fatty acids and their use in cardiology. We make conclusion about efficiency of application and investigation of 99mTc fatty acids radiopharmaceuticals that contain chelate groups EDTA or DTPA. In this study, quantum-chemical modeling of one of such conjugate is conducted and its biavailability is thus confirmed.
Conclusion: The results of myocardial metabolic scintigraphy with 123I-BMIPP may be used as the secondary criteria for selection of patients for CRT and for prediction of the efficacy of this interventional treatment modality in patients with DCMP. 99mTc fatty acids based on chelate groups EDTA or DTPA are the prospective tracers for myocardial metabolism imaging.

BEST POSTERS IN ACUTE CORONARY SYNDROMES

PS225 | BEDSIDE
Troponin positive acute coronary syndrome with unobstructed coronary arteries: improved diagnostic accuracy of early cardiovascular magnetic resonance investigation, and implication for patients
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Background: 7–15% of patients with ACS have non-obstructive coronary artery. In these patients Cardiac MRI (CMR) can identify different underlying etiologies, such as myocarditis, myocardial infarction (MI) with spontaneous recanalization/embolus or Takotsubo cardiomyopathy. However the diagnostic pick-up rate of these aetiologies by CMR is highly variable in the literature.
Aim: To improve CMR diagnostic accuracy in patients with troponin positive ACS and unobstructed coronaries by imaging patients early after presentation.
Methods: Registry data on consecutive patients with troponin positive ACS and unobstructed coronaries by imaging patients early after presentation.

Results: 204 consecutive patients (mean age 55yrs) were included (51% males).
An “early” CMR (≤2weeks from presentation) was performed in 96 patients (mean age 4 days) and 108 patients underwent a “late” (>2weeks from presentation) CMR scan (median 49 days). Overall, a cause for the troponin rise was found in 70% of patients. The diagnostic pick-up rate significantly improved when the scan was done early: 82% vs 54% when CMR performed “late” (p<0.0001). Myocarditis was the most common diagnosis in the early arm (34%) whereas reperfused MI in the late group (26%). Further subgroup analysis revealed a diagnostic pick rate of 87% when the CMR scan done <1week (n=78) from admission (vs 82% when done >2weeks, p=0.40).
Conclusion: In a large cohort of patients with troponin positive ACS and unobstructed coronary arteries CMR was able to establish a final diagnosis in overall 70%. However, the diagnostic value of CMR improves significantly (up to 87%) when carried out within 2 weeks from presentation, with no difference between 1 week and 2 weeks. Accurate diagnosis have a clinical impact on management.

PS227 | BEDSIDE
Dynamic enhancement pattern of unstable coronary plaque: analysis by 320-row area detector computed tomography
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Background: Intraplaque neovascularization is a marker of unstable coronary plaque. We investigated a difference in dynamic enhancement pattern of coronary plaque between stable and unstable angina pectoris, using 320-row area detector computed tomography (CT), which enables whole-heart volumetric acquisition in a single gantry rotation.
Methods: We analysed 106 coronary plaque segments in 33 patients (mean age 69.8±8.3 years, 32 male) with angiographic stenosis in the culprit coronary artery. Patients were divided on the basis of multimodality scintigraphy findings as stable plaque (≤70% stenosis) or unstable plaque. We analyzed non-culprit plaques of stable patients and culprit plaque of unstable patients. In patients with stable angina, we used a reference plaque which was defined as stable plaque. Our multimodality scintigraphy included single photon emission computed tomography (SPECT), myocardial perfusion scintigraphy with 99mTc-sestamibi (MIBI) and with 123I-BMIPP for evaluation of myocardial perfusion and metabolism, respectively. Before and twelve months after, all patients underwent echo-cardiography study to estimate intracardiac hemodynamics.
Conclusion: The results of our study demonstrated that persistent high dynamic enhancement pattern of unstable coronary plaque could be a marker of vulnerable plaque. This pattern could be a potential target for future prediction of coronary events. In future study, a combination of contrast-enhanced CT and multimodality scintigraphy could be a powerful tool in the evaluation of coronary plaque.

PS252 | BEDSIDE
Age dependent association of body mass index with coronary artery calcification: true or false?
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Background and introduction: Obesity is an increasing problem worldwide and recognized as a major risk factor for cardiovascular disease. On the other hand, a protective effect of obesity, known as the “obesity paradox”, has been previously reported.
Purpose: The aim of the present study was to investigate whether there is an age dependent association between body mass index (BMI) and coronary calcium score (CACS) in a large outpatient population.
Methods: We included 4,079 consecutive patients, referred for coronary CT angiography as part of diagnostic work-up. Patients who underwent a CACS scan to determine amount of calcification using the Agatston method and whereby data regarding BMI were available, were included. Patients with known history of previous revascularization, pacemaker or implantable cardioverter-defibrillator, were excluded. Scans were performed between December 2007-May 2014, using 64-slice multidetector CT-scanner (Philips Healthcare; n=1,735) or dual-source CT-scanner (Siemens Definition Flash; n=2,344). Data regarding clinical risk factors: current smoking, diabetes mellitus type 2, positive family history, systolic blood pressure and lipid spectrum were assessed. Missing values according to risk factors were imputed using multiple imputation. Univariable and multivariable
analyses were performed using linear regression. 95% confidence intervals (CI) and two-tailed p-values < 0.05 were used to evaluate statistical significance. This study complies with the ethical principles of the Declaration of Helsinki of the World Medical Association. Results: Univariate regression analysis demonstrated a significant association between age-BMI interaction (B 0.26; 95% CI: 0.22–0.30; p-value < 0.001), no association was observed between BMI and CACS (B 0.92; 95% CI: -2.2–4; p-value < 0.57). Within multivariate regression analysis, including age, BMI and the age-BMI interaction, only age showed a significant independent association with CACS (B 0.92; 95% CI: 2.3–16.2; p-value < 0.009). Including also risk factors, the significant independent predictors for CACS were smoking, diabetes, metilus type 2, family history and total cholesterol (p-value < 0.011).

Conclusion: Within the present study, age and clinical risk factors show a significant independent association with CACS. No age dependent association was observed between BMI and CACS. These data do not confirm the so called “obesity paradox.”

P5229 | BEDSIDE
Association of big endothelin-1 with coronary artery calcification

Background: The coronary artery calcification (CAC) is clinically considered as one of the important predictors of atherosclerosis. Several studies have confirmed that high CAC score plays an important role in the process of atherosclerosis formation. However the relationship of ET-1 and CACS remains uncertain. The aim of this study was to investigate whether big ET-1 is associated with CACS.

Methods: A total of 510 consecutively admitted patients from February 2011 to July 2012 were enrolled in this study. ET-1 plasma levels were analyzed in patients who had undergone computed tomography angiography (CTA) and then divided into the two groups based on the results of coronary artery calcium score (CACS). The clinical characteristics including traditional and calcification-related risk factors were collected and the plasma big ET-1 level was measured by ELSIA. The association of ET-1 with CAC was evaluated.

Results: Patients with CAC had significantly elevated big ET-1 levels compared with those without CAC (0.7±0.5 vs. 0.5±0.4 pmol/L, p<0.001). Patients in higher big ET-1 tertile had elevated CACS (p<0.001). In the multivariate analysis, big ET-1 (OR=101.83, 95% CI: 19.95–519.92, p<0.001) appeared as independent factors predictive of the presence of CAC. There was a positive correlation of the big ET-1 level with CACS (r=0.367, p<0.001). The 10-year Framingham risk (%) was higher in the group with CACS > 0 and the highest tertile of big ET-1 (p<0.001). The area under the receiver operating characteristic curve (AUC) for the big ET-1 level in predicting CAC was 0.83 (95% CI 0.79–0.87, p<0.001), and the optimal cutoff value for the plasma big ET-1 level for predicting CAC was 0.30 pmol/L, with a sensitivity of 70.6% and specificity of 87.7%.

Conclusion: The data, for the first time, demonstrated that the plasma big ET-1 level was a valuable independent predictor for CAC in our study.

BEST POSTERS IN CARDIAC COMPUTED TOMOGRAPHY

P5231 | BEDSIDE
Association of quantitative global plaque volume and Agatston score with major cardiovascular events on long-term follow-up of patients referred for coronary CT angiography

Background: Coronary artery calcification quantified by the Agatston score is considered an established surrogate marker for the global atherosclerotic plaque burden. Nevertheless, little is known about the relationship between calcification, non-calcified plaque in coronary CTA and their respective predictive value regarding major cardiovascular adverse events (MACE) on long-term follow-up.

Methods: 198 patients in whom coronary CT angiography (CTA) was performed between 2005 and 2007 were systematically followed-up by structured telephone interview. The volume of calcified and non-calcified plaque in all coronary segments was quantified using manual planimetry to obtain the global plaque volume burden. Major adverse cardiovascular events (MACE) was defined as a combined endpoint of cardiac death revascularized cardiac arrest, myocardial infarction and/or stroke.

Results: 449 patients lost to follow-up were excluded from the analysis. 585 patients (mean age 59 ±11 years, 59% males) were included. The median follow-up period was 95 months (range 82–109 months). All-cause mortality was 5% on follow-up (3/585). MACE occurred in 45 (7.7%) patients: 2 cardiac deaths, 14 myocardial infarctions, 5 resuscitated cardiac arrests and 26 strokes. The total Agatston score as well as the global plaque volume were significantly higher in patients who suffered MACE on follow up (mean Agatston score 191±378 vs. 140±336, respectively, p=0.03 and mean global plaque volume 2.9±5.5 mm³ vs. 1.8±3.4 mm³, respectively, p=0.009). Agatston score as well as the global plaque volume were not significantly different in patients with and without stroke on follow-up (p<0.5). However, the mean global plaque volume was significantly higher in patients who developed myocardial infarction compared to patients without (5.2±8 mm³ vs. 1.8±3.4 mm³, respectively, p=0.006) whereas the mean Agatston score in patients with and without myocardial infarction was not significantly different (68±16 vs. 137±319, respectively, p=0.07). ROC-curve analysis showed an area under the curve (AUC) of 0.7 (p=0.008) for global plaque volume as a predictor for myocardial infarction versus 0.63 (p=0.63) for Agatston score.

Conclusion: In a large patient cohort, total calcified plaque burden and global plaque burden are significantly higher in patients who develop MACE on follow-up. Global plaque burden is a better predictor of future myocardial infarction than the Agatston score. These data indirectly point to a potential causative role of the non-calcified plaque burden in causing future myocardial infarctions on long-term follow-up.

P5232 | BEDSIDE
Independent prognostic value of coronary artery calcium score and coronary computed tomography angiography in an outpatient cohort of low to intermediate risk chest patients
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Background: Limited studies report on the additional prognostic value of coronary computed tomography angiography (CCTA) to the coronary artery calcium score (CACS) for low to intermediate risk chest patients.

Purpose: This study aimed to evaluate the prognostic value of CCTA independent of clinical risk factors and CACS in a routine clinical cohort of symptomatic patients with low or intermediate pre-test probability (PTP) of obstructive coronary artery disease.

Methods: For a median of 637 days, 1551 chest pain patients from the out-patient clinic with no history of CAD and low or intermediate PTP of CAD were followed for major adverse cardiac events (MACE), defined as death, myocardial infarction and late revascularization. Cox proportional hazards regression was used to evaluate the prognostic value of CCTA, independent of risk factors and CACS.

Results: MACE occurred in 23 patients (1.5%): 3 (0.2%) death, 4 (0.3%) myocardial infarctions and 16 (1.3%) late revascularizations. Both increase in CACS and presence of CAD at CCTA were associated with decreased MACE-free survival (log-rank p<0.01, figure 1). Multivariate analysis, adjusting for risk factors and CACS, showed independent prognostic value of CCTA (p<0.001). CCTA showed obstructive CAD in 3.1% of patients with CACS of zero. No events occurred in patients with CACS of zero without obstructive CAD at CCTA, whereas 2/23 patients (9%) with CACS of zero with obstructive CAD at CCTA had a MACE.

Conclusions: This is the first study to show the prognostic value of CCTA, independent of CACS and risk factors in chest pain patients with low to intermediate PTP of obstructive CAD, in which CCTA is appropriate. Furthermore a non-negligible amount of patients with CACS of zero have obstructive CAD at CCTA. CCTA can be used to identify those patients with CACS of zero at risk for MACE.
Coronary CT angiography anatomic assessment and lesion-specific ischemia: impact of integrating coronary plaque volume and CT density plaque fractals on diagnostic performance

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Background and introduction: The correlation of stenosis assessment by coronary CT angiography (CTA) and downstream ischemia is low. Consequently, coronary CTA is a poor gatekeeper to the cath lab. Both plaque assessment and non-invasive fractional flow reserve (FFR) derived from CTA (FFRct) hold superior diagnostic performance when compared to coronary CTA anatomic assessment in identifying lesion-specific ischemia.

Purpose: The aim of the present study was to evaluate the diagnostic performance of a multi-imaging strategy combining coronary CTA stenosis, plaque assessment, and FFRct.

Methods: As part of a prospective multicentre trial, we performed coronary CTA, FFR, and FFRct in 254 patients suspected of coronary artery disease. A site-read CTA stenosis >50% was considered obstructive. We quantified low-density non-calcified plaque (LD-NCP) volume by semi-automated software (AutoPlaq) from standard CTA images. LD-NCP volume was dichotomized using ROC analysis to define the optimal threshold. ischemia was defined by FFRct or FFR >0.80.

Results: Mean FFR in 484 vessels was 0.87 (±0.13). FFRct was 0.80 in 100 (21%) vessels. Overall, addition of LD-NCP (≥30 mm³) to coronary CTA anatomic measurement in the diagnostic algorithm increased accuracy and specificity for detecting lesion-specific ischemia by FFRct (Table). Adding FFRct to LD-NCP and coronary CTA assessment further improved accuracy, specificity and PPV with no sacrifice in sensitivity or NPV (Table).

Conclusions: Quantification of LD-NCP improves diagnostic performance of coronary CTA and may optimize selection of patients for FFRct analysis. Adding FFRct computation to patients with stenosis and a LD-NCP plaque volume ≥30 mm³ may optimize selection of patients to the cath lab.

BEST POSTERS IN VASCULAR BIOLOGY

Nitroimidazole-streptozotocin-induced type 2 diabetes in uninephrectomized high-fat-fed rats: a novel non-genetic rat model of diabetic nephropathy

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Background: The prevalence of diabetic nephropathy in type 2 diabetes (DM2) raises dramatically, with concurrent increase in associated cardiovascular mortality. One of the optimal strategies for investigation of methods and mechanisms of nephroprotection in DM2 is using an animal model of DN without genetic alteration which mimics natural history of diabetic kidney disease in humans as close as possible, both clinically and morphologically.

Purpose: To develop relatively easy reproducible non-genetic rat model that consequently mimics all stages of DN observed in DM2.

Methods: 3 weeks after unilateral nephrectomy, twenty 9-weeks old male Wis-tar rats were fed high-fat diet with beef tallow for 5 weeks and then successively increased sodium content (NA, 20 mmol/1) and received doses of nitroimidazole-streptozotocin (STZ, 65 mg/kg) intraperitoneally in 15-min interval. One week later, glucose tolerance test was performed, and 17 rats with glucose levels between 8.0 and 14.0 mmol/l were selected. Control uninephrectomized rats received vehicle instead of NA and STZ, and fed normal chow. After 10, 20 weeks, and at the end of the experiment (at week 30), urine and blood samples were collected. Histological examination (PAS and Masson's trichrome stainings) and electronic microscopy were also performed.

Results: HbA1c in diabetic group was considerably higher compared to control rats throughout the experiment, with a significant decrease of serum insulin level by week 20. At week 10, routine blood biochemical markers of kidney dysfunc-tion did not statistically differ between groups with tendency to hyperfiltration, and albuminuria was only slightly but not significantly different between groups. In contrast, early markers of tubular dysfunction (KIM-1 and NGAL) were highly increased in diabetic animals (205±18 ng/ml and 565±50.4 pg/ml, respectively) with p-value <0.05 compared to non-diabetic rats (108±10,2 and 197±30,6, respectively) indicating early stage of DN. Creatinine clearance was significantly decreased in diabetic rats (2.3±0.21 ml/min/kg) until the end of the study (1.8±0.35 ml/min/kg), and was his-terologically mesangial expansion and diffuse glomerular sclerosis, respectively.

Conclusion: Uninephrectomized high-fat-fed rats with NA-STZ-induced diabetes develop all features of DN in DM2.
β-tissue disorder caused by mutations in the fibrillin-1 gene. MFS patients are at risk growth factor suppress the manifestations. Previously, it has been reported that transforming transcription regulator of smooth muscle genes than normal iPSC-VSMCs and SMAD2/3 was found in MFS iPSC-VSMCs than in control iPSC-VSMCs.

Results: Both of MFS and control iPSCs could be differentiated into neuroectodermal in which SOX2, PAX6 and NESTIN expression detected by reverse transcription polymerase chain reaction (RT–PCR). Addition of TGF-β1 increased mRNA level. Immunostaining for smoothelin iPSC-VSMCs than in control iPSC-VSMCs. Addition of TGF-

Conclusions: Despite scientific progresses, TR is still buried by consider- able mortality rates, both early and later after surgery. Type of prostheses im- planted (biological vs. mechanical) does not influence any of the outcomes inves- tigated, whilst incidence of reoperation is increased in small volume centres.

Methods: Dermal fibroblasts obtained from a MFS patient were reprogrammed into induced pluripotent stem cells (iPSCs) using retroviral protocols expressing OCT4, SOX2, c-MYC and KLF4. The MFS iPSCs were coaxed to differentiate into vascular smooth muscle cells (VSMCs) via neuroectodermal lineage from which ascending aorta originates and compared with healthy control iPSC-VSMCs.

Conclusion: Resveratrol treatment did not correlate positively with aortic root dilatation rate. Resveratrol significantly inhib- ited dilatation, even more efficiently than losartan. Resveratrol treatment did not decrease activation of SMAD2 and ERK1/2, which are downstream pathways of the angiotensin-II receptor-1, and blocked by losartan. However, the aortic root of resveratrol-treated mice showed significantly increased nuclear SIRT1, decreased medial area, less elastic lamina breaks and decreased matrix metalloproteinases MMP2, MMP1 and MMP13 expression.

Results: Senescence was observed in the ascending aorta of MFS mice and correlated positively with aortic root dilatation rate. Resveratrol significantly inhibi- ted dilatation, even more efficiently than losartan. Resveratrol treatment did not decrease activation of SMAD2 and ERK1/2, which are downstream pathways of the angiotensin-II receptor-1, and blocked by losartan. However, the aortic root of resveratrol-treated mice showed significantly increased nuclear SIRT1, decreased medial area, less elastic lamina breaks and decreased matrix metalloproteinases MMP2, MMP1 and MMP13 expression.

Conclusion: Resveratrol inhibits aortic root dilatation in MFS mice via a different mechanism of action than is considered for losartan and seemingly via modulation of the extracellular matrix. Resveratrol may hold promise as a novel thera- peutic option for this purpose.

Background: Marfan syndrome (MFS) is an autosomal connective tissue disorder caused by mutations in the fibrillin-1 gene. MFS patients are at risk of lethal aortic aneurysm and dissection. β-blockers and losartan are medication options, however, more treatment possibilities are needed, since losartan is less effective in 67% of the MFS patients. Aneurysm formation can be studied in various mouse models. Spontaneous aneurysm formation occurred in smooth muscle cell-specific sirtuin-1 (SIRT1)-deficient mice. SIRT1 is an NAD+-dependent metalloproteinase-2 (MMP-2) mRNA level. Immunostaining for smootholin (SMTN) and MYH11 were more intense and enhanced nuclear accumulation of trix metalloproteinase-2 (MMP-2) mRNA level. Immunostaining for smoothelin

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Conclusions: To evaluate the diagnostic performance of 3D Area (3DA) in comparison to classic 2D diameter (2DD) for selecting candidates to TV surgery.

Methods: 2DE and 3DTE data sets of the TV were prospectively acquired in 50 patients (Age: 69±9, 82% women) with rheumatic left-side valve disease. FTR was divided in three groups; mild (N: 15), moderate (N: 21) and severe (N: 14). Diastolic 3DA was measured in addition to conventional 2D (2DD). Results: Optimal cut-off points for severe FTR detection using both 3DA (6.5 cm²/m²) and 2DD (21 mm²/m², identical to the described in the literature), were identified by ROC analysis: 2DD: AUC 0.85, Se: 86%, Sp: 72%; 3DA: AUC 0.84, Se 86%, Sp: 78%. Potential selection of candidates for TV surgery, based on the combination of 2DD and 3DA is shown in Figure. Better specificity of 3DA helped to reclassify surgical indication in mild and moderate degrees of FTR.

Conclusions: Although 2DD >21 mm²/m² seems to be a reasonable criterion of marked dilatation of TA in FTR, the combination of diastolic 3DA assessment, cut-off value of 6.5 cm²/m², might improve selection of candidates for TV surgery.

P5244 | BEDSIDE
Tricuspid valve annuloplasty for functional tricuspid regurgitation: immediate outcomes and risk factors for late failure
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Background: Risk factors for recurrent regurgitation after tricuspid valve anuloplasty (TVA) for tricuspid regurgitation (TR) secondary to left-sided heart valve disease (functional TR) remain uncertain.

Purpose: To investigate immediate outcomes and late failure of repair (TVA) for functional TR.

Methods: 524 (mean age: 69±9.6 years) consecutive patients with grade ≥2+ TR (graded from 0 to 3+) underwent TVA at the present authors’ institution from March 1999 throughout June 2014. All patients suffered from left-sided heart valve disease needing surgical treatment. The mean expected operative risk according to EuroSCORE II was 10.4±12.2%. Clinical data and echocardiographic studies were retrospectively reviewed during a mean follow-up of 4.9±3.7 years. Risk factors for late failure of repair were identified by multivariable analysis.

Results: The DeVega suture annuloplasty (SA), rigid rings or flexible bands were used in 15.3, 18.1 and 66.6% of patients, respectively. Thirty-day mortality was 7.1%, and age >70 years (P=0.002), left ventricular (LV) dysfunction (defined as LV ejection fraction <35%, P=0.015), right ventricular (RV) dysfunction (defined as tricuspid annular plane systolic excursion <16 mm (P=0.0023) and RV fractional area change <35% (P=0.0003)) and prolonged (> 48 h) inflation of the balloon (16.3%, low cardiac output (10.2%), acute kidney injury (18%) and mediastinal fluid accumulation (20%) were the most frequent major postoperative complications. The 10-year non-parametric estimates of overall survival and freedom from cardiac death (including hospital mortality) were 51.7% (95% confidence interval (CI): 48.4–55) and 71.5% (95% CI: 68.7–74.3), respectively. TR grade ≥2+ at follow-up was found in 35(67) (7.5) patients, and the 10-year non-parametric estimate of freedom from significant TR was 81.5% (95% CI: 78–85). Predictors of recurrent TR were the use of suture annuloplasty (P=0.023), LV dysfunction (P=0.0022) and RV dysfunction (P=0.0001). At follow-up, significant TR combined with recurrent left-sided heart valve disease (P=0.038) and RV dysfunction (P=0.01) were independent risk factors. Prolonged (>48 h) invasive ventilation (16.3%), low cardiac output (10.2%), acute kidney injury (18%) and mediastinal fluid accumulation (20%) were the most frequent major postoperative complications. The 10-year non-parametric estimates of overall survival and freedom from cardiac death (including hospital mortality) were 51.7% (95% confidence interval (CI): 48.4–55) and 71.5% (95% CI: 68.7–74.3), respectively. TR grade ≥2+ at follow-up was found in 35(67) (7.5) patients, and the 10-year non-parametric estimate of freedom from significant TR was 81.5% (95% CI: 78–85). Predictors of recurrent TR were the use of suture annuloplasty (P=0.023), LV dysfunction (P=0.0022) and RV dysfunction (P=0.0001). At follow-up, significant TR combined with recurrent left-sided heart valve disease (P=0.038) and RV dysfunction (P=0.01) were independent risk factors.

Conclusions: Cardiac operations in patients with functional TR are performed with high early mortality and frequent postoperative complications. On a long-term basis, TR is generally controlled within grade 1+ in patients without preoperative biventricular dysfunction. Late failure of repair is linked to the fate of left-sided heart valve repair and RV function. The use of SA should be discouraged.

P5246 | BEDSIDE
Hypertensive target organ damage and longitudinal changes in brain structure and function in older patients with manifest cardiovascular disease: The SMART-MR study
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Background: High blood pressure has been related to structural and functional changes of the brain. In populations with high cardiovascular risk, hypertensive target organ damage might better represent exposure to high blood pressure than the blood pressure measurement itself.

Methods: To examine the association of hypertensive target organ damage with changes in brain structure and function, data was used from the prospective SMART-MR Study. Renal function, albuminuria, and left ventricular hypertrophy on electrocardiography were measured in 663 patients with manifest cardiovascular disease (mean [SD] age 57 [9] years, 81% men). At baseline and after a mean of 3.9 years of follow-up, 1.5 T brain MRI was performed to quantify progression of global brain atrophy (decrease in brain parenchymal fraction as % of intracranial volume (ICV)) and progression of cerebral small-vessel disease (increase in white matter lesion volume or new lacunar infarcts). Memory and executive functioning were assessed with neuropsychological tests.

Results: Regression analyses showed that an increasing number of signs of target organ damage was associated with more progressive global brain atrophy and more rapid decline in memory performance (Figure). Compared to no target organ damage, mean differences in change in brain parenchymal fraction (95% CI) for 1 and ≥2 signs of organ damage were −0.12 (−0.30, 0.06) and −0.41 (−0.77, −0.05) %ICV/year and mean (95% CI) differences in change in memory performance (z-score) were −0.15 (−0.29, −0.00) and −0.27 (−0.54, −0.01). These results were independent of blood pressure, antihypertensive treatment, and other confounders. Target organ damage was not associated with progression of cerebral small-vessel disease or change in executive functioning

Conclusions and relevance: In this high-risk cardiovascular population, more extensive hypertensive target organ damage was associated with progression of global brain atrophy and greater decline in memory performance. Routinely assessed signs of target organ damage could identify those patients at the highest risk of cognitive decline.

P5247 | BEDSIDE
Results of the cardiac surgery in octogenarians
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Introduction: Cardiac surgery in octogenarians with severely decreased functional status is increasingly common, but outcome data are still limited.

Purpose: The aim of this study was to compare postoperative outcome, medium-term survival and quality of life of low, medium and high risk octogenarians undergoing cardiac surgery.

Methods: 285 octogenarians were included who underwent any cardiac surgical procedure between January 2011 and December 2012. Five out of all twelve national adult cardiac surgical centres participated in the study, representing almost half of all octogenarians operated in our country in that period. Patients were divided into low, medium and high-risk groups according to the operative risk calculated using EuroSCORE II. Preoperative, operative and postoperative data of the patients were collected retrospectively. Follow-up was performed in May 2014 by interviewing the patients by telephone. All patients also completed a questionnaire assessing quality of life by objective and subjective means.

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Conclusions: Although 2DD >21 mm²/m² seems to be a reasonable criterion of marked dilatation of TA in FTR, the combination of diastolic 3DA assessment, cut-off value of 6.5 cm²/m², might improve selection of candidates for TV surgery.
Long-term outcomes of transcatheter aortic valve implantation in elderly patients: Immediate results and medium-term follow-up

P5249 | BEDSIDE
Transcatheter aortic valve implantation in very elderly patients: Immediate results and medium-term follow-up

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Objective: Our aim was to evaluate immediate transcatheter aortic valve implantation (TAVI) results and medium-term follow-up in very elderly patients with severe and symptomatic aortic stenosis (AS).

Methods: Multicenter, observational and prospective study carried out in 3 hospitals. We included consecutive very elderly (>65 years) patients with severe (AS) treated with TAVI. The primary endpoint was to evaluate death from any cause at 2 years.

Results: The study included 160 consecutive patients with a mean age of 87±2.1 years [range, 85–94] and a mean logistic EuroSCORE of 18.8% ± 11.2%, with 57 (35.6%) patients scoring ≥30%. Procedural success rate was 97.5%. 25 (15.6%) patients had acute complications, being major bleed the most frequent. No procedure needed conversion to surgery. Global mortality rate during hospitalization was 8.6% (n=14) and 30-day mortality rate was 10% (n=16). Median follow-up period was 252±243±23.17 days. During the follow-up period, 28 (17.5%) patients died, 17 of them due to cardiac cause. Two year overall and cardiac survival estimated rates using the Kaplan-Meier method were 71% and 86.4% respectively. Cox proportional hazard regression showed that the variable EuroSCORE ≥20 was the unique variable associated with overall mortality.

Conclusion: TAVI is safe and effective in a selected population of very elderly patients. Our findings support the adoption of this new procedure in this complex group of patients.

P5249 | BEDSIDE
Impact of low diastolic blood pressure on risk of cardiovascular death in elderly and late-elderly patients with coronary artery disease after revascularization: the CREDO-Kyoto Registry

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Background: It remains controversial whether low diastolic blood pressure (DBP) is a risk for cardiovascular (CV) events in patients with coronary artery disease (CAD), especially in the elderly.

Purpose: We investigated the impacts of age and low DBP on CV death in CAD patients after coronary revascularization.

Methods and results: We examined 2619 Young/Middle-aged (≤64 years), 2932 Elderly (65–74 years), and 1629 Late-Elderly (75 years) CAD patients who underwent first coronary bypass graft or percutaneous coronary intervention in the CREDO-Kyoto study. Cumulative hazard ratio (HR) for CV death was higher in patients with DBP <70mmHg in Elderly group and in patients with DBP≥60mmHg, but not <70mmHg, in Late-Elderly group, compared with each counterpart (Figure), whereas low DBP was not associated with increased CV death in Young/Middle-aged group. Step-wise logistic regression analysis showed that independent risk factors for CV death in low DBP patients were creatinine clearance (inversely), prior cerebrovascular disease, and hemoglobin (inversely) in Elderly group and creatinine clearance (inversely), prior heart failure, and malignancy in Late-Elderly group. After adjustments with the independent risk factors, cumulative HRs were similar in patients with DBP ≥60 and with DBP<60mmHg in Late-Elderly group and only small difference of HR was shown between patients with DBP ≥70 and with DBP<70mmHg in Elderly group.

Conclusion: In elderly and late-elderly revascularized CAD patients with low DBP, renal dysfunction, co-existing CV disease, and poor general condition were independent risks of CV death, whereas low DBP itself may be a risk marker but not a major risk factor. In elderly and late-elderly CAD patients with low DBP, attention should be paid upon CV and non-CV comorbidity.

BEST POSTERS IN KNOWN AND EMERGING RISK FACTORS AFTER CARDIAC SURGERY

P5251 | BEDSIDE
Blood transfusion and increased hospital morbidity and mortality in patients undergoing coronary artery bypass grafting


Background: The transfusion of blood components has played an important role in hemodynamic management during the perioperative period. Despite its proven benefits, unnecessary transfusions are likely to be associated with unnecessary morbidity and mortality.

Objective: The aim of this study was to evaluate the impact of the transfusion of hemoderivates on clinical outcomes during post-operative period and 30-day mortality.

Methods: A total of 1378 patients who underwent isolated or combined CABG surgery between January 2011 and December 2012 had their transfusional, clinical and hematological data reviewed. The effect of transfusion of blood components was tested in a mutual analysis for the prediction of three coprimary coprimary end points: ischemic, infectious and hospital mortality. Hospital mortality outcome was tested in a stratum of low-risk patients, in order to isolate the effect of pre-operative risk on the outcomes, through the logistic EuroSCORE calculation.

Results: The overall transfusion rate was 63.9%. The transfusion of blood components was associated with greater likelihood of occurrences of the three coprimary end points: infectious composite (OR 2.67; CI 95% 1.70 to 4.19; P<0.001), ischemic composite (OR 2.42; CI 95% 1.70 to 3.46; P<0.001), and hospital mortality (OR 3.07; CI 95% 1.53 to 6.13; P<0.001). When assessing only patients with logistic EuroSCORE ≤2% in both groups, the mortality rate was greater among the ones who underwent blood transfusions [6% vs 0.4% (P<0.001)], contradicting the view that the greatest mortality in the group of transfused patients would result from the most severe condition of the patient.

Conclusion: The blood transfusion in patients who underwent CABG surgery is strongly associated with ischemic events, infectious complications and hospital mortality. This result reinforces the notion that this practice without clear specified criteria should be discouraged due to these risks.

P5252 | BEDSIDE
Smokers undergoing coronary surgery are at a greater risk for perioperative complications


Introduction: Smoking is a known risk factor for cardiovascular diseases, but its effect on operative outcomes is still debated.

Purpose: To analyse patients submitted to CABG, comparing active smokers with past smokers and non-smokers in terms of disease severity, risk factors, surgical indications, surgical outcomes and complications.

Methods: Search the Center’s database for patients submitted to CABG from January 1st 1990 to December 31st 2013.

Results: 10,791 patients were submitted to CABG (9327 male/1464 female), 1208 active smokers, 4,013 past smokers and 5,570 non-smokers. 96.6% of active or past smokers were male, compared to 76.8% in non-smokers (p<0.001). Also significant was the incidence of COPD (4.0% vs. 2.5%, p<0.001), obesity...
Conclusions: but in-hospital mortality was similar (p=0.799). The average length of stay was use of inotropes was greater in active smokers (p=0.012). Although the incidence mortality. Need for postoperative mechanical assistance was not different (p=0.7), but the complication rate was significantly higher than that of patients without MACCE (P=0.010) and...explained in a replication cohort with 646 patients. We have complied with the World function were tested. Cox proportional hazard models were used to identify clini- of 1576 patients, 44 single-nucleotide polymorphisms (SNPs) related to platelet vary significantly in patients related to platelet function are independently associated with MACCE after CABG.

Methods: Two separate cohorts of patients undergoing CABG surgery were ex- and genomic multivariate predictors of MACCE. The positive SNPs were ver- whose troponin values were 1.03) and TnT positive predictive value of 16% and negative predictive value of 97%. The pa- tients were then divided into two groups: TnT ≥50x (99th) and TnT >50x (99th). Twenty-nine percent of the patients had TnT (99th) in the 1st postoperative day with 30-day mortality of 16% compared to 2.9% of death in those with TnT ≥50x (99th) – P < 0.001. Eleven variables were evaluated and three were iden- tified as independent predictors of death after cardiac surgery: age (HR - 1.12; 95% CI - 1.08 to 1.17), cardiopulmonary bypass time (HR - 1.02; 95% CI - 1.01 to 1.03) and TnT >50x (99th) – HR - 4.20; 95% CI - 1.90 to 9.30).

Conclusion: Area under the ROC curve with better sensitivity and specificity for death was 0.77. The cut-off found was the elevation of 47 times the TnT value above the reference value (99th percentile). Setting this value to 50 times did not change the area under the ROC curve and had a sensitivity of 69%, specificity of 74%, positive predictive value of 16% and negative predictive value of 97%. The pa- tients were then divided into two groups: TnT ≥50x (99th) and TnT >50x (99th). Twenty-nine percent of the patients had ≥50x TnT (99th) in the 1st postoperative day with 30-day mortality of 16% compared to 2.9% of death in those with TnT ≥50x (99th) – P < 0.001. Eleven variables were evaluated and three were iden- tified as independent predictors of death after cardiac surgery: age (HR - 1.12; 95% CI - 1.08 to 1.17), cardiopulmonary bypass time (HR - 1.02; 95% CI - 1.01 to 1.03) and TnT >50x (99th) – HR - 4.20; 95% CI - 1.90 to 9.30).

Conclusion: Elevation of the TnT value greater than or equal to 50 times the reference level (99th percentile), regardless of the clinical, electrocardiographic and image findings, was an independent predictor of 30-day mortality after cardiac surgery.
pose of the current study was to assess the interactions between expression of TNF mRNA in skeletal muscle, plasma levels of TNF, changes in skeletal muscle pathology and intramuscular gene expression of enzymes related to skeletal muscle biosynthesis.

Methods: Twenty patients with HF and left bundle branch block who were offered cardiac resynchronization therapy (CRT) were studied. Blood samples and skeletal muscle biopsies were harvested at baseline and after 6 months of CRT. Plasma levels of TNF were measured using a multiplex cytokine immunoassay. Measurements of fibre diameter, interstitial fibrosis, vascular density and inflammation were performed with light microscopy. Point-counting stereology on electron micrographs was used for morphometric registration. Total RNA was extracted from skeletal muscle and quantification of skeletal muscle gene expression of TNF, mitochondrial transcription factor A (TFAM) and nicotinamide phospho- kinase (NAMPT) was performed.

Results: Alterations in plasma levels of TNF correlated statistically significantly with alterations in intramuscular gene expression of TNF (R=0.56, p<0.05) and were negatively correlated to mRNA levels of TFAM (R=−0.81, p<0.01) and NAMPT (R=−0.81, p<0.001) within the skeletal muscle. Alterations in skeletal muscle expression of mRNA levels of TNF were statistically significant correlated with changes in mitochondrial density (r=−0.56, p=0.036 Pearson’s, r=0.475, p=0.086 Spearman’s) and borderline statistical significant correlated with changes in capillary density (r=0.546, p=0.036 Pearson’s, r=0.475, p=0.086 Spearman’s).

Conclusion: This initial study shows novel and early myocardial effects of doxorubicin-induced cardiotoxicity, including changes at the level of myofilaments (titin), apoptotic-gene expression and extracellular matrix. These early changes precede the initial echocardiographic diagnosis of cardiomyopathy, emphasizing the need for an early detection of cardiac damages associated to cancer treatments in order to allow for therapeutic adjustments and prevent the progression of cardiomyopathy.

P5258 | BENCH
Effects of late exercise on cardiac remodeling and myocardial calcium handling proteins in rats with moderate and large myocardial infarction size
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Purpose: Physical exercise is accepted as a non-pharmacological treatment to attenuate myocardial infarct-induced cardiac remodeling. However, it is unsettled whether late exercise modulates post-infarction cardiac remodeling differentially according to infarct size. We investigated the effects of a treadmill exercise protocol started at late stage heart failure on cardiac remodeling and myocardial calcium handling protein expression in rats with moderate and large sized MI.

Methods and results: Three months after inducing MI, rats were assigned into sedentary and exercise groups for three months. Exercise rats underwent treadmill at 16 m/min, 40 min/day, 5 days/week, for three months. Transthoracic echocardiography was performed before and after exercise protocol. After assessing infarct size by histological analysis, rats were subdivided into four groups: moderate-MI sedentary (Mod MI-Sed; n=7), Mod MI exercised (Mod MI-Ex; n=7), Large MI-Sed (n=11), and Large MI-Ex (n=10). Before exercise, cardiac changes in infarcted rats were demonstrated by comparing results to a Sham group; alterations were more intense in rats with large [-40% left ventricle (LV) area] than moderate (30–40% LV area) MI size. Systolic function, evaluated by the variation in LV fractional area change between baseline and after doxorubicin was statistically improved in exercise than sedentary groups. Protein expression was evaluated by Western blot. Phospholamban was higher in Large MI-Sed than Mod MI-Sed. Exercise attenuated phospholamban increase in Large MI-Ex group. Calsequestrin expression increased in both exercise compared to sedentary groups. L-type calcium channel was higher in Mod MI-Ex than Mod MI-Sed. SERCA2a and Na+/Ca2+ exchanger did not differ between groups.

Conclusion: Late aerobic exercise improves systolic function and modulates intracellular calcium signaling protein expression in rats with moderate and large myocardial infarction. This study is the first to show that treadmill exercise increases myocardial calsequestrin protein expression in rats with both moderate and large sized myocardial infarction.

P5259 | BENCH
Myofilament changes in doxorubicin-induced cardiotoxicity
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Introduction: Cardiomyopathies represent important cause of premature death from heart failure. Several studies demonstrate that administration of doxorubicin, results in cardiac toxicity. Alterations in titin have been reported in patients with this kind of cardiomyopathy. The present work aims to evaluate the early myocardial changes of doxorubicin-induced cardiotoxicity.

Methods: Male New Zealand white rabbits were injected intravenously twice weekly for 8 weeks with doxorubicin (DOX-HF, 1mg/kg, n=17) or with an equiv-

clomeric dose of saline (Control, n=18). Echocardiographic evaluation was performed 1 week before the end of protocol. Myocardial samples were collected to evaluate functional properties of isolated skinned cardiomyocytes in terms ofofilaments active and passive tension and calcium sensitivity (pCa50 and nHill). Sirius-red, hematoxylin-eosin and TUNNEL stained samples were used to quan-

tify the percentage of myofibril necrosis, respectively. BAX, BCL-2, NF-KB, BECLIN and PINK-1 expression were measured. Titin isoform expression, phosphorylation and degradation were quantified.

Results: DOX-HF group presented cardiac hypertrophy as evidenced by an increase in heart to body weight (2.38±0.09 vs 2.17±0.06mg/g) and by the increased right ventricle (RV) and left ventricle (LV) cardiomyocyte area (RV: 268±12 vs 235±16μm2 and LV: 380±20 vs 331±27μm2). Concerning cardiomyocytes function, DOX-HF group presented increased active tension (21.4±1.9 vs 16.5±1.1nN/μm2) without significant changes in electrical activity. Nevertheless, an increase in systolic tension or myofila-

dents sensitivity to Ca2+. DOX-HF group showed a decrease in total titin phos-

phorylation (49.0±6.1 vs 85.2±9%), more pronounced in N2B isoform (62.6±9.1 vs 31.0±4.4%), as well as an increase in the ratio between the compliant isofrom and the stiffer isofrom (N2B:N2A: 0.5±0.1 vs 0.3±0.1%). Despite similar percent-

age of apoptotic nuclei DOX-HF presented a significant increase in Bax/Bcl-2 ratio (2.5±0.4 vs 1.3±0.2AU). The extracellular matrix was shown marked alterations as confirmed by the significant increase in myocardial interstitial fibrosis in LV from DOX-HF group (12.1±1.4 vs 7.8±1.2%).

Conclusion: This study presents novel and early myocardial effects of doxorubicin-induced cardiotoxicity, including changes at the level of myofilaments (titin), apoptotic-gene expression and extracellular matrix. These early changes precede the initial echocardiographic diagnosis of cardiomyopathy, emphasizing the need for an early detection of cardiac damages associated to cancer treatments in order to allow for therapeutic adjustments and prevent the progression of cardiomyopathy.

BEST POSTERS IN HYPERTENSION IN SPECIFIC POPULATIONS

P5261 | BENCH
Nationwide prevalence, awareness, treatment and control of hypertension among the adult population in Bangladesh
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Objective: To evaluate the prevalence, awareness, treatment and control of hypertension among elderly individuals in Bangladesh.

Methods: Socio demographic and anthropometric data and on blood pressure were obtained for 7839 adults aged 35 years or more from the biomarker sample of the 2011 Bangladesh Demographic and Health Survey (DHS), which was nationally representative based on a stratified, multistage, cluster sampling design. Blood pressure values considered normal are less than 120 mmHg for SBP and less than 80 mmHg for DBP. An SBP value of 120–139 mmHg or a DBP value of 80–89 mmHg is classified as pre-hypertension.

Results: Overall prevalence of hypertension – defined by systolic blood pressure ≥140 and/or diastolic blood pressure >90 or reporting history of hypertension – was found to be 32% in Bangladeshi adult women and 19% in adult men. An additional around 28 percent of women and men are pre-

hypertensive. Higher rate of hypertension is seen in urban population than in rural population. 15.9% of survey participant were told by a doctor having high blood pressure. Hypertension has significant association with age, BMI, educational level, working status, geographical region, wealth status, presence of diabetes. Forty-five percent of women and 57 percent of men are not aware that they have elevated blood pressure. Eleven percent of women and 8 percent of men are aware of their hypertension, but are not treating it. Forty-five percent of women and 36 percent of men with hypertension are taking medication to lower the blood pressure, but are unsuccessful in controlling the elevated blood pressure.

Conclusion: Our findings emphasize the need to implement effective and low cost intervention programs based on absolute levels of cardiovascular risk appropriate for the economic context. From a public health perspective, the only sustainable approach to the high prevalence of hypertension in Bangladesh is through a strategy to reduce the average blood pressure in the population.
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**Background:** Systolic blood pressure (SBP) and arterial stiffness (AS) are closely related and may behave reciprocally as cause or effect and interact in a vicious cycle. Systolic blood pressure is a risk factor for the development of cardiovascular disease. There have been insufficient data for age-related change of blood pressure and brachial-ankle pulse wave velocity in native Papuan populations. In this study, we evaluated the age-related changes of SBP and AS in the Papuans.

**Methods:** During the 2014 “World Hypertension Day”, health care providers from 50 hypertension centers affiliated to the Italian Society of Hypertension, spread all over the country, anonymously interviewed individuals spontaneously participating in this campaign. Information on demography, cardiovascular risk factors and other cardiovascular risk factors in participants in this initiative. Even considering that these individuals may not be fully representative of the general Italian population, our data, obtained in Italy at the time of the 2014 World Hypertension Day campaign in Italy, are relevant since main body of heart failure patients are elderly with high cardiovascular risk factors in participants in the 2014 “World Hypertension Day” campaign in Italy.

**Objective:** Aim: The aim of the present study was to investigate a possible association between hypertension and the loci in six candidate genes in individuals of Tatar origin.

**Background:** Genome-wide association studies have identified different hypertension-susceptibility loci in the populations of European ancestry. However, fine-mapping of blood pressure related loci has been complicated by the existing differences in genetic variation across populations. The population of Tatars residing in the Volga-Ural region of Russian Federation, particularly in the Republic of Bashkortostan, has a distinct genetic structure characterized by combination of Mongoloid and Caucasoid components, which makes it an interesting object for genetic study.

**Methods:** We performed screening for SNPs in CXCL13, CCL8, CCL16, CCL17, CCL18, and CCL23 genes in the group of 522 Tatars from the Republic of Bashkortostan, Russia (213 patients with essential hypertension (mean age 42.24±8.27) and 309 healthy individuals (mean age 43.58±7.13) without history of cardiovascular or any other chronic disease.

**Results:** An association was detected between CXCL13 rs5356889 polymorphism and essential hypertension; “T” genotype and “T” allele were associated with an increased risk of hypertension (OR=2.51, P=3.06*10–6 and OR=1.87, P=0.0001, respectively), while heterozygous genotype and “G” allele carrier status indicated a decreased risk of the disease (OR=0.35, P=2.13*10–6 and OR=0.053, P=0.0001, respectively). Analysis of association between EH and allele/genotype combinations revealed many combinations, which differed in frequency in the group of EH patients and in control group. Eleven combinations remained significantly associated with EH after the correction for multiple testing was applied. The most significant association was observed for CXCL13*T/T+CCL8*T+CCL17*T combination, that was more frequent in the group of patients with essential hypertension (OR=2.62, P=0.0009) and two combinations that appeared to be protective against hypertension – CXCL13*C+CCL8*C+CCL17*T (OR=0.32, P=0.0002), and CXCL13*C+CCL8*T (OR=0.33, P=0.0002). Conclusion: CXCL13 rs5356889 polymorphism was found to be significantly associated with essential hypertension in Tatars, both individually and in combination with other chemokine genes.

**Discussion:** Our data, obtained in Italy at the time of the 2014 World Hypertension Day campaign in Italy, are relevant since main body of heart failure patients are elderly with high cardiovascular risk factors in participants in the 2014 “World Hypertension Day” campaign in Italy.
Background: Previous studies on digoxin use in patients with atrial fibrillation (AF) and the risk of all-cause and cardiovascular mortality have reported conflicting results. Most of these studies were not able to take into account the severity of possible associated HF. We analyzed the effects of digoxin on mortality in unselected AF patients.

Methods: We conducted a population-based retrospective cohort study of patients admitted to a cardiology department from January 2000 to January 2011. Survival analysis used a Cox model controlled with propensity scores derived from multivariate logistic regression model based on all characteristics including NYHA functional class, eGFR, and BNP at baseline. In 8871 patients with AF, digoxin was prescribed to 618 (28.3%) by whom 618 (28.3%) received it transiently. Digoxin was defined as "full dose" treatment (0.25mg daily) for 1202 patients (55.7%) and "low dose" treatment (0.125mg daily) for 957 patients (44.3%).

Results: Patients treated with digoxin were significantly older, with more heart failure and lower use of beta-blockers than non-users. Crude mortality was higher in patients on digoxin (17.1% vs 11.3%; Hazard Ratio [HR] 1.27; 95% Confidence Interval [CI] 1.12–1.44; p<0.0001), especially for those on low dose treatment (HR 1.54; 95% CI 1.32–1.81; p<0.0001). Based on individual propensity scores, there was no longer a significant difference in mortality related to digoxin use per se (HR 0.89; CI 0.70–1.13), regardless of the presence (HR 0.90; CI 0.78–1.04) or absence (HR 0.94; CI 0.72–1.23) of underlying heart failure, digoxin dose regime (HR 1.16; 95% CI 0.92–1.45) or persistence of treatment (HR 1.06; 0.83–1.35).

Conclusion: In a large contemporary cohort of AF patients with more granular data than claims based studied, digoxin use was associated with an increased mortality. When differences in patient characteristics were accounted for, digoxin use had a non-significant effect on all-cause mortality regardless of dose, persistence of use, or underlying HF.

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**Table 1**

<table>
<thead>
<tr>
<th>LA thrombus</th>
<th>N</th>
<th>Odds ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA diameter</td>
<td>≥42.5mm</td>
<td>97</td>
<td>4.32 (12.8%) VS265 (3.1%)</td>
</tr>
<tr>
<td></td>
<td>&lt;42.5mm</td>
<td>108</td>
<td>8/6 (17.4%) VS262 (3.2%)</td>
</tr>
</tbody>
</table>

Left atrial size further stratify stroke risk in different CHA2DS2Vasc score.

Conclusion: LA enlargement was an independent risk factor of LA thrombus in patients with non-valvular persistent AF.

Acknowledgement/Funding: High Levels Talent in Health in Beijing (Project 215, No. 2013-3-007)

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**Table 2**

<table>
<thead>
<tr>
<th>n</th>
<th>CHA2DS2-VASC</th>
<th>Odds ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4/32 (12.8%) VS265 (3.1%)</td>
<td>4.50</td>
<td>0.78-26.02 0.090</td>
</tr>
<tr>
<td>1</td>
<td>108/6 (17.4%) VS262 (3.2%)</td>
<td>6.32</td>
<td>1.27-31.34 0.017</td>
</tr>
</tbody>
</table>

Left atrial size further stratify stroke risk in different CHA2DS2Vasc score.

Conclusion: LA enlargement was an independent risk factor of LA thrombus in patients with non-valvular persistent AF.

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**Table 3**

<table>
<thead>
<tr>
<th>n</th>
<th>CHA2DS2-VASC</th>
<th>Odds ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>12/7 (17.4%) VS7 (9.8%)</td>
<td>1.69</td>
<td>0.60-9.40 0.137</td>
</tr>
</tbody>
</table>

Left atrial size further stratify stroke risk in different CHA2DS2Vasc score.

Conclusion: LA enlargement was an independent risk factor of LA thrombus in patients with non-valvular persistent AF.

Acknowledgement/Funding: High Levels Talent in Health in Beijing (Project 215, No. 2013-3-007)
Atrial fibrillation as an independent risk factor for depression in elderly population

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Background: Depression is a frequently comorbid condition in cardiovascular diseases. In contrast to coronary artery disease and heart failure we have a limited amount of data documenting the increased prevalence of depression in patients with atrial fibrillation (AF). Available results from studies with a small number of patients suggest a significant and perhaps two-way relationship between the two diseases. Due to the increasing with age incidence of both atrial fibrillation and its complications, the above issue is a particularly important in elderly patients.

Aim: To determine the frequency of depression in patients with a history of AF in a large group of patients: 65 years of age.

Methods: The data were collected as part of the nationwide PoiSenior project (2003–2011). Of 4,979 individuals (age range 65–104 years), data on self-reported history of AF were available for 4,677 subjects (93.9%). Finally, the 4,049 participants without suspected moderate or severe dementia in Mini Mental State Examination test were assessed with the 15-item Geriatric Depression Scale (GDS), and a score of 6 points and more was regarded as suspected depression.

Results: Mean age±SD of the study population was 78.1±8.3 years; 52% were males. The history of AF was reported by 788 (19.5%) subjects. The proportion of female subjects, obese individuals and the number of cardiovascular comorbidities, frequency of reported diabetes, strokes, falls, osteoporosis/fractures were higher in AF subgroup. In univariate analysis the self-reported AF history was connected with 41% increase of suspected depression (29% vs 41%; p=0.001).

In multivariable logistic regression AF remained an independent predictor of depression (OR=1.42, 95% CI: 1.16–1.73), stronger than heart failure, diabetes or coronary artery disease.

Conclusions: In geriatric population AF is connected with higher frequency of depression than other cardiovascular comorbidities and stroke history and certainly influences the quality of life of these subjects.

Acknowledgement/Funding: The study was implemented under the publicly-funded project No. PBZ-MEIN-9/2/2006 by the Ministry of Science and Higher Education in Poland.

Prevalence of erectile dysfunction in atrial fibrillation patients - cross-sectional, epidemiological study

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Introduction: Sexual dysfunctions, especially erectile dysfunction (ED) are a major problem in cardiovascular patients. They are caused by cardiovascular risk factors including low-grade inflammation process, endothelial dysfunction, oxidative stress, and vascular alterations. The same mechanisms are some of the main causes and/or consequences of atrial fibrillation (AF). To this day, literature provides no cross-sectional data on the prevalence of sexual dysfunction in AF patients.

Methods: A cross-sectional survey of adult male patients with a primary diagnosis of AF was conducted at University Cardiology Departments from 2013 to 2014. During the enrolment participants were either electively hospitalized with a primary diagnosis of AF, or had a scheduled outpatient visit. Sexual dysfunctions were assessed using IIEF score.

Results: 129 consecutive AF patients (mean age 57±11.8 years) were analyzed. Hypertension was present in 60.5%, diabetes in 22.5%, dyslipidemia in 46.5%, smoking in 18.6% and 45.7% had a family history of cardiovascular disease. 86.8% of patients had any kind of sexual dysfunction. ED was present in 57.4% of patients. 44.2% of patients had orgasmic dysfunction, 69.0% had lowered sexual desire, 65.1% had lowered intercourse satisfaction, and 55.8% had lowered overall satisfaction.

Conclusions: Sexual dysfunctions are highly prevalent in AF patients and are not only limited to ED, but also include dysfunction of orgasmic function, desire, or general satisfaction. In part, the presence of the sexual dysfunctions is probably caused by classical cardiovascular risk factors highly prevalent in AF patients, but the impact of AF itself, cannot be underestimated.

The association of non-O blood groups with spontaneous echo contrast.

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Introduction: Non-O blood groups have an association with a higher risk of the arterial and venous thrombosis owing to the relation of non-O blood groups with vWF and VIII levels. Spontaneous echo contrast (SEC) as a manifestation of red cell aggregation, constitute a risk for thromboembolism and mortality. We aimed to assess the relation of ABO blood groups with SEC in non-valvular AF patients.

Materials and methods: 349 patients who were diagnosed as non-valvular AF and performed TEE before cardioversion or AF ablation procedure between 2010–2015, were included. The patients were categorized into two groups as non-O blood groups (228 patients) and 0 blood group (121 patients).

Results: Non-O blood groups had higher SEC prevalence than O blood group (54.8% vs 43.4%; p=0.019). In the subgroup analysis, A blood group had higher SEC prevalence than other groups (49.3% p=0.013). CHA2DS2-VASc score was correlated with the grade of SEC (r=0.534; p<0.001). Also, A blood group was quantified as an additional risk factor and incorporated into CHA2DS2-VASc score by adding 1 point. New score was significantly correlated with SEC grade (r=0.577; P<0.001). In ROC analyses, a cut off value 1.5 score for new risk score has 61.8% sensitivity and 71.4% specificity for prediction of SEC with a higher area under the curve comparing with CHA2DS2-VASc score (AUC=0.739 and AUC=0.697, respectively).

Prevalence of erectile dysfunction in atrial fibrillation patients - cross-sectional, epidemiological study

A.E. Platek, F.M. Szymanski, K.J. Filipiak, G. Opolski, Medical University of Warsaw, 1st Department of Cardiology, Warsaw, Poland

Conclusion: In conjunction with other risk factors, non-O blood types, especially A blood type were demonstrated as independent predictors of SEC in non-valvular AF. Our study proposed A blood group as an additional risk factor to traditional risk scores for thromboembolism. There is a necessity of prospective, larger studies to evaluate the effect of blood groups on thromboembolic events.

Sex-related differences in epidemiologic and clinical presentation of atrial fibrillation in the Balkan countries - insights from the BALKAN AF Snap Shot Survey

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Background: Compared to other European Regions, data on sex-related differences in epidemiologic and clinical aspects of atrial fibrillation (AF) in the Balkan Region are sparse.

Purpose: We report an interim analysis from the Balkan-AF Survey addressing sex-related differences in epidemiologic and clinical presentations of AF patients.

Methods: A 12-week prospective snapshot survey (December 2014-February 2015) of consecutive non-valvular AF patients seen by internal medicine specialists or cardiologists in university/non-university centres in- and outside the capital.
Atrial fibrillation // Atrial fibrillation II

cities was conducted in Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Montenegro, Romania and Serbia (a region with ~45 million inhabitants). Data were collected via an electronic case report form.

**Results:** The interim analysis included a total of 2080 AF patients. Principal sex-related differences in clinical presentation are presented in the Table.

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Females (n=936)</th>
<th>Males (n=1144)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average/mean SD</td>
<td>71.6±9.7</td>
<td>67.0±11.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inclusion setting – hospitalization (%)</td>
<td>71.6</td>
<td>69.3</td>
<td>0.267</td>
</tr>
<tr>
<td>Emergency admissions (%)</td>
<td>73.1</td>
<td>65.4</td>
<td>0.002</td>
</tr>
<tr>
<td>First-diagnosed AF (%)</td>
<td>23.7</td>
<td>23.3</td>
<td>0.795</td>
</tr>
<tr>
<td>Paroxysmal AF (%)</td>
<td>30.7</td>
<td>24.9</td>
<td>0.011</td>
</tr>
<tr>
<td>Symptomatic AF (%)</td>
<td>80.9</td>
<td>77.2</td>
<td>0.040</td>
</tr>
<tr>
<td>Palpitations (%)</td>
<td>51.7</td>
<td>57.6</td>
<td>0.066</td>
</tr>
<tr>
<td>Chest pain (%)</td>
<td>30.9</td>
<td>29.4</td>
<td>0.581</td>
</tr>
<tr>
<td>Dyspnoea (%)</td>
<td>64.8</td>
<td>59.2</td>
<td>0.022</td>
</tr>
<tr>
<td>Fatigue (%)</td>
<td>54.4</td>
<td>48.8</td>
<td>0.026</td>
</tr>
<tr>
<td>General non-well being (%)</td>
<td>30.5</td>
<td>25.4</td>
<td>0.023</td>
</tr>
<tr>
<td>Fear/anxiety (%)</td>
<td>16.3</td>
<td>16.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>82.3</td>
<td>78.6</td>
<td>0.041</td>
</tr>
<tr>
<td>Coronary artery disease (%)</td>
<td>27.6</td>
<td>34.6</td>
<td>0.001</td>
</tr>
<tr>
<td>Coronary angiography (%)</td>
<td>36.7</td>
<td>59.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SLET implantation (%)</td>
<td>18.6</td>
<td>33.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart failure, HF (%)</td>
<td>43.3</td>
<td>43.7</td>
<td>0.589</td>
</tr>
<tr>
<td>HF-Preserved ejection fraction (%)</td>
<td>15.8</td>
<td>12.6</td>
<td>0.036</td>
</tr>
<tr>
<td>Mild valvular heart disease (%)</td>
<td>80.0</td>
<td>67.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>27.2</td>
<td>24.3</td>
<td>0.143</td>
</tr>
<tr>
<td>Peripheral arterial disease (%)</td>
<td>2.9</td>
<td>6.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>COPD (%)</td>
<td>9.6</td>
<td>15.8</td>
<td>0.003</td>
</tr>
<tr>
<td>Chronic kidney disease (%)</td>
<td>13.6</td>
<td>16.3</td>
<td>0.085</td>
</tr>
<tr>
<td>Anaemia (%)</td>
<td>17.9</td>
<td>11.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dementia (%)</td>
<td>4.1</td>
<td>1.8</td>
<td>0.003</td>
</tr>
<tr>
<td>Thyroid disease (%)</td>
<td>16.5</td>
<td>6.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke/TIA (%)</td>
<td>3.9</td>
<td>12.3</td>
<td>0.236</td>
</tr>
<tr>
<td>Systemic embolism (%)</td>
<td>1.2</td>
<td>0.8</td>
<td>0.141</td>
</tr>
<tr>
<td>Pulmonary embolism (%)</td>
<td>2.7</td>
<td>1.2</td>
<td>0.022</td>
</tr>
<tr>
<td>Previous bleeding events (%)</td>
<td>5.8</td>
<td>5.2</td>
<td>0.561</td>
</tr>
<tr>
<td>CHA2DS2-VASc ≥ 2 (%)</td>
<td>87.1</td>
<td>77.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HASBLED ≥ 3 (%)</td>
<td>34.2</td>
<td>26.1</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Conclusions:** Female AF patients in the BALKAN AF Survey were older, more symptomatic, with more comorbidities and required more emergency hospitalizations. The rate for AF was higher in females, bearing implications for antithrombotic treatment.

**Methods:** This prospective study, 116 patients underwent catheter ablation of persistent AF. Left atrial geometry (LA) was reconstructed with a 3.5 mm tip ablation catheter with fill-in threshold 10 in CARTO system. The mapping catheter was stabilized at each endocardial location for at least 3 seconds for recording. The electrogram recordings at each endocardial location were analyzed with a custom software embedded in the CARTO mapping system. Interval confidence level (ICL) was used to characterize complex fractionated atrial electrograms (CFAEs). As the default setting of the software, ICL more than or equal to 7 was considered sites with a highly repetitive CFAEs complex. CFAEs index was defined as the fraction of area of ICL more than or equal to 7 to the left atrial surface. The CFAEs index and outcome of catheter ablation among different CHA2DS2-VASc groups were compared.

**Results:** Of the 116 patients, 33 patients had CHA2DS2-VASc = 0, 31 patients had CHA2DS2-VASc = 1, 52 patients had CHA2DS2-VASc ≥ 2. There are significant differences of left atrial surface (121.2±18.9 cm², 133.6±23.8 cm², 133.9±16.1 cm², P=0.008), left atrial volume (103.6±24.8 ml, 118.3±27.8 ml, 120.9±20.9 ml, P=0.05) and CFAEs index (44.6±22.4%, 54.2±22.2%, 58.7±23.1%, P=0.023) among the three groups. There are no difference of ICLmax, ICLmin, CFAEs spatial distribution among the three groups. After a mean follow-up of 13±8 months, the recurrence rate was 36.4%, 35.5%, 58.8% among the three groups (P=0.025) (Figure 1).

**Conclusion:** A high CHA2DS2-VASc score was associated with extensive AF substrate and poor outcome of catheter ablation of persistent AF. **Acknowledgement/Funding:** High Levels Talent in Health in Beijing (Project 215, No. 2013-3-007)

**ATRIAL FIBRILLATION II**

**P5274 | BEDSIDE**

**CHAD2DS2-VASc score predicted extensive substrate and poor outcome of catheter ablation of persistent atrial fibrillation**


**Objective:** This study sought to explore if CHAD2DS2-VASc score can predict substrate for persistent atrial fibrillation (AF) and outcome of catheter ablation of AF.

**Methods:** In this prospective study, 116 patients underwent catheter ablation of persistent AF were enrolled. Left atrial geometry (LA) was reconstructed with a 3.5 mm tip ablation catheter with fill-in threshold 10 in CARTO system. The mapping catheter was stabilized at each endocardial location for at least 3 seconds for recording. The electrogram recordings at each endocardial location were analyzed with a custom software embedded in the CARTO mapping system. Interval confidence level (ICL) was used to characterize complex fractionated atrial electrograms (CFAEs). As the default setting of the software, ICL more than or equal to 7 was considered sites with a highly repetitive CFAEs complex. CFAEs index was defined as the fraction of area of ICL more than or equal to 7 of the left atrial surface. The CFAEs index and outcome of catheter ablation among different CHAD2DS2-VASc groups were compared.

**Results:** Of the 116 patients, 33 patients had CHA2DS2-VASc = 0, 31 patients had CHA2DS2-VASc = 1, 52 patients had CHA2DS2-VASc ≥ 2. There are significant differences of left atrial surface (121.2±18.9 cm², 133.6±23.8 cm², 133.9±16.1 cm², P=0.008), left atrial volume (103.6±24.8 ml, 118.3±27.8 ml, 120.9±20.9 ml, P=0.05) and CFAEs index (44.6±22.4%, 54.2±22.2%, 58.7±23.1%, P=0.023) among the three groups. There are no difference of ICLmax, ICLmin, CFAEs spatial distribution among the three groups. After a mean follow-up of 13±8 months, the recurrence rate was 36.4%, 35.5%, 58.8% among the three groups (P=0.025) (Figure 1).

**Conclusion:** A high CHA2DS2-VASc score was associated with extensive AF substrate and poor outcome of catheter ablation of persistent AF. **Acknowledgement/Funding:** High Levels Talent in Health in Beijing (Project 215, No. 2013-3-007)

**ATRIAL FIBRILLATION II**

**P5275 | BEDSIDE**

**Diastolic electrocardiographic parameters and diastolic index predict postoperative atrial fibrillation**


**Background:** Postoperative atrial fibrillation (POAF) is an important cause of morbidity and mortality. Diastolic dysfunction (DD) has significant pathological effect on atrial structure and function, many of which are proarrhythmic. It has been shown that diastolic ECG parameters like PQ, QTc, Tend-P, Tend-Q and a combined novel ECG index (Tend-P/QTc X Age) provides a good diagnostic performance for the recognition of DD. In our study, we aimed to investigate the relation between diastolic ECG parameters, novel diastolic ECG index and POAF in patients undergoing elective coronary artery bypass surgery (CABG).

**Methods:** Patients who will undergo CABG electively without a history of atrial fibrillation were included in the study. POAF was defined as at least 30-second
duration of AF detection. PQ interval was calculated from the beginning of the P wave to the beginning of the QRS complex manually. The QTc interval was calculated using the Bazett formula, Tend-P and Tend-Q intervals were calculated as: RR minus PQ minus QT for Tend-P and RR minus QT for Tend-Q. Diastolic ECG index was calculated as follows; Tend-P PQ x Age. Results: A total number of 311 patients (age 60±18.7 years, %34.1 women) were included in our study prospectively. Only 71 (22.8%) of them developed POAF during their postoperative follow-up. Patients were divided into two groups according to observation of AF: Group-1 (POAF+) and Group-2 (POAF-). Demo-graphics and transthoracic ECG parameters are similar between two groups. QT intervals were similar in both groups, however PQ interval (161.4±32.6 vs 147.0±15.1 ms, p=0.01) and QTc (449.3±38.3 vs 426.9 vs 47.6) was significa- ntly longer in Group-1. Mean heart rate was significantly higher in Group-1 and CHADS2. Tend-P, Tend-Q and CHADS2 intervals were significantly shorter in Group-1. Di- astolic ECG index was significantly different between two groups (0.04±0.017 vs 0.058±0.010, p=0.01). Diastolic ECG index was also significantly negatively correlated with POAF (r=−0.463, p<0.01). Univariate analysis revealed age, hy- pertension, preoperative calcium levels, heart rate, Tend-P, Tend-Q, PQ intervals and QTc may be predictors of POAF occurrence. Multivariate analysis showed ECG parameters like Tend-P, Tend-Q, QTc, PQ intervals with heart rate were only statistically significant predictor of POAF.

Conclusion: Diastolic ECG parameters and novel diastolic index predicts POAF aha (p=0.03). Conclusion event rate of primary outcome

Conclusion: This research received no grant from any funding agency in the public, commercial or not-for-profit sectors.

**P5276 | BEDSIDE**

Risk prediction in atrial fibrillation. Comparison between the CHADS2, CHA2DS2-VASc score in a large contemporary cohort of patients with incident non-valvular atrial fibrillation

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Introduction: The 2 most commonly used risk scores to predict thromboembolic events in patients with atrial fibrillation - AF are the CHADS2 and the CHA2DS2-VASC. There is a controversy as to which score performs better.

Aim: To compare and describe the predictive ability of these risk scores in a large contemporary cohort of patients with non-valvular atrial fibrillation.

Methods: We used a computerized database of 2,420,000 adults, includes data of community clinic visits, hospital discharge records, medical diagnoses, med- ications, medical interventions and laboratory test results. During 2004-2012, 98,811 patients had nonvalvular AF.

Results: The distribution of risks is presented in figure. The rate of stroke and death (heart failure) is shown based on risk category in table. The predictible ability of CHADS2 was somewhat better for prediction of stroke (c-statistic 0.65) as compared to the CHADS VASC score (c statistic 0.64), and they performed similarly for predicting mortality (c-statistic of 0.69 for both) and the net reclassification index was decreased when moving from the CHADS2 to CHA2DS2-VASC score by 14% for mortality and by 7% for stroke.

Death and stroke based on risk category

<table>
<thead>
<tr>
<th>Risk class</th>
<th>Percent in population (%)</th>
<th>Stroke rate (%)</th>
<th>Death rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHADS2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>25.0</td>
<td>1.4</td>
<td>10.1</td>
</tr>
<tr>
<td>1</td>
<td>22.8</td>
<td>3.3</td>
<td>12.3</td>
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<tr>
<td>2</td>
<td>22.0</td>
<td>6.6</td>
<td>31.3</td>
</tr>
<tr>
<td>CHA2DS2-VASc</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>57.0</td>
<td>0.8</td>
<td>8.5</td>
</tr>
<tr>
<td>1</td>
<td>20.1</td>
<td>1.6</td>
<td>10.1</td>
</tr>
<tr>
<td>2</td>
<td>22.9</td>
<td>5.8</td>
<td>41.1</td>
</tr>
</tbody>
</table>

Conclusions: Both risk scores perform similarly but the CHADS2 performed somewhat better for ischemic stroke prediction and significantly better for pre- diction of mortality.

Acknowledgement/Funding: Pfizer

**P5277 | BEDSIDE**

Effectiveness of structured hospital based nurse-led atrial fibrillation clinics: A comparison of a real-world population versus a clinical trial population


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Aims: A randomized trial has documented that structured nurse-led Atrial Fibril-

lation (AF) service is superior to conventional AF service, but there is a need for more data, confirming feasibility and outcome in a real-world setting. We com- pared patient outcome in nurse-led structured hospital AF clinics between real- world patients from Denmark (DK) and from the randomised trial on efficacy of a nurse-led AF clinic reported from the Netherlands (NL), with respect to a com- plete outcome of CV hospitalization and CV death.

Methods: Real-world data consisted of baseline and follow-up data. All patients were referred by cardiologists. The AF nurse specialist provided patient educa- tion, risk factor control, and stimulated empowerment and compliance in these patients. During follow-up treatment was adjusted according to clinical guidelines, supervised by a cardiologist. Patient education was repeated and compliance was controlled. The study size was powered as a non-inferiority study. Outcome mea- sures were adjudicated by same principles in both countries.

Results: 985 patients from DK and 356 patients from NL were included. There were no significant differences between groups with respect to age, body mass index, type of AF, CHA2DS2VASC score and co-morbidity. The composite primary end point occurred with an incidence rate of 8.0 in DK and 8.3 per 100 person years in NL, crude HR 0.83 (95% CI 0.56–1.23). Adjustment for covariates and medical treatment did not substantially change HR.
Background: Non-Valvular Atrial Fibrillation (AF) patients show high residual cardiovascular risk despite oral anticoagulants. Urinary 11-dehydro-thromboxane B2 (TXB2) is associated with an increased rate of CVEs in anticoagulated patients with AF.

Method: Prospective single-center cohort study, including 864 AF patients treated with vitamin K antagonists (VKAs). Mean time of follow-up was 30.0 months yielding 2062 person-years of observation. Urinary 11-dehydro-TXB2 was measured at baseline. The primary end-point was the occurrence of a CVE including fatal/nonfatal myocardial infarction and ischemic stroke, transient ischemic attack, cardiac revascularization and cardiovascular death.

Results: Mean age of patients was 73.1 years, and 43.6% were women. Median 11-dehydro-TXB2 levels were 100 [IQR 50–187] ng/ml of urinary creatinine. Overall, the anticoagulation control was adequate (63.9% of mean time in therapeutic range). A CVE occurred in 98 (11.3%) patients, 55 were cardiovascular events and 43 were cerebrovascular events. Cox proportional hazards analysis showed that tertile of 11-dehydro-TXB2 (3rd vs. 1st hazard ratio [HR] 4.71 95% confidence interval [CI] 2.46–9.03, p < 0.001, age >75 years (HR: 1.79 95% CI 1.17–2.74, p = 0.007), diabetes (HR: 1.72 95% CI 1.07–2.76, p = 0.0245), history of stroke/TIA (HR: 1.96 95% CI 1.24–3.10, p = 0.0042) and myocardial infarction (HR: 1.62 95% CI 1.04–2.53, p = 0.0322) were predictors of CVEs.

Conclusions: Urinary 11-dehydro-TXB2 levels predict residual risk of CVEs and cardiovascular mortality in AF patients despite treatment with oral anticoagulants.

P5280 | BEDSIDE
Rate control or rhythm control - what do we choose more often in patients with higher thromboembolic risk? Data from a multicenter real-life registry

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Introduction: In atrial fibrillation (AF) patients both management strategies - rate control or rhythm control seem to be equally safe and effective. Decision on the way of patients treating depends on patients and doctors preferences. However, in everyday clinical practice we observe some disparities between patients on rate and rhythm control strategies.

Purpose: The aim of this study was to compare the group of persistent AF patients in whom the rhythm control strategy is taken and those in whom the rate control strategy is chosen.

Methods: We analyzed data from a prospective multicenter registry of continuous AF patients. All patients included in the study were hospitalized in one of the participating clinics with a primary diagnosis of paroxysmal AF between 2011 and 2014. Patients had their medical data collected by a qualified physician basing on the medical records or a de novo diagnosis during the current hospitalization. Thromboembolic risk of patients was assessed using CHADS2 and CHA2DS2-VASc scores.

Results: Out of the 1205 hospitalization due to AF occurring in the given time period we chose 341 cases of unique AF patients. Mean age of the study population was 69.6±13.2 years, a their mean body mass index (BMI) was 29.4±6.4 kg/m2. Persistent AF patients in whom the rhythm control strategy was chosen were younger (65.2±13.6 vs. 74.0±11.1; p < 0.001). There were no differences in terms of thromboembolic risk despite oral anticoagulants. Urinary 11-dehydro-thromboxane B2 (TXB2) is associated with an increased rate of CVEs in anticoagulated patients with AF.

Conclusions: Persistent AF patients in whom the rhythm control strategy is taken are younger and have less comorbidities, therefore their thromboembolic risk in both CHADS2 and CHA2DS2-VASc scores is lower than in patients on rate control strategy (permanent AF). Total thromboembolic risk is one of the factors taken into consideration in choosing treatment strategy in real-life AF patients.

P5281 | BEDSIDE
Being diagnosed with atrial fibrillation/flutter is associated with lower perceived physical health - a Danish cross sectional study

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Background: Reports on self-reported health-related quality of life and health status in patients living with atrial fibrillation (AF) have been deviating; from being similar to those of patients who have sustained and survived a myocardial infarction to no difference, when compared with healthy subjects. Low sample sizes have, however made stratification on gender impossible in earlier studies.

Purpose: To investigate the association between the diagnosis of AF and self-reported health status.

Methods: An observational, cross-sectional study was conducted, using data from the Danish Diet, Cancer and Health cohort. Information on health status was obtained using the Danish Short Form 36 version 2 (SF-36v2) questionnaire. The analyses were stratified on gender. In adjusted analyses, we considered potential confounding from comorbidity expressed by the Charlson Comorbidity Index and effect modification by age.

Results: We included 42,598 participants in the study; 873 of the participants had the diagnosis of AF and/or atrial flutter. We found a lower adjusted physical health score in previously known AF patients compared with a non-AF participant of 2.63 points [95% CI: 1.77; 3.48] for men and 3.44 points [95% CI: 1.84; 5.04] for women. The mental component score was 0.28 [95% CI: −0.63; 1.19] lower in men and 0.98 points [95% CI: −0.67; 2.63] lower in women.

Conclusion: Being diagnosed with AF report a clinically relevant and statistically significantly lower physical health component score compared with the remaining participants in the cohort, but no systematical differences in the mental component score. When caring for patients living with AF, it is important to be aware that even though patients with AF do not need much physical attention, they report a lower physical component score and therefore their individual perception of symptoms leading to physical limitations should be articulated.

Acknowledgement/Funding: The study was financially supported by a research grant from the Danish Council for Strategic Research (grant number 09-066965).

P5282 | BEDSIDE
Atrial fibrillation/flutter underdiagnosed in general practice - the PROFIL FA awareness campaign results in patients above 80y

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Introduction: AF in patients above 85 y is a strong risk factor for stroke and anticoagulation should be considered. But early diagnosis is often difficult and in up to 20% of AF related strokes, AF is discovered too late at the time of the stroke. Use of a symptom targeted questionnaire in general practice (GP) was shown to improve early AF diagnosis if the PROFIL FA campaign. In patients 80+, AF is highly prevalent and stroke is a big concern, in relation to disability and dementia burden.

Methods: During one week, GP asked all their consecutive patients above 60 y if they had ever had palpitations, chest pain, shortness of breath, or dizziness. If AF episodes could be suspected, the patient was referred to a cardiologist for confirmation or not. Risk scores for stroke and anticoagulation therapy were obtained.

Results: 6301 patients from 622 GP were questioned, 2126 aged >80y (group 80+) (85y, 53% F) and 4175 aged >80y (group AF) (71y, 42% F). AF was previously known more frequently in older patients: in 564 patients in 80+ (26%) vs 653 in 80- (26%). Following questionnaire, AF was similarly suspected in 232 in 80+ (11%) vs 422 in 80- (12%). Out of these AF suspected patients, AF was newly diagnosed by the cardiologist in 46 in 80+ (26%) and 318 in 80- (30%). Symptoms of palpitations, dizziness, or chest pain, and more often shortness of breath were highly prevalent in AF older patients, respectively for 23%, 14%, 6.2%, and 38% in 80+, and for 24%, 12%, 6.6% and 28% in 80-. An irregular pulse was related to AF only in 1 out of 2 patients, similarly in 80+ (49%) and in 80- (58%). CHADS2 scores were higher in 80+.

Following the campaign, anticoagulation was initiated similarly in 80+ (61%) and 80- (78%), at a level as already 22% and 19% were on anticoagulation.

Conclusion: Systematic symptoms search is worthy in 80 y old patients, and can yield AF diagnosis in 26% of patients. Anticoagulation was increased in 61% of these patients. A symptoms targeted questionnaire approach should be recommended in family practice.
P5283 | BEDSIDE
Stroke history as predictive criteria for further atrial fibrillation diagnostic: French screening campaign of atrial fibrillation (PROFIL FA) in general practice

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Purpose: Atrial fibrillation (AF) (750 000 patients in France) is a severe disease with important consequences in terms of morbidity and mortality but still under-diagnosed. Boehringer Ingelheim pursued in 2014 the screening campaign begun in 2013 (PROFIL FA) among family physicians in France, with a simple questionnaire based on heartbeat measurement, AF linked symptoms and thromboembolic risk.

The main objective of this second part of the study was to confirm or not the most predictive factors of the disease identified in the first part, and to provide a simple tool to improve screening and diagnosis of AF in patients over 65.

Methods: Main predictive factors of AF were identified, from questionnaire results, using a logistic regression model. A prognostic score was estimated and its predictive performance investigated using the ROC curve.

Results: 6 301 patients were screened. 612 were oriented to a cardiology specialist and 155 were diagnosed with AF. The statistical analysis was performed on the sample of oriented patients. The logistic regression model identified 3 predictive factors of AF: irregular heartbeat (OR=13.5, p<0.0001), stroke history, transient ischemic attack or peripheral embolism (OR=2.1, p=0.04) and presence of at least two of the following symptoms: faintness, palpitations, chest pain and shortness of breath (OR=2.7, p=0.0001). An AF prediction based only on irregular heartbeat (1st criteria) showed a sensitivity of 77.2% and a specificity of 81.2%, its positive predictive value was 58.1%. It represents the main predictive criteria of AF.

The presence of at least two symptoms in patients having a stroke history improves sensitivity (81.9%) while maintaining good specificity (78.7%).

Screening campaign showed that applying strictly those latest criteria to patients of the screened cohort could have potentially led to diagnosis of 94 additional AF.

However, 27 patients (all with regular heartbeats) with FA would have been missed.

Further investigations were conducted on the sample of patients over 80. Two predictive factors of AF were identified: irregular heartbeat (OR=13.2, p<0.0001) and history of lipothyroidism (OR=2.6, p<0.02). Analyses are still underway.

Conclusion: This complementary study confirms that measure of heartbeat is the main predictive criteria in patients over 65, but patients with a regular heartbeat should also be considered. They should systematically be referred to a cardiologist in case they present at least two symptoms and a stroke history.

P5284 | BEDSIDE
Risk of incident atrial fibrillation in patients presenting with retinal artery or vein occlusion: a nationwide cohort study

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Background: Retinal artery or venous occlusions are associated with cardiovascular risk factors. Whether a presentation with retinal artery or venous occlusions could predict the occurrence of silent AF has not been established yet. The aim is to assess prevalence and predictors of silent AT with continuous 7-day ECG Holter monitoring applied in patients at risk for AF.

Methods: We enrolled consecutive patients, 65 years of age or older, with left atrium diameter at echocardiographic exam, defined as left atrium indexed volume >108 ml/m2 detected at transcranial echocardiography (TTE), and the presence of at least one of the following clinical risk factors: hypertension with left ventricular hypertrophy, defined as left ventricular mass >108 g/m2 for women and >131 g/m2 for men, and >131 ml/m2 detected at TTE; heart failure with left ventricular ejection fraction <35%; previous myocardial infarction with left ventricular ejection fraction <35%; previous cerebral ischemic event defined as transient cerebral ischemic attack. All patients underwent continuous 7-day ECG Holter monitoring and TTE.

Results: Of 1712 screened patients, 142 were included in the study (mean age 72.6±7.4 yrs, 65% males). The mean CHA2DS2 Vasc Score was 3.5±1.3, with a mean HAS-BLED score of 2.0±0.5. Subclinical AT detected by continuous 7-day Holter monitoring had occurred in 31 patients (22%). Mean duration was 30 s (10s-90s), with a mean of 6 episodes/patient. At the univariate comparison, patients with AT had a higher body mass index (BMI; 23±3 vs 29±5; P=0.002), had more often significant mitral stenosis (27% vs 5%; P=0.006) and intraventricular septum thickness (14±3 vs 12±2 mm; P<0.02). At the multivariate logistic regression analysis, mitral stenosis (OR=8.09, CI 95% 1.65–39.8, P=0.01) and interventricular septum thickness (OR=1.46 CI 95% 1.11–1.94, P=0.01) were identified as independent predictors of AF, whereas a higher BMI had a protective effect (OR=0.81, CI 95% 0.66–0.99, P=0.03).

Conclusion: In a high risk population, the occurrence of silent AT detected is not uncommon and is predicted by mitral stenosis, intraventricular septum thickness, and BMI.

P5286 | BEDSIDE
The relationship between the frequency of paroxysmal episodes of atrial fibrillation and left atrial function as measured by strain imaging

K.G. Adamyan1, A.L. Chilingaryan2, L.G. Tunyan3, L.R. Turnasyan4, 1Institute of Cardiology, Yerevan, Armenia

Objective: The objective of the study were (i) to reveal the role of strain (S) and strain rate (SR) imaging (SRI) and their prognostic power in the left atrial (LA) function changes among patients (pts) with paroxysmal atrial fibrillation (PAF); (ii) to establish the LA reservoir function by SRI for the relationship between the frequency of symptomatic arrhythmic episodes and echocardiographic data.

Methods: 54 pts with lone PAF for 4-15 years, 36 m were assessed by the standard echo-Doppler study (LA diameter, minimum and volumes, LA compliance index) and by Doppler myocardial imaging (velocity, S, and SR of LA). The difference between LA maximum and minimum volumes divided by the minimum LA volume was used as an index of LA compliance.

Pts were divided into two groups. Based on the frequency of their symptomatic AF paroxysms. The first group (n=28) included pts with paroxysms frequency of no more than one time in a three-month period. The pts of the second group (n=26) had more than one paroxysm during the same three-month period. AF paroxysms numbers in all groups were between 1 to 12 months.

Results: In the second group the S from both the septal (S-LAs) and lateral (S-Lae) portion of the LA were significantly lower compared to the first group (S-LAs (%): 24.5±2.5 vs. 13.5±4.1, P<0.001; S-Lae (%): 8.0±2.5 vs. 0.5±2.1, P<0.001). Frequent AF paroxysms correlated significantly with LA ejection force (r=−0.57, P<0.005), emptying fraction (r=−0.61, P<0.005) and S-LAs (r=−0.54, P<0.005). Both the LA diameter and volumes were significantly increased in the second group (P<0.005). Atrial myocardial velocities and deformation indices were sig-
nificantly compromised in the second group (P < 0.005). Significant negative correlation was found between the LA myocardial velocity and LA volumes (R = 0.58; P < 0.05). Peak systolic LA myocardial S and SR were significantly correlated with LA volumes (R = 0.56; P < 0.05; SR: R = −0.49; P < 0.05; compliance index (S: R = 0.47; P < 0.05; SR: R = −0.48; P < 0.05), ejection fraction (S: R = 0.53; P < 0.05; SR: R = −0.51; P < 0.05).

In multivariate analysis, the best predictor of repeated AF paroxysms was LA peak systolic LR average with a sensitivity of 85%, specificity of 81%.

Conclusion: LA myocardial deformation properties, assessed by SRI, are abnormal in AF paroxysms group. The degree of this impairment is predictor of AF paroxysms and this could be used as an indicator of gradual mechanical remodeling of the LA, which may favor recurrence and perpetuation of AF.

ATRIAL FIBRILLATION II

P5287 | BENCH

Predictors of atrial fibrillation: Late Gadolinium Enhancement MRI study to assess atrial fibrosis

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Introduction - Atrial fibrillation (AF) is a common arrhythmia in patients with rheumatic heart disease (RHD). Late Gadolinium Enhancement (LGE) MRI can identify atrial scarring. Data on in vivo distribution of atrial scarring in RHD patients is lacking. We lack LGE to quantify atrial scarring in RHD and to define predictors for developing AF.

Methods: Consecutive patients with mild to moderate rheumatic mitral valve disease were prospectively studied. After sample-size calculation, we planned to include 35 consecutive patients and 30 in sinus rhythm (SR). Clinical, echo and LGE MRI data were analyzed.

Results: Mean age was 32.6 years, 63% were females and 83% had isolated mitral valve disease. Mean left atrial (LA) diameters was 4.6±0.51cm and volume was 73.0±7.3 ml. All patients were on beta blockers and 7 were on amiodarone. Median duration of AF was 12 months (range 6-48). Atrial fibrosis was more common in AF patients compared to those in SR (100% vs. 33%, P < 0.001) with more involvement of the LA than the right atrium (44% vs. 20% in the SR group and 86.7% vs. 63.2% in the AF group). The posterior wall was the most frequently involved (26.7% in the SR group and 86.7% in the AF group). Severe fibrosis was more common in long standing AF (n=11) compared to persistent (n=9) and paroxysmal (n=10) (100% vs. 44% vs. 0, P < 0.001). LA fibrosis was the most important predictor of AF (OR 5.8, 95% CI 2.63–13, P < 0.001). Atrial fibrosis maintained its statistical significance among clinical and echocardiographic data using Stepwise multiple regression analysis with R=0.8 and P < 0.001 (Standardized Coefficients Beta was 0.58, 0.56 and 0.26, P value was <0.001, <0.001 and 0.47 for LA fibrosis, LA volume and mitral valve area respectively).

Conclusions: AF is associated with more atrial fibrosis in RHD patients. Severity of atrial fibrosis is a stronger predictor of AF compared to valve disease severity or LA size which may play a role for patient selection for catheter ablation in this subset of AF.

P5288 | BEDSIDE

Predictors for atrial fibrillation in patients with coronary artery disease: a cross-sectional analysis of BOREAS registry data


Background: Atrial fibrillation (AF) is the most common cardiac arrhythmia and is associated with increased cardiovascular morbidity and mortality. Previous studies have shown that hypertension, valvular disease, heart failure, age and male gender are the predictors of AF in general population. However, differences in the predictors of AF in general population. However, differences in the predictors of AF in general population. However, differences in the predictors of AF in general population. However, differences in the predictors of AF in general population. However, differences in the predictors of AF in general population. However, differences in the predictors of AF in general population.

Methods and results: We analyzed data from 14731 patients in the BOREAS-CAD2 Registry. Patients with moderate or severe mitral valve disease and those with history of coronary angioplasty were excluded (n=960), and thus 911 patients contributed to the present analysis. Patients were divided into two groups: patients with CAD and 6% of patients in the CAD group had AF. In both the non-CAD and CAD groups, age, and proportions of males, hypertension and diabetes were similar in patients with and without AF. In the non-CAD group, patients with AF had larger left atrial dimension (LAD: 43±7.8 vs. 39±6.9 mm), lower left ventricular ejection fraction (LVEF: 55±13.9 vs. 61.8±11.8%), lower estimated glomerular filtration rate (eGFR: 56±21.7 vs. 67.1±23.4 ml/min/1.73m2) and higher brain natriuretic peptide (BNP: 274±276 vs. 113±209 pg/ml) than those without AF, while body mass index (BMI) was similar in patients with or without AF. In the CAD group, AF patients had larger LAD, lower LVEF, lower eGFR (51.7±26.8 vs. 65.7±30.5 ml/min/1.73m2), higher BNP, higher uric acid (6.6±2.8 vs. 6.0±1.7 mg/dl) and lower BMI (22.4±3.9 vs. 24.5±3.8 kg/m2) than patients without AF. Multivariate logistic regression analysis revealed that larger LAD and higher BNP were significantly associated with AF in the non-CAD group, whereas that higher uric acid and lower BMI were significantly associated with AF in the CAD group.

Conclusions: Predictive factors for AF are different between patients with and without CAD. Renal dysfunction may have greater impact on the development of AF in patients with CAD that in those without CAD.

P5290 | BEDSIDE

Predictors of non valvular atrial fibrillation in a large cohort of ambulatory patients. A survey from a large data base of a GP group

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Background: Non Valvular Atrial Fibrillation (NVAF) is a common condition in the general population. The prevalence of NVAF is reported to be 2% in several studies. However, prevalence varies with age and sex. Furthermore, there is evidence of significant heterogeneity in estimations and availability of population-based data. In our area General Practitioners (GPs) are organized in groups and work with a common medical practice management software (Millewish). All clinical information from patients are prospectively recorded and are stored in a common database. Aim of this survey was to evaluate the prevalence, age distribution and therapeutic choices from the common database offered by the common informatic platform of the GPs.

Methods: We identified 10 GPs with a sufficient quality of data recording and a large number of assisted patients. Data of a recent on site was checked by verifying the adherence to a program of proactive assistance which included the assessment of the cardiovascular risk in their patients. Only those GPs reaching a target >90% of adherence to the protocol were invited to the data collection of this survey.

Results: Data from 14731 pts (16 years were collected and analysed. NVAF was found in 563 Patients, thus representing a prevalence in this population of 3.82%. The gender distribution was similar (50.8% Males, 49.2% Females). Among the NVAF group, 9.2% of the patients were less than 65 years old, while the oldest age was older (62.7% in the Group 65–84 years old). 30% of patients with NVAF was older than 85. Patients older than 85 years old represent 5.22% of the whole population examined. In this older group of patients the prevalence of NVAF was 16%. Fifty-seven percent of these NVAF patients were on treatment with oral anticoagulation (VKA and NOAC). The percentage of treated patients increased to 68% when considering only permanent NVAF.

Conclusions: The prevalence of NVAF in this population-based cohort is higher than that reported in previous studies. This may depend on a different age distribution of our population with respect to previous studies. Our results confirm and reinforce the concept that NVAF is a common condition in the general population particularly in the oldest subjects. In the real world more than 40% of NVAF patients do not receive an adequate antithrombotic therapy. Access to GPs Medical records allow to gain real-world information that can be used to promote and monitor public health actions.

P5290 | BEDSIDE

Critical coronary atherosclerosis in patients with recent onset atrial fibrillation and troponin rise

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Background: In patients with atrial fibrillation (AF), the presence of comorbidity (excluding coronary artery disease (CAD)) could contribute to excess mortality, beyond systemic embolism. Evidence to look for the presence of CAD that in those without AF and severe comorbidities were enrolled. Baseline characteristics in those with troponin rise versus those without were adjusted with the propensity score matching for possible confounders. SPSS software allowed estimation of the propensity-score using logistic regression and specifying nearest neighbor matching in prior-stroke, heart-rate, hypertension, TIMI-risk score, GRACE score, CHADS2/ Vasc score. Patients with a troponin rise or adverse cardiovascular event (CVE) were considered for angiography. The primary endpoint was the composite of ACS, critical coronary stenosis > 70%, revascularization and cardiac death at the follow-up; the secondary endpoint was stroke.

Results: Out of 10250 patients with supraventricular tachyarrhythmias, 6203 with recent onset AF and without severe comorbidities were considered, 3627 with recent onset AF, 905
were enrolled and 3541 completed the study (86 patients lost at follow-up); finally 202 (6%) showed a troponin rise, 91 (3%) a CVE. After matching no difference existed in baseline characteristics. On multivariate analysis, in the entire cohort, troponin rise, know CAD and hypertension were predictors of the primary end-point, whereas only troponin rise (Odd Ratio: OR, 10. Confidence Interval 95%, CI: 4.8–22, p < 0.001) and TIMI score >2 (OR 4.1, CI 2.9–5, p < 0.001) in the matching cohort, suggesting the role of CAD in poor outcomes. Patients with or without troponin rise achieved the endpoint in 38 (19%) and 43 (1%), respectively (p < 0.001). Stroke occurred in 4 (2%) and 20 (1%), respectively (p = 0.018). “Critical” CAD account for 23 (12%) and 15 (1%), respectively (p < 0.001). In the matching cohort, only stroke did not reach the statistical significance. Interestingly, the best cut-off level for decision making was 0.30 ng/L which, on Receiver Operator Curve analysis, was associated with 68% of sensitivity and 60% specificity: the value best correlated with history and ejection fraction (p=0.04). In this real-life study, Spanish patients newly diagnosed with NVAF were elderly, with a small majority of women, and frequently had comorbidities of cardiovascular importance such as hypertension and diabetes. VKA was the most prescribed anticoagulant for AF in this time period. As more patients treated with NOACs accumulate in Spain, research should continue to address NVAF patient population.

Acknowledgement/Funding: This study was funded by Bristol-Myers Squibb.

P5293 | BEDSIDE Does routine function affect clinical course and management in patients with atrial fibrillation?
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Background: There are scarce data concerning renal function in population with valvular and non-valvular atrial fibrillation (AF).
Methods: We assessed renal function in patients with AF, the association between eGFR and AF perpetuation. The patients with impaired renal function (eGFR <60ml/min) were older (p=0.001), they were more frequently females (p=0.001), had more often per- manent AF (p=0.001), diabetes (p=0.001) anaemia (p=0.001, p=0.001), respectively. The reason of admission to hospital was more frequently exacerbation of chronic heart failure (p=0.001), acute heart failure (p=0.001) and non-ST elevation myocardial infarction (p=0.006). There were more frequently given reduced dose of non-VKA (p=0.001), also less often VKA (p=0.01) and not given antithrombotic treatment at all despite it was indicated (p=0.05). The use of non-VKA was similar in both groups (p=0.7). Cardioversion in the group with CKD was done less frequently (p=0.03). Patients with eGFR <60ml/min had also lower ejection fraction (p=0.004), and larger left atrium (p=0.04). The patients with CKD had higher hospital mortality (p=0.04), Paroxysmal type of AF was less observed (p=0.001, p<0.001) and more likely female, had a higher CHA2DS2-VASc score, had more HT and DM, and were more likely to receive VKA/NOAC (p=0.001). They also had more cases of stroke (p=0.001), in this period but discontinued therapy before stroke; and 11.4% received VKA/NOAC only at time of stroke.
Conclusion: In this real-life study, Spanish patients newly diagnosed with NVAF were elderly, with a small majority of women, and frequently had comorbidities of cardiovascular importance such as hypertension and diabetes. VKA was the most prescribed anticoagulant for AF in this time period. As more patients treated with NOACs accumulate in Spain, research should continue to address NVAF patient population.

Acknowledgement/Funding: Our study was supported by Leading National Research Center in Bialystok, Poland (KNOW)

P5294 | BEDSIDE The impact of new onset atrial fibrillation on mortality and morbidity in patients with acute coronary syndrome
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Background: There is a strong evidence that patients (pts) with atrial fibrillation (AF) and acute coronary syndrome (ACS) constitute a high-risk population, however the prognostic importance of new onset AF in these pts remains unclear. The aim of this study was to determine in-hospital and long-term mortality in pts with ACS and new onset AF.
Methods: We conducted the cohort study, which included consecutive 644 pts with ACS diagnosed according to the ESC guidelines, hospitalized in the Depart-
mortality in follow-up, in pts with ACS. In pts with ACS and new onset AF follow-up revealed higher rate of LVEF in TTE (RR 0.95; 95% CI (0.93–0.97); p < 0.001), higher heart rate at admission to the hospital (111 ± 78/min; p < 0.001). Blood examination revealed higher serum creatinine level (101 ± 87 μmol/l; p < 0.001). TTE showed larger LVEDD (53.1 ± 50.8 mm; p=0.04), whereas in coronary angiography more often left main coronary artery disease was diagnosed (14.1% vs. 6.5%; p < 0.05), in contrary to one- vessel disease (24.4 vs. 39.4%; p=0.007). In these pts we also observed higher rate of cardiac arrest during hospitalization (9.8 vs. 1.6%; p<0.001). In-hospital mortality rate in the ACS-AF group was 2.3 vs. 0.7% (p<0.15). Follow up revealed differences in both groups in all-cause mortality (24.7 vs. 6.1%; p <0.001), stroke-related mortality (4.3 vs. 0.6%; p=0.009) and cardiovascular disease- related mortality (8.5 vs. 2.5%; p=0.008). Cox proportional hazards model revealed three independent predictors of all-cause mortality in both groups: new onset AF during ACS (RR 2.1; 95% CI (1.1–3.8); p=0.01), age (RR 1.09; 95% CI (1.05–1.13); p<0.001) and LVEF in TTE (RR 0.95; 95% CI (0.93–0.97); p < 0.001).

Conclusions: In pts with ACS and new onset AF follow-up revealed higher rate of all-cause mortality, stroke-related mortality and cardiovascular disease - related mortality. Age, AF during ACS and LVEF were independent predictors of all-cause mortality in follow-up, in pts with ACS.

P5295 | BEDSIDE

Lone atrial fibrillation: work up and predictors of recurrences

Background: Mechanisms and best treatment choice of “lone atrial fibrillation (AF)" are still debated. Due to the risk of major complications and recurrences after anticoagulant therapy for atrial fibrillation, patients are often considered as first line therapy. The aim of this study was to report on clinical work up and long term efficacy and safety of ablation procedure in the highly selected subgroup of lone AF patients.

Methods: We retrospectively analyzed 855 patients referred to our centre for a first AF ablation between 2011 and 2014. Among them 72 (8%) met diagnostic criteria for lone AF (mean age 45±4 years; 68% males; mean LA diameter 343±3 mm; no cardiovascular comorbidities). 58 (81%) patients underwent pulmonary veins isolation (PVI) for paroxysmal AF; 14 (19%) underwent PVI and additional substrate modification (PVI+SM, n=22). Atrial ablation and/or linear lesions for persistent AF. Immediately after ablation, all AADs were stopped in all patients.

Results: The median preoperative AF history was 24 [9–48] months. 12 (16%) patients were unsuccessfully treated with AADs as first line therapy. After a median follow up of 458±347 days, 78% of patients were free from recurrences without AADs. The risk of recurrences after ablation procedure was not influenced either from AF duration, or from type of AF (paroxysmal vs persistent). In the Cox- proportional hazard’s model, atrial fibrillation duration (p=0.001; HR=3.02) and early recurrences in the blanking period (p<0.001; HR=11.8) were associated with a higher risk of clinical recurrences in the long term follow up. Major peri-procedural adverse events did not occur, no strokes or mortalities were registered during long-term follow-up.

Conclusions: This retrospective study shows that catheter ablation in young healthy patients with AF is highly effective and safe. The outcomes are maintained at long-term follow-up, irrespective of preoperative AF history. Smoke, AV Block I and early recurrences are associated with higher risk of recurrences at long term follow up.

P5296 | BEDSIDE

More advanced electroanatomical remodeling of left atrium and contractile dysfunction of left atrial appendage increase the risk of stroke for women in comparison to men in atrial fibrillation

Background: The risk of stroke imposed by atrial fibrillation (AF) is significantly greater in women than in men; however, the mechanism behind the observed differences is still unclear.

Purpose: We hypothesized that the higher stroke rate in women with AF can be explained by gender differences in electroanatomical remodeling of left atrium (LA) and contractile function of LA appendage (LAA) in association with left ventricular (LV) diastolic dysfunction.

Methods: A total of 493 AF patients (173 women and age- and AF type matched 320 men, 60.7±10.4 years old, 73.6% paroxysmal AF) who underwent AF catheter ablation were enrolled in the study. Gender differences of LA volume index (TTE), LAA emptying flow velocity (FV, TEE) and LA voltage were analyzed in low (0 men, 1 women), intermediate (1 men, 2 women) and high (>2 men, >3 women) risk groups, into which patients were divided according to their CHA2DS2-VASc scores.

Results: 1. Contractile dysfunction of LAA (LA-AFV) was more significant in women than in men (p<0.001), but not in the low or intermediate risk groups. 2. Women also showed a greater LA volume index than their male counterpart in the high risk (p<0.001) group, but not in the low or intermediate risk groups. 3. Women showed lower LA voltage than men in the intermediate (p=0.17) and high (p<0.001) risk groups. 4. LA volume index (OR 1.134, CI 1.013–1.269, p=0.029) was independently associated with the history of stroke in women but not in men among AF patients.

Conclusions: More extensive LA remodeling and deterioration in mechanical function of LAA were noted in women with intermediate to high risk of stroke in AF, but not in those with a low risk.

P5297 | BEDSIDE

Atrial fibrillation with or without valvular disease: is the prognosis different?
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Background: European guidelines defined valvular atrial fibrillation (V-AF) in the presence of prosthetic valve or rheumatic heart disease. Recently it was proposed to restrict V-AF to mitral stenosis and mechanical prosthetic valves. The remaining pts with AF are therefore those without valvular disease (AF-WVD) or with other valvular disease/prosthetic valves (AF-VD). There are scarce data directly comparing these two populations.

Aim: We assessed demographic and clinical baseline characteristics and incidence of thromboembolic (TE) and major events (hospital admissions, major bleeding and death) during follow up, in a real-world population of outpatients with AF-WVD and AF-VD.

Methods: Between calendar 2009 and 2013 years, we enrolled 3379 AF-WVD pts and 1268 AF-VD pts. Clinical data were derived from the E-data chart for outpatient clinic. After a median follow up of 29 months we considered the incidence of TE and major events in the two groups. Data were obtained from Hospital Discharge Database and ICD9 code reports and regional Registry of Births and Deaths.

Results: Considering baseline characteristics of 3379 AF-WVD pts (mean age 75, 56% males) versus (vs) 1238 AF-VD pts (mean age 78, males 50%), the prevalence of obesity was 21% vs 16% (p<0.001), coronary artery disease 27 vs 3% (p<0.001), Charlson Index was ≥5 in 9.4 vs 13.9% (p<0.001), mean CHA2DS2-VASc 4 (2–5) vs 4 (3–5) (p<0.001), HASBLED ≥3 in 30% vs 39% (p<0.001), previous stroke/TIA 11.8 vs 11.4% (p=ns), glomerular filtration rate (GFR) <60ml/min/m2 27% vs 35% (p<0.001), >5 drugs 62 vs 72% (p<0.001), oral anticoagulants (AT) 53 vs 63% (p<0.001). During follow up we recorded TE events in 7.5% AF-WVD vs 8.7% AF-VD pts (p=NS), hospital admission in 53% vs 60% (p<0.001), CV hospitalizations 27% vs 37% (p<0.001), major bleeding 9.4% vs 13% (p<0.001), deaths 13% vs 19% (p<0.001). Also considering patients treated with AT, less TE occurred in AF-WVD vs AF-VD: 6.9 vs 9% (p<0.001).

Conclusions: 1) In a real world registry, AF-WVD vs AF-VD pts are different groups, being the former pts are younger, more obese, without complex heart disease or comorbidities, lower CHA2DS2-VASc/HASBLED and less frequent on AT treatment; 2) During follow up TE events in the 2 groups were not different, but considering patients on AT therapy, TE events were significantly increased in AF-VD pts. During follow-up, the incidence of hard prognostic events was higher in AF-VD pts, probably related to demographic and clinical characteristic of these more complex and frail pts.

P5298 | BEDSIDE

Guideline adherence for stroke prevention and risk of mortality in patients with atrial fibrillation
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Background: Although the current European guideline had clear recommenda-
tions for stroke prevention in patients with atrial fibrillation (AF), whether patients who received treatments adherent to guidelines had a lower risk of mortality re-

Methods: This study used the “National Health Insurance Research Database” in Taiwan. According to the 2012 ESC AF guideline, adherences to guideline rec-

Results: From 1996–2011, the Taiwan AF cohort included 354,652 AF patients. Among the study population, 45,595 and 309,057 patients were defined as guide-

Conclusions: In this nationwide AF cohort, the risk of mortality was lower for patients who were adherent to ESC guideline for stroke prevention. The finding of the present study emphasized the importance of guideline adherence.

ATRIAL FIBRILLATION IV

PS299 | BEDSIDE

Combination of bilevel positive airway pressure and airway insertion is an effective strategy during atrial fibrillation ablation


Background: Adaptive servo-ventilation was reported to be useful during pul-

Methods: Two hundred twenty seven AF patients who underwent PVI using NavX were studied (paroxysmal AF, n=155; non-paroxysmal AF, n=72). Combination of dexmedetomidine and thiopental, or propofol was used for sedation. We divided into 3 groups: they underwent AF ablation using bilevel positive airway pressure (BiPAP) system (BiPAP group, n=70), using BiPAP system and oral airway inser-

Results: BiPAP-Airway group was lower frequency of patient restlessness compared with BiPAP and control groups (1.2±2.3 times versus 6.1±1.7, and 2.4±1.8 times, P<0.01 and P<0.01, respectively) and minimum SpO2 was higher in only BiPAP-Airway group than in control (88.8±1.1% versus 97.9±1.8%; P<0.05). At the ablation procedure data, procedure duration for PVI was shorter in BiPAP-Airway 

Conclusion: Combination of bilevel positive airway pressure and oral airway insertion is an effective strategy during atrial fibrillation ablation.

PS300 | BEDSIDE

Which components of the CHA2DS2-VASc score are the most important in obstructive sleep apnea patients with atrial fibrillation?

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Introduction: Elevated thromboembolic risk is observed in patients with different diseases of the cardiovascular system, with the most prevalent of them being atrial fibrillation. The arrhythmia often co-exists with other diseases like ob-

Results: The finding was consistently observed after the propensity match analysis. This study used the “National Health Insurance Research Database” in Taiwan. According to the 2012 ESC AF guideline, adherences to guideline rec-

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Conclusions: Combination of BiPAP and oral airway insertion during AF ablation suppresses patient restless and stabilized patient respiratory condition as com-

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Results: The mean age of the study population was 57.6±10.1 years, and 65.0% of the subjects were male. Moderate to severe OSA was diagnosed in 16.5% of patients. In OSA patients the following risk factors included in the CHA2DS2VASc score were significantly higher: hypertension (59.3 vs. 70.9%; p<0.01), diabetes mellitus (26.1 vs. 6.8%; p<0.003), history of vascular disease (23.9 vs. 8.2%; p=0.006). Non-significant differences were noticed in the history of stroke, age categories, or sex. After dis-

Conclusion: This study demonstrated that in 24h Holter monitoring (HM) characteristics, the patients who received treatments adherent to guidelines had a lower risk of mortality than in control (98.8±1.1% versus 97.9±1.8%, P<0.05). Atrial fibrillation (AF) represents a tremendous challenge. Despite some studies have defined clinical 

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Conclusions: Clinical and HM parameters are able to predict new onset AF at long term in a non-selected population. These patients should be closely followed in order to assess AF incidence.

PS302 | BEDSIDE
Opportunistic screening for atrial fibrillation in hospitalized geriatric patients
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Introduction: The clinical presentation of atrial fibrillation (AF) in the elderly is often atypical. Nevertheless it is a major source of increased morbidity especially because of the increased risk of stroke in this population.

Purpose: To assess (1) the added value of daily short-term rhythm strip recordings in AF detection in hospitalized geriatric patients (pts) on top of routine clinical care (history, physical examination, ECG and 24 hour ECG recording in selected pts) and (2) to assess its potential therapeutic implications.

Methods: A hand held device storing a bipolar electrogram during one minute automatically classifying the rhythm as AF or non-AF was used for daily recording. During 2 months all patients (n=327) admitted to the Department of Geriatric Medicine were screened. Patients with severe mental (n=29) or motoric impairment (n=24) and implantable cardiac stimulators (n=38) were excluded (n=224 eligible patients). All rhythm strips were evaluated by experts.

Results: Based upon routine clinical care (data from ECGs available in 214 pts), AF was known in 71 pts (33%). If experts only reviewed tracings automatically labeled as AF, another 15 pts with AF (7%) were identified. If experts reviewed all tracings, 28 patients (13%) with AF were identified on top of routine clinical care. All of these patients had a CHADS2VASc score of at least 3. No contraindications for anticoagulation were present in respectively 10/15 (67%) and 21/28 (75%) of identified patients.

Conclusions: On top of routine clinical care, daily short-term rhythm strip recordings identify 7-13% (depending on the scoring approach) of elderly hospitalized patients with AF. This has significant therapeutic implications with respect to initiation of anticoagulation.

PS303 | BEDSIDE
The clinical impact of atrial fibrillation complicating ST-segment elevation myocardial infarction depends on location of infarction and timing of arrhythmia - data from a 10-year prospective study
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Introduction: Atrial fibrillation (AF) is the most common supraventricular tachyarrhythmia in patients with ST-segment elevation myocardial infarction (STEMI). AF is a well-established marker of poor short- and long-term prognosis in STEMI patients. According to current guidelines as well as to the scoring AF-ON in STEMI is associated with a 10-year mortality in patients with different locations of STEMI.

Purpose: The aim of the study was to assess the clinical significance of new-onset AF in patients with STEMI according to a location of infarction and timing of arrhythmia.

Methods: We analyzed 4363 consecutive STEMI-patients treated invasively, who were analyzed 4363 consecutive STEMI-patients treated invasively, who were included into further analysis, as 264 patients were excluded because of previous permanent/paroxysmal AF. Among them, 1800 (43.91%) subjects with anterior infarction were included into Group 1, whereas Group 2 encompassed 2299 (56.09%) patients with non-anterior infarction. Data on in-hospital follow up were screened to identify subjects who experienced major adverse cardiovascular events during index hospitalization.

Results: New-onset AF was recognized in 225 patients (5.49%) during index hospitalization – 96 (5.33%) with anterior infarction (Group AF1) and 129 (5.61%) with non-anterior infarction (Group AF2). The incidence of arrhythmia onset within 24 hours (early-onset) after admission was significantly higher in Group AF2 than in Group AF1: 71.33% vs. 35.42% (p<0.001). In Group 2, only late onset of AF (>24 hours after admission) was associated with significantly higher in-hospital mortality (13.51% vs. 4.24% p<0.05), whereas mortality in patients with early onset of AF did not differ significantly in comparison with AF-free subjects (7.61% vs. 4.24% p>0.05). On the contrary, in Group 1 in-hospital mortality in patients with early and late onset of AF was 2- and 4-fold increased compared with AF-free population (17.65% and 27.42% respectively vs. 6.34%; p<0.05). Additionally, new-onset AF was the independent predictor of death only in Group 1 (HR 2.16 and this effect was found in 100% of patients who developed AF and 24% (32/100) died in 0.19 and 0.97 for the re-expressed MDRD-4 equation (34.1%).

Conclusions: New-onset AF was associated with significantly worse in-hospital outcome in STEMI-patients treated invasively. However, the predictive value of new-onset AF was the independent predictor of death only in Group 1 (HR 2.16)

PS304 | BEDSIDE
Prognostic usefulness of the glomerular filtration rate estimation in patients with non-valvular atrial fibrillation on vitamin K antagonists: the new CKD-EPI versus the re-expressed MDRD-4 equation

Background: In atrial fibrillation, renal dysfunction entails more adverse events. Limited data exist on the prognostic value of the re-expressed Modification of Diet in Renal Disease equation (MDRD-4) versus the new Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) in atrial fibrillation.

Purpose: We compared the performance of the re-expressed MDRD-4 equation versus the new CKD-EPI equation at predicting major adverse outcomes in a real world cohort of patients with non-valvular atrial fibrillation (NVAF) on vitamin K antagonists (VKAs).

Methods: Retrospectively, we identified 911 consecutive patients with NVAF on VKAs who were attending the outpatient Cardiology consultation of a tertiary hospital between January 2011 and February 2013. The performance of each equation with respect to either a composite endpoint of major bleeding, thromboembolic events and all-cause mortality or each individual component of the composite endpoint was assessed using continuous and categorical <60, 50–<60, and >50–<60 ml/min/1.73 m² estimated glomerular filtration rate.

Results: During 102±3 months of follow up, the composite endpoint occurred in 98 (10.8%) patients: 30 patients developed major bleeding, 18 had thromboembolic events, and 60 died. The new CKD-EPI equation provided lower prevalence of renal dysfunction <60 ml/min/1.73 m² (32.9%), compared with the re-expressed MDRD-4 equation (34.1%). Estimated glomerular filtration rate from both equations was an independent predictor of the composite endpoint (hazard ratio=0.98 for the re-expressed MDRD-4 and the new CKD-EPI, respectively; p<0.0001) and all-cause mortality (hazard ratio=0.98 for both equations, p<0.0001). Strong association with thromboembolic events was observed only when estimated glomerular filtration rate was -30 ml/min/1.73 m², hazard ratio=5.1 for the re-expressed MDRD-4 equation, and hazard ratio=5.0 for the new CKD-EPI.

No significant association with major bleeding was observed for both equations.

Conclusions: The new CKD-EPI equation reduced the prevalence of renal dysfunction in a community based cohort of patients with NVAF on VKAs. Both equations performed similarly in predicting major adverse outcomes.

PS305 | BEDSIDE
Atrial ectopy and NT-proBNP as predictors of atrial fibrillation
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Background: Atrial fibrillation (AF) is a common arrhythmia associated with increased morbidity. Models for prediction of AF can be relevant in identifying subjects who might be at increased risk for AF. The Framingham Heart Study AF risk score is validated risk score that predicts the 10-year risk for incident AF. Studies have shown an association between increased risk of AF and increased rate of premature atrial contractions (PAC) and elevated levels of N-terminal pro-BNP (NT-proBNP).

Purpose: We aimed to investigate whether addition of the biomarkers NT-proBNP and PAC improved the model performance of the Framingham AF risk score.

Methods: Subjects from the population-based cohort in the Copenhagen Holter Study, consisting of 646 men and women between 55 and 75 years of age and without any history of prior atrial fibrillation, stroke or cardiovascular disease, were followed for the diagnosis of incident AF or death (median follow-up time 14.4 years). Baseline examination included physical examination, laboratory testing and 48-hour ambulatory ECG monitoring. In order to investigate the predictive ability of PAC (log-scale) and NT-proBNP (log-scale) we computed the time-dependent area under the ROC curve (AUC) for the AF status 10 years after the baseline examination. Risk reclassification and calibration of the models was assessed and compared to the Framingham AF risk prediction model.

Results: Two hundred and eighty nine subjects (41.6%) were women, mean systolic blood pressure was 156.2 mmHg and 72 subjects (11.1%) had diabetes. Median NT-proBNP was 6.7 mmol/l (IQR: 3.6–13.5) and median PAC count was 1.4 beats/hour (IQR: 0.6–4.5). During the 14.4 years of observation 71 (11.0%) developed AF and 24 (3.5%) died (HR 1.61; 95% CI: 1.16–1.87; p=0.001; HR 1.22 [95% CI: 1.08–1.37] p=0.002). The addition of PAC to the Framingham AF risk model significantly improved AF risk discrimination (AUC 65.7 vs. 72.2; p=0.007), while the addition of NT-proBNP did not (AUC 68.4; p=0.23). The addition of both PAC and NT-proBNP to the Framingham risk score also improved the AF discrimination capability (AUC 72.1; p=0.013).

Conclusion: AF risk discrimination was significantly improved by addition of PAC to the Framingham AF risk prediction model, but not by addition of NT-proBNP.
P5306 | BEDSIDE
Anthropometric measures and risk of atrial fibrillation - a cohort study of 1.2 million young men
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To investigate associations of body height, body weight, body surface area and disease, tall stature has been proposed as a risk factor for atrial fibrillation.

**Background:** While tall stature has been related to lower risk of cardiovascular disease, tall stature has been proposed as a risk factor for atrial fibrillation.

**Aim:** To investigate associations of body height, body weight, body surface area and body mass index with risk of atrial fibrillation, and to investigate joint effects of these measures and potential mediators of effect.

**Study design:** Cohort study

**Study population:** All Swedish men who participated in the mandatory military conscription at age 18 between August 1st 1972 and December 31st 1995. Outcomes were defined using the national in-patient and cause-of-death registries.

**Results:** During a median of 26.3 years of follow-up of 1,173,547 men, higher body height was associated with higher risk of atrial fibrillation (HR 2.80; 95% CI 2.63–2.98; for 5th vs. 1st quintile) and so was weight (HR 2.52; 95% CI 2.34–2.70; for 5th vs. 1st quintile). Higher body surface area was also associated with higher risk of atrial fibrillation (HR 2.63; 95% CI 2.52–2.70; for 5th vs. 1st quintile). Thus, there were clearly determined to be factors responsible for the increased incidence of atrial fibrillation other than changes in the population pyramid attributable to an increase in the size of the elderly population.

**Conclusion:** Higher body height and weight in adolescence are strongly associated with higher subsequent risk of atrial fibrillation. These associations are multiplicative, and are reflected in a strong association of body surface area with risk of atrial fibrillation. The mechanisms remain unknown but we suggest that the increased volume load related to larger body size could be a mediating factor.

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P5307 | BEDSIDE
The incidence of atrial fibrillation increased significantly among men in their sixties and seventies
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**Background:** There has been a remarkable increase in the incidence of atrial fibrillation in Japan. Atrial fibrillation is known to increase with age. Although the increase in the incidence of atrial fibrillation may be due to the increase in the size of the elderly population, it is not clear as to whether or not the incidence of atrial fibrillation is increasing at a rate greater than the increase in the size of the elderly population due to other factors.

**Subjects and methods:** We annually recorded and analyzed the electrocardiograms of healthy residents of Iwate Prefecture, Japan who are living in their own using 16 specially equipped buses capable of recording electrocardiograms. In this study, we divided subjects ranging in ages from 40 to 79 years old into four groups for every 10 years of age, and investigated the incidence of atrial fibrillation for four rounds of analysis. In this study, we divided subjects ranging in ages from 40 to 79 years old into four groups for every 10 years of age, and investigated the incidence of atrial fibrillation at five year intervals during the 15 year period from 1997 to 2012.

**Results:** The average number of subjects during the four rounds of analysis was 201,000, and the population coverage rate was 29.1% of the number of residents in the prefecture of the same age groups of 690,000 (as of 2012). The incidence of atrial fibrillation, as determined by correcting the age composition in each analyzed year for the age composition in 2012, among men was 1.47% in 1997, 1.55% in 2002, 1.71% in 2007 and 1.79% in 2012, thereby demonstrating a significant increase. On the other hand, there were no significant increases observed among women. In looking at individual age groups, although the incidence among men in their forties in 2012 was 0.33% and that among men in the fifties was 0.33% and there were no significant differences observed, the incidence among men in their sixties increased from 2.27% in 1997 to 2.95% in 2012 and the incidence among women in their seventies increased from 4.17% in 1997 to 5.63% in 2012, demonstrating significant increases of 0.68% and 1.46%, respectively. In addition, the size of the increase was larger among men in their seventies than men in their sixties.

**Conclusions:** Although the incidence of atrial fibrillation among men in Iwate Prefecture during the 15 year period from 1997 to 2012 did not exhibit any changes among men in their forties and fifties, significant increases were observed among men in their sixties and seventies. Thus, there were clearly determined to be factors responsible for the increased incidence of atrial fibrillation other than changes in the population pyramid attributable to an increase in the size of the elderly population.

P5308 | BEDSIDE
Duration of diabetes mellitus and thromboembolic events in atrial fibrillation: a nationwide cohort study
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**Background:** Guidelines advocate anticoagulant treatment to all patients with atrial fibrillation and concomitant diabetes mellitus. The potential refinement to thromboembolic risk stratification that may spring from subdividing diabetes mellitus is unexplored.

**Purpose:** To investigate duration of diabetes mellitus as a predictor of thromboembolism and anticoagulant-related bleeding in patients with atrial fibrillation.

**Methods:** Using nationwide Danish registries, we identified all patients discharged from hospital with incident atrial fibrillation from 2000–2011. Hazard ratios [HRs] with 95% confidence intervals [CIs] for thromboembolism and bleeding according to years of diabetes duration in categories (0–4, 5–9, 10–14, and ≥15) and as a continuous variable were calculated using Cox regression.

**Results:** The study population comprised 137,222 patients with atrial fibrillation, of which 12.4% had diabetes mellitus. Compared with patients without diabetes and after adjustment for anticoagulant treatment and CHA2DS2-VASc components, the risk of thromboembolism was lowest in the 0–4 years duration category (HR 1.11, 95% CI 1.03–1.20), and highest in the longest duration category of ≥15 years (HR 1.48, 95% CI 1.29–1.70). As a continuous variable, duration of diabetes was associated with risk of thromboembolism in a dose-response dependent manner, but not with a higher risk of bleeding during anticoagulant treatment.

**Conclusion:** Higher body height and weight in adolescence are strongly associated with higher subsequent risk of atrial fibrillation. These associations are multiplicative, and are reflected in a strong association of body surface area with risk of atrial fibrillation. The mechanisms remain unknown but we suggest that the increased volume load related to larger body size could be a mediating factor.

P5309 | BEDSIDE
Acute ranolazine plus amiodarone vs amiodarone alone for conversion of recent-onset atrial fibrillation: a prospective clinical study
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**Background and Introduction:** Amiodarone (AMIO) is frequently used to convert atrial fibrillation (AF) in patients with or without heart failure. However, because AMIO needs several hours or days for converting AF into sinus rhythm, it has recently been started to combine it with ranolazine (RAN) in an attempt to accelerate termination of this arrhythmia in clinical practice. RAN is a new antiarrhythmic agent with additional electrophysiologic properties, partially consisting of a selective open-state Na+ channel inhibition at atrial level.

**Purpose:** To compare the antiaarrhythmic effectiveness of AMIO + RAN vs AMIO alone in a prospective, single-blinded, randomized study.

**Methods:** We enrolled 65 patients with recent-onset (~48 h duration) AF who

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**Thromboembolism and bleeding**

**Conclusion:** In patients with atrial fibrillation, longer duration of diabetes mellitus was associated with a higher risk of thromboembolism, but not with a higher risk of antiarrhythmic-related bleeding. Considering the critical balance between preventing thromboembolism and avoiding bleeding, longer duration of diabetes mellitus may favour initiation of anticoagulant therapy.
were eligible for pharmacologic cardioversion. A number of 29 patients (16 male/13 female, 62±11 years) received only AMIO infusion (loading dose 5 mg/kg followed by maintenance dose of 50 mg/h), while the remaining 36 patients (9 male/27 female, 67±10 years) were treated with AMIO plus a single oral dose of RAN 1g. Left ventricular ejection fraction (LVEF), left atrial diameter (LAD), and P-wave duration (PW) were evaluated in all patients.

Results: Patients in the AMIO+RAN group compared with the AMIO-only group showed significantly shorter time to conversion intervals (8.1±2.2 vs 24.4±4.1 h; P<0.0001, Mann-Whitney test). AMIO+RAN vs AMIO-only patients had LVEF (54.3±5.9 vs 54.5±3.8%, P=NS), LAD (39.1±3.8 vs 39.1±7.7 mm, P=NS), and PW (90.2±28 vs 91.1±26 ms, P=NS), respectively. All aforementioned variables were expressed as mean±SD and considered significant at the 0.05 level. No sinus bradycardia or QTc excessive prolongation (>440 ms) were observed after cessation of AMIO in the AMIO+RAN group.

Conclusion: These findings demonstrate a superior antiarrhythmic efficacy of AMIO+RAN therapy to AMIO alone in patients with recent-onset AF and LAD ≤46 mm. We suppose that RAN might selectively depress atrial conduction and increase postrepoliration refractoriness which is more than AMIO alone thereby potentially enhancing its antiarrhythmic effect.

P5310 | BEDSIDE
A multidisciplinary atrial fibrillation clinic is superior to standard outpatient treatment
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Background: Atrial fibrillation (AF) is the most common tachy-arrhythmia and it is associated with an increased risk of stroke and mortality. Anticoagulation therapy reduces the risk of stroke in patients with AF. Despite a simple empiric scoring system (CHA2DS2-VASc) only 50–80% of patients receive correct anticoagulation therapy according to guidelines. We hypothesized that a structured multidisciplinary approach to AF patients will ensure optimal anticoagulation therapy superior to standard outpatient treatment.

Methods: The present study compares the proportion of patients with AF in anti-coagulation treatment according to guidelines in three different settings. In the “AF clinic group” patients were treated in a structured multidisciplinary AF clinic that comprised of two dedicated cardiologists and two nurses, one nurse with expert knowledge of anticoagulation treatment, and another with echocardiographic skills. The “first usual care group” comprised of patients with AF seen in the same outpatient setting prior to the establishment of the AF clinic. The “second usual care group” comprised of data from the EURObservational Research Programme on Atrial Fibrillation (EORP-AF) Pilot General Registry.

Conclusion: The present study demonstrates that a structured multidisciplinary approach ensures optimal anticoagulation therapy in patients with atrial fibrillation. This contributes to a better protection against stroke and a lower bleeding risk. We encourage establishment of structured multidisciplinary AF clinics to ensure optimal antithrombotic treatment and adherence to current guidelines.

ATRIAL FIBRILLATION V

P5311 | BEDSIDE
Stroke severity in relation to duration of atrial fibrillation and supraventricular runs in patients with cerebral ischemia
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Background: Atrial fibrillation (AF) is a frequent cause of ischemic strokes. The AF-definition includes only typical episodes ≥30 seconds, but the minimal duration of AF that increases the risk of thromboembolism is unknown. The relevance of shorter supraventricular (SV) runs, which are frequently revealed by enhanced ECG-monitoring, remains unclear. As AF-related strokes are known to be more severe, we applied stroke-related physical impairment as a surrogate marker for cardioembolic pathogenesis in patients with various durations of paroxysmal AF and SV-runs.

Methods: Retrospective analysis from the prospective observational Find-AF trial (ISRCTN46104198). Those without AF at presentation received 7-day Holter-ECG-monitoring. The longest SV-run was determined in a 24-hour interval free from AF. Stroke severity was assessed using the National Institute of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS).

Results: 258 patients were included in presentation. 215 received Holter-monitoring: 27 (12.5%) had paroxysmal AF, 69 had SV-runs <5 beats and 119 had neither AF nor SV-runs. Stroke severity was equally increased in those with various durations of manifest AF. Even those with prolonged SV-runs had significantly milder strokes, in the range of those without any supraventricular arrhythmias.

Conclusion: Although stroke-related physical impairment is only a surrogate marker of cardioembolic pathogenesis, our results imply that even short AF-episodes could be associated with thromboembolic events. On the other hand, even prolonged SV-runs do not appear to induce cardioembolism. It remains to be determined, whether subgroups with short AF-episodes or those with SV-runs effectively benefit from oral anticoagulation.

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P5312 | BEDSIDE
A severity of sleep-disordered breathing with atrial fibrillation ablation candidates is associated with the long-term outcome after pulmonary vein antrum isolation
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Background: Sleep-disordered breathing (SDB) may be associated with pulmonary vein antrum isolation (PVAI) failure. The aim of the present study was to investigate the impact of the severity of SDB for the outcome after PVAI.

Methods: From December 2011 to March 2014, 269 consecutive patients underwent PVAI. Known SDB cases with continuous positive airway pressure (CPAP) therapy, cases without appropriate oxygen desaturation data, and ablation failure cases due to the complications were excluded. A total of 244 patients were analyzed. After the procedure, we measured the oxygen desaturation index (ODI) by pulse oximetry overnight as an indicator of SDB, and classified SDB severity by 3% ODI as normal (ODI <5 events/h), mild (ODI ≥5 to <15 events/h) or moderate-severe (ODI ≥15 events/h).

Results: At the mean follow-up period (18±11 months), 82.2% of normal, 74.0% of mild, and 59.2% of moderate-severe SDB group were free of atrial fibrillation (PVAI) failure. Known SDB cases with continuous positive airway pressure (CPAP) therapy, cases without appropriate oxygen desaturation data, and ablation failure cases due to the complications were excluded. A total of 244 patients were analyzed. After the procedure, we measured the oxygen desaturation index (ODI) by pulse oximetry overnight as an indicator of SDB, and classified SDB severity by 3% ODI as normal (ODI <5 events/h), mild (ODI ≥5 to <15 events/h) or moderate-severe (ODI ≥15 events/h).

Results: At the mean follow-up period (18±11 months), 82.2% of normal, 74.0% of mild, and 59.2% of moderate-severe SDB group were free of atrial fibrillation (PVAI) failure. Known SDB cases with continuous positive airway pressure (CPAP) therapy, cases without appropriate oxygen desaturation data, and ablation failure cases due to the complications were excluded. A total of 244 patients were analyzed. After the procedure, we measured the oxygen desaturation index (ODI) by pulse oximetry overnight as an indicator of SDB, and classified SDB severity by 3% ODI as normal (ODI <5 events/h), mild (ODI ≥5 to <15 events/h) or moderate-severe (ODI ≥15 events/h).

Conclusions: Our study suggests that baseline SDB is associated with increased PVAI failure and the moderate-severe SDB was an independent predictor for the recurrence after single PVAI. We recommend that pulse oximeter testing become a routine part of the procedural work-up before AF ablation.
PS314 | BEDSIDE
Time course of atrial fibrillation in patients with a congenital heart defects

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Background: Atrial fibrillation (AF) occurs frequently in patients with congenital heart defects (CHD). Whereas regular AF has extensively been studied, studies about AF in CHD patients are rare, despite the increasing incidence of AF.

Aims: To examine the development of AF in patients with a variety of CHD 2) to investigate the coexistence of AF with regular AT 3) to study the progression of paroxysmal to long-standing persistent/permanent AF during long-term follow-up.

Methods: CHD patients derived from databases of the participating centers with known AF. AF episodes on an ECG or 24-hour Holter registration were in-cluded. All available ECGs and 24-hour Holter registrations were also reviewed.

Results: We examined the clinical course of 8962 consecutive patients with AF seen between 2000–2010 in an academic institution and identified their causes of death. Of the patients with a yearly ECG (N=112), progression to long-standing persistent/permanent AF was frequently observed and occurred relative fast; therefore, aggressive therapy of regular AT and AF is reasonable.

Conclusions: Patients with CHD develop AF at a relative young age compared to patients without CHD, especially patients with ‘complex’ CHD. Thirty-three percent of the patients with AF also developed regular AT; initial episodes of AF were documented before as well as after regular AT. Progression of paroxysmal to long-standing persistent/permanent AF was frequently observed and occurred relative fast; therefore, aggressive therapy of regular AT and AF is reasonable.

PS315 | BEDSIDE
Does renal dysfunction predict new onset of atrial fibrillation in the Japanese general population?

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Purpose: Several conditions have been proposed as a risk factor contributing to the new onset of atrial fibrillation (AF). Chronic kidney disease is reported as a risk factor for the new onset of AF in hypertensive patients, whereas their relation-ship has not been intensively investigated in general population. We tested the hypothesis that the risk of new AF increases with deterioration of estimated glomerular filtration rate (eGFR) in the general population.

Methods: Consecutive 14,558 participants without a history of AF (male=8,924, 52±10.2 year-old) who visited our hospital for a physical check-up from July 2001 to June 2013 were enrolled in this study. After baseline evaluation, they were followed up for the median of 1,638 days with the endpoint being the new onset of AF. The relationship between baseline eGFR and the incidence of AF during the follow-up was analyzed. Kidney function was categorized into 4 groups according to the classification of chronic kidney disease: stage 1, eGFR ≥90; stage 2, 60 < eGFR < 90; stage 3, 30 < eGFR < 60; and stage 4, eGFR < 30 mL/min per 1.73 m².

Results: During the follow-up, 99 subjects suffered from paroxysmal or chronic AF (1.19 person-year), with the incidence being more frequent in male than in female subjects (1.55 vs. 0.58 per 1000 person-year, p<0.0001). The incidence of AF in stage 1, 2, 3, and 4 was 0.59, 1.58, 3.77 and 27.46 per 1000 person-year, respectively. The risk of new AF increased across the kidney function categories at baseline (the hazard ratio [95% confidence interval] in stage 1, 2, 3, and 4 was 1, 2.2, 3.5, and 5.5, respectively). After adjustment for gender, body mass index, systolic blood pressure, heart rate, uric acid, fasting plasma glucose, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and current smoking habit at baseline, multivariable Cox proportional hazard regression analysis, where eGFR was taken as a continuous variable, revealed that decreased eGFR was the significant predictor of new AF (hazard ratio [95% confidence interval: 0.981 [0.967–0.996]).

Conclusions: The risk of the new onset of AF increases with decreasing eGFR. Racial dysfunction may be a useful predictive factor for the incidence of AF in the general population.

PS316 | BEDSIDE
Impact of non-rheumatic valvular heart disease on mortality in patients with atrial fibrillation: Results from the German AFNET registry

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Atrial fibrillation (AF), the most common arrhythmia, is associated with substantial morbidity and an increased risk of death. Recent data from large randomized trials have highlighted that mortality in anticoagulated AF patients remains high and is often due to heart failure or sudden death. Data on the impact of valvular disease on mortality in AF patients are limited. We therefore analysed mortality rates and baseline prognostic factors for all-cause mortality in AF patients with and without native valve disease.

Methods: A total of 9574 AF patients were enrolled 2004–2006 in the prospective long-term registry of the German Atrial Fibrillation Competence NETwork (AFNET). Survival information was available for 96.8% of patients. Corresponding to the definition of non-valvular AF, patients with mitral stenosis or valve prostheses were excluded for this study. A total of 2722 patients with missing values on prognostic factors, the study population consisted of 8260 patients (516 men, mean age 66.2±11.2 years; 3091 women, 71.6±10 years). Patients were grouped by type of valvular disease (VD) to aortic stenosis (AS, n=314 (3.3%)), Other VD (n=2232 (28.8%)), and No VD (n=5564 (67.4%)) as assessed by the enrolling physician.

Results: Median follow-up time was 6.4 years and total number of deaths was 2259. Patients with AS were older, had higher NYHA classes, and more comor-
bleeding and the composite endpoint of death and stroke. Among patients with normal kidney function. On multivariate analyses eGFR was lower chance of being treated with Warfarin (only 15.2% of the patients compared to 89.1% of the controls). Mortality was directly correlated with severity of CKD. Highest risk of Af were identified. Mean follow-up time was 48.8 months. The incidence rate of AF was 14.5 per 1000 person-years. The average age was highest among the patients with moderate CKD, but mortality rate increased with decreased eGFR throughout the entire range of CKD. The use of Warfarin among patients with severe renal impairment was associated with improved survival.

Conclusion: In this large real world cohort of patients with "non-valvular" AF, aortic stenosis was independently associated with an increased risk of death from all causes, whereas other valvular disease was not. Specific diseases therefore have a major impact on mortality in AF, illustrating the need to target concomitant diseases to improve survival in AF.

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P5319 | BEDSIDE
Comparison of emerging blood biomarkers, NTproBNP and the CHA2DS2-VASc score in the prediction of paroxysmal atrial fibrillation in patients with continuous rhythm monitoring

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Background: Atrial fibrillation (AF) is the most common sustained arrhythmia associated with increased morbidity and risk of stroke. Paroxysmal AF (PAF) is often asymptomatic, and diagnosis and management may be delayed with sporadic rhythm monitoring. Risk factors of AF were combined in the CHA2DS2-VASc score (heart failure, age, diabetes, hypertension, stroke, vascular disease, gender) and also serum biomarkers (e.g. NTproBNP) have been associated with AF. We compared the predictive value of emerging biomarkers, NTproBNP and CHA2DS2-VASc for AF diagnosis with continuous rhythm monitoring.

Methods: Patients with dual chamber pacemaker and sinus rhythm at presentation were divided according to the absence (SR, N=44) or presence (AF, N=49) of atrial tachyarythmias >6 min duration in the device event history. CHA2DS2-VASc score was assessed and set of biomarkers were determined in serum or plasma taken during sinus rhythm from all patients. Regulation of 16 selected biomarkers was tested in univariate analysis in two subgroups of patients with the highest incidence of AF (N=20) and no (0 min) AF (N=20). The predictive value (AUC) of significantly regulated biomarkers was tested than in all patients in univariate and bivariate models.

Results: In the PAF and SR subgroups levels of Hsp27, TGF1, cysteine C, matrix metalloproteinases MMP-2,-3,-9, albumin and serum uric acid were not different between SR and PAF. In contrast, tissue inhibitors of metalloproteinases (TIMP)−1,−2,−4; proANP (1–98), NTproBNP, IL-6 and serum amyloïd protein A (SAA) were significantly different in PAF vs SR (subgroups and full cohort; p<0.05), with the highest AUC for TIMP−4 (78%). Patients with NTproBNP value >150 pg/ml had an odds ratio of 12.9 for AF (sensitivity: 92%; specificity: 46.5%). Combining two of the best performing biomarkers vs. a single biomarker added predictive value for AF detection (e.g. TIMP−4 vs TIMP−4 with NTproBNP, TIMP−4 with NTproBNP, TIMP−4 with proANP (1–98); both p<0.05). AUC for CHA2DS2-VASc was lower than for the biomarkers (TIMP−1, proANP (1–98), NTproBNP). Combination of CHA2DS2-VASc with the top biomarkers significantly added predictive value.

Summary: We identified biomarkers (TIMP−1,−2,−4; proANP (1–98), NTproBNP, IL-6 and SAA) that are regulated in patients with a history of PAF presenting in sinus rhythm. TIMP−1, proANP (1–98), NTproBNP performed better that the CHA2DS2-VASc score in identifying patients with PAF.

P5320 | SPOTLIGHT
Increasing incidence of non-valvular atrial fibrillation (AF) between 2001-2013 in the UK: largely due to non-primary AF hospital diagnosis in the elderly

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Background: The incidence of non-valvular atrial fibrillation (AF) is increasing, though many studies have calculated incidence rates from only one source, usually hospital discharges, disregarding any contribution of general practice to AF diagnosis.

Purpose: To examine recent temporal trends in AF incidence rate and place of hospital diagnosis.

Methods: The UK Clinical Practice Research Datalink with additional hospital discharge data from Hospital Episode Statistics (HES) was used to identify a cohort of 91,707 patients aged over 45 with incident AF from 2001 to 2013. Age and gender-standardized incidence rates of AF in the UK population were calculated and stratified by calendar year and place of AF presentation.

Results: Overall, 39% of incident AF presentations were in general practice (GP), 15% were primary admissions to hospital with AF, and 46% were diagnosed during an inpatient admission with non-AF secondary hospital diagnosis. There was a gradual linear increase of incidence rate from 5.9 to 6.9 new AF/1000 person-years between 2001 and 2013, almost entirely due to an increase of non-primary hospital AF diagnoses, while incidence rates in GP and for primary AF hospital admis-
Atrial fibrillation V / Atrial fibrillation VI

Conclusions: GP diagnosis of AF without hospital admission constitutes a large proportion of incident AF, often overlooked in epidemiological studies. There has been a gradual and significant rise in incidence rates of AF in the last 13 years, largely due to an increasing incidence of hospital diagnosis of AF in the elderly admitted for a cause other than AF. This needs to be considered when addressing the increasing burden of AF as the population ages.

**PS522 | BEDSIDE**

Usual blood pressure, atrial fibrillation and vascular risk: evidence from 4.3 million adults


**Purpose:** To determine the age-specific association between usual blood pressure and risk of atrial fibrillation and to further determine the associations between atrial fibrillation and a range of vascular events in a large contemporary cohort.

**Methods:** Linked electronic health records, validated for epidemiological research, were used to assemble a cohort of 4.3 million adults, aged 30 to 90 years and free of pre-existing vascular disease. Cox proportional hazards models were used to examine the association between baseline blood pressure and incident atrial fibrillation, and the association between baseline atrial fibrillation and risk of nine different vascular events.

**Results:** After adjusting for regression dilution, a 20 mm Hg higher systolic blood pressure was associated with a higher risk of atrial fibrillation (hazard ratio [HR] 1.21 95% confidence interval [CI] 1.19, 1.22). The strength of the association declined with increasing age, from an HR of 1.91 (CI 1.75, 2.09) in age 30–40 to an HR of 1.01 (CI 0.97 1.04) at age 80–90 years.

Atrial fibrillation without antithrombotic use at baseline was associated with a greater risk of any vascular event than atrial fibrillation with antithrombotic usage (2.15 CI 2.05, 2.24 vs. HR 1.15 CI 1.12, 1.18; p interaction <0.0001). Atrial fibrillation without baseline antithrombotic usage was associated with an increased risk of ischemic stroke (HR 2.21 CI 1.98, 2.47), hemorrhagic stroke (HR 2.22, CI 1.60, 3.08), unspecified stroke (HR 2.59 CI 2.25, 2.99), ischemic heart disease (HR 2.52 CI 2.23, 2.84), heart failure (HR 3.80 CI 3.50, 4.12), chronic kidney disease, peripheral arterial disease and vascular dementia, but not aortic aneurysm.

**Conclusions:** The association between elevated blood pressure and atrial fibrillation attenuates significantly with increasing age. Atrial fibrillation without antithrombotic usage is, in turn, associated with increased risk of stroke, ischemic heart disease, heart failure, chronic kidney disease, peripheral arterial disease and vascular dementia.

**ATRIAL FIBRILLATION VI**

**PS523 | BEDSIDE**

Accessory pathway ablation is enough to suppress atrial fibrillation in patients without elevated B-type natriuretic peptide level among those with WPW syndrome and atrial fibrillation (WPW-AF study)

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**Introduction:** Paroxysmal atrial fibrillation (AF) often occurs in patients with Wolff-Parkinson-White (WPW) syndrome. It has been reported that successful accessory pathway (AP) ablation suppressed AF. **Methods:** Ninety-one WPW syndrome patients (55±14 years, 70 men) with clinical AF underwent catheter ablation between 2007 and 2014 at 8 centers.

**Results:** Sixty patients underwent only AP ablation (only-AP group) and 31 underwent pulmonary vein isolation simultaneously (+PVI group). There was no significant difference between baseline clinical and electrophysiological findings between the groups. During follow-up (median 711 days), AF was observed in those who are in AF. These findings question the value of strict heart rate control in CHF patients with atrial fibrillation, thus necessitating further research in this area.

**Conclusion:** Although higher heart rate was associated with worse survival for CHF patients in sinus rhythm, it does not appear to be associated with survival in...
The incidence of AF after the ablation did not show a significant difference between the groups. In the on-demand AF group, those with residual AF were significantly older and had significantly higher BP levels and more concomitant hypertension than those without AF. Among risk factors for residual AF (age > 60 years, BP > 40 mm Hg, or accompanied hypertension), BP > 40 mm Hg was the only independent predictor of remaining AF (95% confidence interval 0.023 to 0.491; p = 0.004) using multivariate Cox regression.

Conclusions: In WPW syndrome patients with AF, a BP level > 40 mm Hg is a strong and independent predictor of AF after ablation. This finding has important implications for identifying patients at higher risk of post-procedural AF who could be considered for additional ablation for AF.

PS324 | BEDSIDE
Increased cardiovascular risk after treatment for hyperthyroidism
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Background: Hyperthyroidism is a common disease affecting 1–2% of the population at some time. Previous studies have shown increased long-term morbidity in patients treated for hyperthyroidism, largely due to cardiovascular disease. However, controversy remains regarding which cardiovascular subgroups are responsible for this increased risk. It is also not clear whether the type of hyperthyroidism - Graves disease (GD) or Toxic Nodular Goiter (TNG) - matters.

Purpose: To perform a detailed investigation of incident cardiovascular disease in previously hyperthyroid subjects.

Methods: We analysed a register of 29662 patients treated for hyperthyroidism with either radioiodine or surgery between the years 1976–2012. An additional cohort of 42630 euthyroid patients was used as a control group. Data on comorbidities were collected from the Swedish National Inpatient Register. Age, sex, and cardiovascular risk factors at baseline were adjusted for.

Results: For hyperthyroidism as a whole, statistically significant increases in hazard ratios (HR) were seen for the following overall categories of cardiovascular diagnoses: Valvular disease (1.20, 95% confidence interval (CI) 1.09–1.30), ischaemic heart disease (HR 1.05, CI 1.01–1.10), arrhythmias (HR 1.15, CI 1.10–1.20), heart failure (HR 1.41, CI 1.35–1.47) and cerebrovascular disease (HR 1.18, CI 1.13–1.24). No significant excess risk was seen for disorders of the pulmonary circulation or arterial disease. When GD and TNG were analysed separately, few significant differences between GD patients and controls remained, while HRs were further increased among TNG patients in all cardiovascular disease categories examined. Additional analyses of more specific diagnosis groups revealed increased risk for pulmonary embolism (HR 1.16, CI 1.02–1.32), bradyarrhythmias (HR 1.30, CI 1.14–1.50), atrial fibrillation (HR 1.31, CI 1.23–1.38) and cardiac arrest (HR 2.03, CI 1.58–2.60) among TNG patients but not among patients with GD.

Conclusion: In our cohort, hyperthyroidism is associated with an increased risk of cardiovascular disease for several types of cardiovascular disease. This excess risk appears to be almost solely attributed to patients with a TNG diagnosis. Furthermore, the connections seen between TNG and pulmonary embolism, bradyarrhythmia and cardiac arrest due to our knowledge not been previously described.

PS325 | BEDSIDE
Ectopies with a short coupling interval may trigger atrial fibrillation
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Background: Ectopies with a short coupling interval may trigger atrial fibrillation (AF). The elimination of AF-trigger ectopies is an essential procedure in AF ablation. However, the identification of AF-trigger ectopies is often difficult because of insufficient AF inducibility by drugs such as an isolated infusion.

Purpose: To compare the coupling intervals (CI) between AF-trigger and non-AF-trigger ectopies.

Methods: This study consisted of 59 patients with AF (paroxysmal AF, 35 (59%) patients; male, 43 (73%) patients; age, 66 ± 10 years old) who underwent an initial radiofrequency catheter ablation. Prior to the ablation procedure, we investigated the AF triggers as follows. If patients were in AF, they were converted to sinus rhythm by electrical cardioversion. Then, isoproterenol was infused to provoke ectopies and AF. We measured the CI of all ectopies provoked by an isoproterenol infusion. An ectopy was defined as an AF-trigger ectopy when it preceded AF or atrial firing. The %CI was calculated as the CI of the ectopy/P-P interval of the preceding 2 beats.

Results: Out of a total of 132 ectopies, 32 (24%) were AF-trigger ectopies. Most (97%) originated from pulmonary veins. AF-trigger ectopies had a significantly shorter CI (20±55 ms vs. 74±15 ms, p < 0.001) and %CI (0.31±0.11 vs. 0.56±0.13, p < 0.001) than those of non-trigger ectopies (Figure). An ROC analysis revealed that a %CI of 0.40 was the best cut-off value for the differentiation between AF-trigger and non-AF-trigger ectopies. (AUC=0.92, sensitivity=93%, specificity=78%).

Conclusion: AF-trigger ectopies had a short CI and %CI. These findings may be useful for estimating whether the ectopies are AF-trigger or not.

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PS326 | BEDSIDE
Evaluation of colchicine on the incidence of atrial fibrillation in open heart surgery patients: a prospective randomized open-label single-center study
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Background: Atrial fibrillation (AF) is a common rhythm disturbance in patients undergoing open heart surgery (OHS). It occurs in up to 25% of such patients and results in significant morbidity and increased hospital stay. Different strategies have been tested to decrease its incidence with variable success.

Purpose: This study was designed to determine if colchicine administered preoperatively to patients undergoing OHS and continued during their hospitalization is effective in reducing the incidence of postoperative AF.

Methods: This is a multicentre prospective randomized open label study. Consecutive patients with no history of supraventricular arrhythmia and scheduled for OHS (n = 360) were randomized to colchicine (n = 179) or no colchicine (n = 181). Main exclusion criteria were history of supraventricular arrhythmias or absence of sinus rhythm at enrolment, and contraindications to colchicine. Colchicine was orally administered 12 to 24 hours preoperatively and continued until hospital discharge (2 mg at enrolment and 0.5 mg twice daily in patients ≥ 70 kg, 1 mg at enrolment and 0.5 mg once daily in patients < 70 kg). Cardiac rhythm was monitored continuously in the coronary care unit and, by daily and symptom-prompted 12-lead electrocardiograms in the ward. The primary end point was colchicine side effects.

Results: The baseline characteristics were similar in both groups. In-hospital mortality was 3.3% (12 patients, 5 in the colchicine and 7 in the no-colchicine groups). The primary end point of AF occurred in 63 patients (17.5%), 26 (14.5%) in the colchicine group and 37 (20.5%) in the no-colchicine group (RR: 28.3% (p = 0.17). Of the 63 patients who developed AF, 33 (52.4%) developed their AF on the second post-operative day, and the majority of AF episodes (n = 53, 84.1%) occurred in the first 3 days after surgery. Diarrhoea occurred in 54 patients, 44 (24.6%) on colchicine and 10 (5.5%) on no-colchicine (p = 0.001). Colchicine was discontinued in 23 patients (52%) because of diarrhea.

Conclusion: Colchicine administered preoperatively to patients undergoing OHS and continued until hospital discharge failed to reduce the incidence of early postoperative AF. 2. Most AF episodes developed shortly after OHS. 3. Diarrhoea was the most common side effect of colchicine prompting discontinuation in more than half of patients.

PS327 | BEDSIDE
Comparisons of the effect of anticoagulation therapies on the coagulation system including the tissue factor pathway between vitamin K antagonist and the factor Xa inhibitors
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Background and introduction: The effects of the factor Xa inhibitors (FXa-inh) on the tissue factor pathway, are unclear. In addition, the anti-coagulation effect of NOACs during the trough drug concentration periods has not been well clarified.

Purpose: The purpose of this study was to evaluate the effects of FXa-inh and vitamin K antagonist (VKA) on the coagulation system including the tissue factor pathway inhibitor (TFPI).

Methods: In the consecutive 16 patients with atrial fibrillation who underwent catheter ablation therapy and 6 patients with paroxysmal supraventricular tachycardia or idiopathic ventricular tachycardia as control, we assayed the various markers of the coagulation system including tissue factor pathway inhibitor (TFPI). Of those 22, 11 were treated with factor Xa inhibitors (FXa-inh group), 5 with vitamin K antagonist (VKA) and 6 controls without anticoagulation therapy. The markers of the coagulation system were collected before punctures of femoral artery

Distribution of CI and %CI

Conclusion: AF-trigger ectopies had a short CI and %CI. These findings may be useful for estimating whether the ectopies are AF-trigger or not.

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and veins (corresponding to the trough concentration periods of FXa-inh), 15 minute after administration of 5,000 unit of unfractionated heparin intravenously, and 15 minute after punctions of femoral artery and veins during catheter operation.

Results: (1) The non-endothelial binding TFPI level was not different among the three groups (P = 0.22, ANOVA) control group: 94±32 ng/dl. VKA group: 69±28 ng/dl. and FXa-inh group: 93±20 ng/dl, respectively). However, the endothelial TFPI binding level was significantly higher in the FXa-inh group than in the control group (P = 0.02, 280±55 ng/dl vs. 199±43 ng/dl) and in the VKA group (P = 0.01, 280±55 ng/dl vs. 187±58 ng/dl).

(2) The basal levels of protein C, protein S and factor VII were lower in the VKA group than in other two groups.

(3) The prothrombin fragment 1+2 (F1+2) was a marker of thrombin generation, before the puncture was higher in the control group (228±52 pmol/L), compared with other two groups (P = 0.01, vs. FXa-inh group: 113±41 pmol/L). In addition, F1+2 after the punctures was lower in the VKA group (67±34 pmol/L) compared with other two groups (P = 0.01, vs. control group: 245±82 pmol/L; P = 0.03, vs. FXa-inh group: 171±75 pmol/L).

Conclusion(s): Endothelial TFPI was augmented by FXa inhibitor treatment, which could account for the anticoagulation effect in the period of the trough drug concentration. As compared to FXa-inh, VKA inhibited thrombin generation in response to vascular injury, which could explain about the lower risk of hemorrhagic complications in paroxysmal atrial fibrillation.

P5328 | BEDSIDE
The prevalence and risk factors for atrial fibrillation in beta-thalassemia major: a cross-sectional study in a UK specialist cardio-haematology clinic
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Background: The reason why some episodes of atrial fibrillation are symptomatic while others are asymptomatic remains unclear. The purpose of this study is to evaluate the electrocardiographic (ECG) differences between these episodes of paroxysmal atrial fibrillation (PAF).

Methods: Thirty consecutive patients (mean age 67±9 years; 14 men) who received an implantable loop recorder-IR (Reveal XT 9526, Medtronic, Minneapolis, Minnesota, USA) after the first symptomatic episode of paroxysmal atrial fibrillation (AF) were enrolled. All the patients were instructed to activate the device after the onset of symptoms indicative of the arrhythmia. We analyzed episodes of PAF that initially were asymptomatic but became symptomatic later on. In all these episodes we calculated the heart rate (HR) and the heart rate variability (HRV) the first 2 minutes of the episode and 2 minutes before the activation of the device by the patient. HRV was defined as the standard deviation (SD) of RR intervals. Coefficient of variation (CV) defined as SD/mean RR X 100.

Results: In 73 episodes of PAF from 17 patients (10 male). The major symptom was palpitation. The average time between the onset of AF and the activation of the device was 244 min (range 30–645 min). The mean duration of the episodes was 13±9. The average HR at the onset of AF was 104±28bpm while during the symptomatic period was 145±30bpm (p < 0.001).

The mean HRV was 170±68mséc and 84±32mséc (p < 0.001), while the mean CV was 24±5,3.9 and 18±4,5% (p < 0.001) respectively.

Conclusion: In this study we found that in episodes of PAF recorded by an ILR with an asymptomatic period preceding the symptomatic, onset of symptoms was characterized by higher HR and lower HRV. This finding related to the presence of autonomic imbalance due to the arrhythmia remains to be investigated.

P5330 | BEDSIDE
Relationship between inflammatory markers and coagulation cascade in patients with atrial fibrillation
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Background: Atrial fibrillation (AF) is associated with a prothrombotic or hypercoagulable state, which may be contributed to an increased risk for stroke and systemic embolism. There is a plausible evidence linking inflammation to the initiation and perpetuation of AF and AF-related thrombosis. Various inflammatory markers such as interleukin-8 (IL-8) and c-reactive protein (CRP) have been associated with AF. Several prothrombotic factors have been found to be elevated in AF, indicating abnormal thrombogenesis. Abnormalities of haemostasis, fibrinolysis, endothelium and platelets have all been described increasing the risk of stroke and thromboembolism. The aim of this study is to investigate a relationship between inflammation and the prothrombotic state in the setting of AF, including the impact of this relationship on clinical presentation and outcome of AF patients.

Methods: 141 patients with non-valvular AF (mean age 64.6±9.7) who enrolled in this study. After the enrollment the echocardiography examination and 24-hour ambulatory Holter monitoring ECG were registered in each patient. We measured plasma indexes of inflammation (CRP, IL-8) and the prothrombotic state, including markers of the coagulation cascade such as tissue factor (TF) and fibrinogen (F) in all observed patients with AF and 21 healthy control subjects. Sample calculated for 80% power, assuming a standard deviation difference of 1/3; significant p if p<0.05. All data were analyzed with SPSS 13.

Results: The obtained results shown that compared with controls, AF patients had higher levels of IL-8 (p=0.043), CRP (p=0.002), TF (p=0.026), and F (p=0.025). Plasma CRP levels were higher among AF patients at “high” risk compared with those at “low” risk (p=0.001). The mean levels of F and IL-8 are markedly elevated in patients with dilated left atrium, poorly functioning left atrial appendage and longer duration of AF.

Conclusion: Increased plasma of IL-8 and CRP are related to indexes of the coagulation cascade and may be contribute to structural remodeling of left atrium in patients with AF.

P5331 | BEDSIDE
Comparison among CHADS2, CHA2DS2-VASc and R2CHADS2 score in Japanese patients with paroxysmal non-valvular atrial fibrillation without receiving anticoagulant therapy
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Aim: It remains unclear which of CHADS2, CHA2DS2-VASc or R2CHADS2 score is most available for the risk stratification of ischemic stroke/systemic thromboembolism (IS/SE) in Japanese patients with paroxysmal non-valvular atrial fibrillation (PNVAF). We retrospectively investigated incidence of IS/SE on the basis of CHADS2, CHA2DS2-VASc, and R2CHADS2 scores in 332 paroxysmal non-valvular atrial fibrillation (PNVAF) patients (224 men, mean age 65±13 years) who was not administered anticoagulation therapy but who administered antiarrhythm drug therapy to maintain sinus rhythm between August 1995 to July 2008 based on the Japanese Circulation Society guideline was issued (mean follow-up periods 53±35months).

Results: (1) Annual rates of IS/SE underlying antiarrhythmic drugs therapy were as follow (Table). All higher CHADS2, CHA2DS2-VASc and R2CHADS2 scores
were associated with greater annual rates of IS/SE (P < 0.001). (2) A multivariate logistic regression analysis adjusted for the potentially confounding variables, CHADS2 scores (odds ratio [OR] 4.74, 95% confidence interval [CI] 2.80–8.00, P < 0.001), CHA2DS2-VASc scores (OR: 4.15, 95% CI: 2.57–6.71, P < 0.001), and R2CHA2DS2 scores (OR: 1.94, 95% CI: 1.48–2.53, P < 0.001) were significant independent predictors for IS/SE, respectively. (3) Area under receiver-operator characteristic curve for predicting IS/SE was 0.89 in CHA2DS2-VASc, 0.87 in CHADS2 scores and 0.85 in R2CHA2DS2 scores (all, P < 0.001), respectively, whereas there were not a significant difference among three scores.

Conclusion: In Japanese patients with PNVI, all CHA2DS2, CHA2DS2-VASc and R2CHA2DS2 scores are useful schemes for the risk stratification of ischemic stroke or systemic embolism.

P5332 | BENCH
The prevalence of left atrial enlargement in unselected atrial fibrillation patients
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Methods: We evaluated 138 asymptomatic CKD patients (90, 38 and 10 patients in stages G3, G4 and G5, respectively). A non-contrast computed tomography (CT) for ACS were included in this study. Blood samples were drawn on admission in patients with acute coronary syndrome (ACS). The presence of non-IRA-CTO in patients with ACS was associated with severe CAC score (OR 1.91, 95% CI 1.18–3.11; P = 0.008). On univariate analysis, MPV was a significant predictor of early and late mortality. Both mean platelet volume (MPV) and serum uric acid (SUA) were associated with adverse cardiovascular events in patients with ACS. Conclusion: We aimed to investigate the relationship between presence of non-IRA-CTO with MPV and SUA levels in ACS. Methods: A total of 1024 patients who underwent urgent coronary angiography (CA) for ACS were included in this study. Blood samples were drawn on admission before CA. Patients were dichotomized into two groups: non-IRA-CTO (+) group and non-IRA-CTO (−) group. Results: 230 patients (22.5%) had a non-IRA-CTO. MPV and SUA levels on admission were significantly higher in non-IRA-CTO (+) group when compared with non-IRA-CTO (−) group (9.26±0.98 vs. 8.35±0.69; P = 0.001 and 1.98±1.73 vs. 5.26±1.29; P < 0.001, respectively). At multivariate analysis, MPV [odds ratio (OR) 4.705, 95% confidence interval (CI) 2.842–7.790; P < 0.001] and SUA (OR 2.535, 95% CI 1.891–3.398; P < 0.001) levels were still independent predictors of non-IRA-CTO as well as age, hemoglobin, LVEF, and NSTE-ACS.

P5333 | BENCH
Obesity paradox in patients with coronary artery disease treated with percutaneous coronary intervention
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Results: Among the subjects, abdominal aortic calcification was present in 121 patients (88.0%) as defined by ACI >0 and median ACI was 12.9%; severe CAC score (≥400 AU) was present in 35 patients (25.4%). ACI showed a significant positive correlation with CAC score in CKD patients. (r = 0.549, P < 0.001). After adjusting for age, diabetes, systolic blood pressure, eGFR, and intact-PTH, ACI was independently associated with severe CAC score (OR 1.91, 95% CI 1.18–3.11; P = 0.008). ROC curve analysis showed that the ACI optimal cut-off value predicting severe CAC score was 15.5% (AUC 0.833, P < 0.001).

Conclusion: High abdominal aortic calcification is strongly associated with severe coronary artery calcification in CKD patients. The value of ACI 15.5% allows us to predict the presence of severe coronary artery calcification in these patients.

P5334 | BENCH
Coronary artery disease and comorbidities I
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Purpose: The area under the receiver operating characteristics curve (AUC) for predicting non-IRA-CTO was 0.72 (95% CI 0.65–0.79, P < 0.001). Conclusion: The area under the receiver operating characteristics curve (AUC) for predicting non-IRA-CTO was 0.72 (95% CI 0.65–0.79, P < 0.001).
endothelial dysfunction and impaired coronary flow reserve. However, the effect of subclinical hypothyroidism or thyroid autonomy on variant angina has yet to be determined.

**Materials and methods:** Among 385 consecutive patients without associated cardiovascular risk factors, who underwent coronary angiography with the ergonomics test (EPT) (165 had a positive EPT [EPT(+)], 159 had a negative EPT [EPT(−)]. The relationship between coronary artery spasm and the presence of subclinical thyroid dysfunction as well as serum thyroid peroxidase autoantibody (TPOAb) was evaluated.

**Results:** The proportion of patients with subclinical hypothyroidism among those who were EPT(+) was significantly higher than that in those who were EPT(−) (18% vs. 11%, p<0.001). However, there was no significant difference in the proportion of patients with subclinical hyperthyroidism between the groups. Moreover, we identified more positive TPOAb (33% vs. 14%, p<0.001) than those with EPT(−). There was a positive correlation between EPT(+) and TPOAb positivity (r=0.226, p<0.001), subclinical hypothyroidism (r=0.112, p=0.033), and body mass index (r=0.123, p=0.018). Binary logistic regression analysis revealed that the significant predictors of EPT(+) were body mass index (adjusted odds ratio [OR]=1.042, 95% confidence interval [CI]: 1.005–1.080), presence of subclinical hypothyroidism (OR=3.047, 95% CI: 1.083–8.572), TPO Ab titer (OR=1.028, 95% CI: 1.015–1.041) and the presence of TPO Ab (OR=4.904, 95% CI: 1.544–15.567).

**Conclusion:** Subclinical hypothyroidism and the presence of TPO Ab are significantly associated with coronary vasospasm in patients without cardiovascular risk factors.

**P3537 | BEDSIDE**

**Impact of coronary artery disease on outcomes after transcatheter aortic valve implantation**

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**Background:** Coronal artery disease (CAD) negatively prognostic of patients undergoing surgical aortic valve replacement and revascularization is generally recommended at the time of surgery. Implications of CAD in the setting of transcatheter aortic valve implantation (TAVI) are not known. The aim of this study was to determine the prevalence and impact having coronary artery disease in patients undergoing percutaneous valve implantation.

**Methods:** Between April 2008 and December 2010, we treated 372 patients with severe symptomatic aortic valve stenosis who were treated with high surgical risk, percutaneous aortic CoreValve prosthesis. All patients underwent coronary angiography prior.

**Results:** A total of 150 (40.3%) had coronary disease. In 95 patients were performed PCI, 23 had CABG and 23 had both techniques. Revascularization was complete in 64.6%. Patients with CAD were characterized by increased incidence of ventricular dysfunction than patients without CAD (24.8% vs. 12.6%, p=0.002). In-hospital (23% vs. 3.4%, p<0.001) and 6m (35.4% vs. 7.5%, p<0.001) mortality were higher in patients with CAD. After multivariate analysis, CAD was as independent predictor of in-hospital mortality (HR 2.1; 95% CI: 1.25–3.55, p=0.002). Patients with CAD had higher 6m mortality when presenting with GFR < 60 mL/min (48% vs 13%, p<0.024), severe LVSD (63% vs 27%; p<0.04), lower mean AVA (0.2±0.1 cm2 vs 0.4±0.2 cm2; p=0.03) and higher euroSCORE (11.6±8.6, 7.1±5.2, p=0.04). P who underwent aortic valve replacement also had higher 6m mortality (48% vs 15% p<0.05). Only AVA and aortic valve replacement persisted as independent predictors of 6m mortality in sAE.

**Conclusion:** The coexistence of sAE and ACS is rare, but is associated with a poor in-hospital and medium term outcome.

**P3539 | BEDSIDE**

**Lipid profile and paraoxonase 1 enzyme activity in patients with type 2 diabetes mellitus and different genotypes of paraoxonase 1 gene**

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**Aim of study:** We assumed lipid profile and paraoxonase 1 (PON 1) activity in patients with type 2 diabetes mellitus and different genotypes of paraoxonase 1 gene.

**Material and methods:** PON 1 enzyme activity, lipid profile and PON 1 192 gene polymorphism were determined in 118 patients (27 males and 91 females) with type 2 diabetes mellitus (DM) (age - 48.7 ±10.7 years old). 110 patients (93.2%) were overweight and obesity. 112 patients (94.9%) had arterial hypertention. 20 patients (17.2%) were smokers. Family history of cardiovascular disease was in 63 patients (53.4%) and family history of DM was in 43 patients (36.8%). 77 patients (67.5%) had hypercholesterolemia, 73 patients (61.9%) had ischemic heart disease and 16 patients (13.6%) had myocardial infarction (MI). PON 1 enzyme activity was evaluated by kinetic method, parameters of lipid profile - by enzyme method. PON 1 192 gene polymorphism were determined by PCR.

**Results:** We identified PON 1 genotype Q192R in 76 patients (64.4%), PON 1 genotype Q192R - in 39 patients (33.1%). PON 1 genotype R192R was revealed only in 3 patients (2.5%). PON 1 enzyme activity was higher in patients with PON 1 Q192Q genotype versus patients with PON 1 Q192R and PON 1 R192R genotypes (9.8±5.7 FA/mmol and 7.3±4.9 FA/mmol, p<0.03). Lipid profile in patients with type 2 DM and different PON 1 192 genotypes didn’t differ. We revealed correlations between level of high density lipoproteins and PON 1 enzyme activity (r=0.2, p=0.04). Lipid profile in patient with and without MI didn’t differ.

**Conclusion:** Paraoxonase 1 activity is increased in patients with type 2 diabetes mellitus and paraoxonase 1 Q192Q genotype. Lipid profile in patients with type 2 diabetes mellitus and different PON 1 192 genotypes didn’t differ.

**P3540 | BEDSIDE**

**Prognostic value of elevated high-sensitivity cardiac troponin T levels in patients with stable coronary artery disease**

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**Background:** Coronary artery disease (CAD) remains one of the leading causes of morbidity and mortality worldwide despite advanced primary and secondary prevention.

**Purpose:** To investigate the prognostic implications of elevated high-sensitivity cardiac troponin T (hs-cTnT) values in presumably stable ambulatory CAD patients treated for secondary and non-secondary prevention.

**Methods:** We conducted a retrospective, single-center pilot observational study in a low-risk population. All patients received routine measurement of hs-cTnT at the time of coronary angiography and follow-up visits. Endpoints were all-cause mortality and a composite of all-cause mortality, acute myocardial infarction, stroke and rehospitalization for acute coronary syndrome and heart failure.

**Results:** 965 consecutive patients presenting to our outpatient clinic between June 2009 and June 2010 were screened for eligibility. 893 patients with a stable clinical course at index visit, at least one hs-cTnT value and at least one follow-up visit qualified for analysis. Follow-up was 796 days. 547 patients (78.9%) had hs-cTnT values below 14 ng/L and 146 patients (21.1%) had values above 14 ng/L. We observed 13 deaths (all-cause mortality) including 4 patients with a cardiovascular death. Age, NT-proBNP levels and impaired renal function were independently associated with an elevated hs-cTnT in a multivariate analysis. hs-cTnT values >14 ng/L were strongly associated with all-cause mortality (HR 12.9, 95% CI:
Methods: We consecutively registered 4248 type 2 diabetic patients with CAD between 2008 and 2014. Patients were registered if their HbA1c was above 7%, usual if 7–8% and uncontrolled if above 8% during the follow-up.

Results: During 15717 patients-years of follow-up, 630 primary outcomes occurred. There was no association between baseline Hb A1c (below or above 7%) and primary outcome. Risk for primary outcome (HR 1.52, p=0.0014) and all-cause death (HR 1.51, p=0.0077) in very tight glycaemic control group was significantly higher than that in tight control group. Risk for primary outcome in either usual control group or uncontrolled group was not higher than that in tight control group.

Conclusion: Tight glycaemic control among type 2 diabetic patients with CAD was not associated with improved cardiovascular outcomes compared with patients having usually controlled or even uncontrolled HbA1c.

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CORONARY ARTERY DISEASE AND COMORBIDITIES II

P5343 | BEDSIDE
Myocardial revascularization using exclusive skeletonized internal thoracic artery grafting in diabetic multivessel-disease patients
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Objectives: The left internal thoracic artery (ITA) is acknowledged as the best coronary conduit for coronary artery bypass grafting surgery (CABG). In diabetic multivessel-disease patients, CABG can be performed by using exclusively both ITAs with multiple sequential side-to-side coronary anastomoses. The purpose of this study is to evaluate the clinical status of the patients by stress test and the patency of ITA, and the quality of ITA grafts, and coronary anastomoses by angiographic control.

Methods: Between May 2008 and February 2014, 112 diabetic and multiple vessel disease patients underwent CABG by exclusive ITAs. The technique consisted of connecting the right ITA divided at its origin and connected to the left ITA left in situ, in a Y fashion; the left ITA is used to revascularize anterior coronary arteries, and the right ITA, coronary arteries of lateral and posterior aspect of the heart. A total of 409 anastomoses were performed (3.6 anastomoses per patients; range, 3 to 5).

Results: There was 1 death on the seventh post operative day by right ventricular failure. There was no postoperative myocardial infarction or stroke. There was no mediastinitis or wound infection or sternal healing problem. Ninety three patients (83%) had stress test control with no major abnormalities, except 3 patients in whom the test was interrupted because of arrhythmia for two patients and high blood pressure for the other one. Angiographic control was performed in 53 patients (total of 204 anastomoses; 3.8 anastomoses per patients; range, 3 to 5); all Y anastomoses were patent and the 204 ITA-coronary anastomoses were patent; moderate stenosis was found in 2 side to side anastomoses between the right ITA and marginal arteries, and competitive flow related to moderately stenosed right coronary artery was found in 4 patients, without clinical consequences.

Conclusions: In diabetic multiple vessel disease patients this method of myocardial revascularisation can be performed safely, with good early postoperative results. In terms of angiographic control the patency of all the anastomoses is excellent.
in blood samples of 40 diagnosed patients with CHD by coronary angiography and 40 health controls. Routine anthropometric and serologic data were collected.

Serum betatrophin, fasting glucose, lipid protein profiles, homocysteine and high-sensitivity C-reactive protein (hs-CRP) were measured. Serum betatrophin levels were significantly higher in CHD patients than in healthy control subjects (569.09 pg/ml; 95% CI 444.52–798.85 pg/ml vs. 410.46 pg/ml; 95% CI 339.02–526.41 pg/ml; p < 0.001). Importantly, serum betatrophin associated positively with the severity of coronary branch luminal narrowings (ρ=0.304, p < 0.05), homocysteine (ρ=0.278, p < 0.01) and high-sensitivity C-reactive protein (ρ=0.179, p < 0.05) in CHD patients, whereas there was no significant association with blood lipids and glucose. In CHD subjects, multivariate regression analyses showed that the homocysteine was independent factors influencing serum betatrophin levels.

Conclusions: Serum betatrophin levels are significantly increased and associated positively with the severity of coronary branch luminal narrowings in patients with CHD. Our results suggest that betatrophin may play a role in the pathogenesis of CHD.

**Purpose:** To determine the prevalence and prognostic value of ID in P with ACS.

**Methods:** Prospective, unicentric study including 543 P admitted with ACS over 1 year and a minimal 6 months follow-up. Serum iron, ferritin, total iron binding capacity and transferrin saturation were evaluated in the first 24 hours of hospitalization.

**Results:** ID was defined as a transferrin saturation <20% and was further classified as absolute (ferritin <100µg/L), when iron stores were depleted; or functional (ferritin >100µg/L), when iron delivery to cells was restricted. The clinical event study was 6 months mortality (GM).

**Results:** ID was diagnosed in 37.9% (n=189) of P and was more often functional (n=144) with ID had a higher prevalence of anemia (p<0.001). P with ID had more often history of diabetes (p<0.001) and surgical coronary revascularization (p<0.001). At admission they presented more frequently with heart failure (p<0.028) and have heart failure (p<0.001). They had lower mean levels of glomerular filtration rate (p<0.001) and higher mean levels of RDW (p<0.001), C reactive protein (p<0.001) and type B natriurethic peptide (p<0.001). At echocardiographic examination, they had more moderate/severe left ventricular systolic dysfunction (p<0.001) and a higher mean level of sggFR (p<0.001). By ROC analysis, a cut-off of 1200 mg/L for haptoglobin was considered as the optimal cut-off to identify CAD patients with significant coronary endothelial dysfunction and is correlated to coronary microvascular endothelial dysfunction. We investigated the value of RH-PAT as a noninvasive tool to identify CAD patients with reduced coronary flow reserve (CFR).

**Conclusion:** Using RH-PAT (PAT = PAT Index), digital pulse volume changes during reactive hyperemia were assessed in 89 patients with angiographically documented CAD and >70% stenosis of LAD. The PAT device consists of two finger-mounted probes, which include a system of inflatable latex air-cushions within which a blood pressure cuff is placed on one upper arm (study arm), while the contralateral arm serves as a control (control arm) RH-PAT index was calculated as the ratio of the digital pulse volume during reactive hyperemia divided by that at baseline using the Endo-PAT apparatus. Coronary flow reserve (CFR) of the LAD after adenosine infusion was assessed using Doppler echocardiography Patients were categorised to those with either normal (>2.5) or impaired (<2.5) CFR.

**Results:** A decreasing CFR was related with decreasing RH-PAT index (r=−0.45 p<0.001). The RH-PAT index was significantly lower in patients with CFR ≤2.5 compared with those with CFR>2.5 (1.4±0.3 vs. 1.85±0.4, p<0.006). By ROC analysis, an RH-PAT index >1.5 was found to have a sensitivity of 75% and a specificity of 77% to identify patients with CFR<2.5.

**Conclusions:** Digital hyperemic response, as measured by RH-PAT, is attenuated in patients with impaired CFR suggesting a role for RH-PAT as a noninvasive test to identify CAD patients with significant coronary endothelial dysfunction and thus adverse prognosis.

**PS544 | BEDSIDE**

**Objective:** To identify an optimal cut-off point for the GRACE risk score that maximizes the area under the ROC curve for the estimation of hospital and 1-year mortality in ACS patients.

**Methods:** We included all ACS patients in a single centre in a 4 years time period. Patients were divided on the basis of the high (≥2.5) or intermediate (<2.5) risk groups.

**Results:** We included 1237 patients and 438 (35.4%) age 65 years and older patients with ACS (GRACE risk ≥ 2.5). Patients with GRACE risk ≥ 2.5 had higher IHM (13,8% vs 2,3%, p<0.001), mortality during follow-up (41,8% vs 12,7%, p<0.049) but not MACE (26,2% vs 54,7%, p=0,011). In multivariate analysis UC was a better IHM (CI 95%; OR 8,6, p=0,001) compared with cystatin C (p=0,079).

**Conclusions:** When compared with cystatin-C our variable was a better predictor of IHM.

**PS545 | BEDSIDE**

**Objective:** To assess the accuracy of the GRACE score in elderly ACS patients with intermediate coronary stenosis (50–70%). Peripheral arterial tonometry after measurement of reactive hyperemia (RH-PAT) and cystatin-C were correlated to IMH and IMH＜2.5. The methodology is based on the hypothesis that reactive hyperemia and its impairment are markers of endothelial dysfunction and is correlated to ischemia.

**Methods:** We used a prospective, multicentre study including 217 patients with ACS over 1 year. RH-PAT and cystatin-C were performed at admission. IMH＜2.5 was defined using the cut-off of 1200 mg/L for haptoglobin.

**Results:** At admission patients with IHM＜2.5 had higher IHM (13,8% vs 2.8% (p<0.01), mortality during follow-up (41.8% vs 12.7%, p<0.049) but not MACE (26.2% vs 54.7%, p=0.011). In multivariate analysis UC was a better IHM (CI 95%; OR 8.6, p=0.001) compared with cystatin C (p=0.079).

**Conclusions:** When compared with cystatin-C our variable was a better predictor of IHM.
log-rank=0.21) or high-risk (18.8% vs. 13.0%; log-rank=0.24) categories. Multivariate analysis, performed by Cox-regression, showed that age > 75 years was independently associated to higher 1-year mortality (HR: 2.51 95% CI 1.38–4.58; p < 0.01) as well as the GRACE score (1.01 95% CI 1.01–1.02). When divided in GRACE score risk categories, age > 75 year was associated to mortality only in low-risk group (1.00% 95% CI 1.00–1.00).

Conclusions: The GRACE score risk is useful for risk prediction in elderly patients admitted for ACS although it might underestimate the risk in low-risk category.

P5349 | BEDSIDE

The role of acute kidney injury in acute myocardial infarction
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Myocardial infarction (MI) and renal pathology - two serious diseases. Even moderate acute kidney injury (AKI) may lead to increased mortality.

Aim of the work: To study the influence of systemic inflammatory on the course of MI, accompanied by AKI in patients without chronic kidney disease.

Materials and methods: The study included 343 patients without chronic kidney disease (CKD) who had an AKI and 340 control patients (n=683). Between the patients with AKI and the control group (n=683) there were no differences in age (53.4 ±17.8 vs 53.5 ±17.6 years; p>0.05) and sex (35% female vs 33%; p>0.05).

Results: QMI was from 74.6% in group III to 79.2% in I. Leukocytosis at admittance was in 2 patients of group II. Mortality: I - 7.4%, II - 21.0%, III - 6.3%.

Conclusion: Cystatin C was significantly increased in patients of group II vs 10,14±0,15*109/l, P<0.01. Respiratory rate at admission in all groups were above normal: 20,29±0,85, 23,57±1,08, 18,60±0,90 per minute. Between II and III groups P<0.01. Heart rate: 92,56±3,25, 93,40±3,30, 86,70±2,50 beats per minute. Between II and III groups P<0.01. Cystatin C was significantly increased in patients of group II vs: 989,23±51,34 vs 721,37±12,78 ng/ml. Neutrophilic lipocytosis was elevated in all groups but between I and III: 20,29±0,85, 23,57±1,08, 18,60±0,90 per minute. Between II and III groups P<0.01. Between I and II: 164,69±9,74 vs 103,40±5,69 ng/ml, P<0.01.

P5350 | BEDSIDE

Impaired glucose tolerance and coronary artery spasm in non-diabetic patients underwent acetylcholine provocation test
B.G. Choi, S.W. Rha, S.Y. Choi, J.K. Byun, J.J. Lee, J.B. Kim, E.J. Kim, C.G. Park, H.S. Seo, D.J. Oh. Korea University Guro Hospital, Seoul, Korea, Republic of Background: Impaired glucose tolerance (IGT) is known to be a risk factor of significant coronary artery disease (CAD) and endothelial dysfunction. However, currently there is no enough available data regarding the impact of newly-diagnosed IGT on coronary artery spasm (CAS) in real world clinical practice.

Methods: A total of eligible 4,745 consecutive non-diabetic patients (pts) without significant CAD underwent acetylcholine (Ach) provocation test were enrolled. IGT was defined as follows: [fasting glucose, 100–125 mg/dl; or HbA1c%, 5.7–6.4%]. Significant CAS was defined as >70% of narrowing by incremental intracoronary Ach injection of 20, 50 and 100 μg into left coronary artery. Pts were divided into two groups based on the presence of IGT: the IGT group (n=1,345) and the control group (n=3,400). To adjust potential confounders, a propensity score matched (PSM) analysis was performed using the logistic regression model.

Results: After PSM analysis, 2 propensity-matched groups (1,337 pairs, n=2,674, C-statistic=0.654) were generated and the baseline characteristics of the two groups were balanced. Major angiographic and clinical parameters during Ach provocation test were not different between the two groups. IGT was an independent predictor of Ach-induced CAS (58% vs.59%, p=0.609; HR=0.960; 95% CI: 0.823 - 1.120).

Conclusions: In this study, despite the expected endothelial dysfunction, IGT was not associated with Ach induced CAS, suggesting that the mechanisms and risk factors of CAS may be different from those of atherosclerotic CAD.

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Long term mortality and risk of myocardial infarction associated with presence and extent of coronary artery disease
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Introduction: Coronary angiography (CAG) is the current state-of-the-art in determining presence and extent of obstructive coronary artery disease (CAD) to assess risk of future myocardial infarction (MI). Atherosclerosis is one of several potential causes of ischemic stroke but studies comparing the extent of CAD and the risk of ischemic stroke is lacking.

Purpose: To examine the potential association between severity of CAD and long-term clinical outcomes: death, MI and ischemic stroke.

Methods: We performed a population-based cohort study of every CAD registrered at our institutions from January 1st 2003 to December 31st 2012. In case of multiple CAG examinations during the period, only the first CAG was included. Patients were stratified into three groups: I < 2-VD, II ≥ 2- and 3- vessel disease (VD), and finally diffuse CAD. Left main stenosis was defined as ≥ 2-VD. Patients were followed for a maximum of 7 years. End-points were all-cause mortality, ischemic stroke and MI. Crude and adjusted hazard ratios were estimated using Cox proportional hazards model. Subgroup analyses were performed according to level of comorbidity and procedural priority.

Results: A total of 84,025 patients were eligible for analyses, 31,734 had 0-VD, 26,656 had 1-VD, 1,355 had 2-VD, 9,871 had 3-VD, and finally 6,173 had diffuse CAD. Mean follow up was 4.4 years. Patients with 3-VD had the highest all-cause mortality risk during follow-up, followed by patients with 2-VD, diffuse CAD and 1-VD, while patients without obstructive CAD had the lowest mortality risk. Risk of death was highest among patients with 3-VD followed by 2-VD and 1-VD, while patients with 0-VD or diffuse CAD had the lowest MI rates. Patients with diffuse CAD and 3-VD had the highest risk of ischemic stroke followed by 2-VD, 1-VD and lastly 0-VD. Death, MI and ischemic stroke rates all increased with increasing level of comorbidity and per procedure procedural priority.

Conclusions: Presence and extent of CAD was associated with increasing risk of death, MI and ischemic stroke. Diffuse CAD (alongside 3-VD) was found to be associated with the highest risk of future ischemic stroke, despite remaining in lower risk of future MI.

P5352 | BEDSIDE

Differences on prognosis among patients with previous ischemic heart disease versus cerebrovascular disease admitted with acute coronary syndrome?

Background: It is known that patients with previous vascular disease (PVD) have a poorer outcome than those without and prognosis worsens as the number of affected vascular beds increases.

Aim: To evaluate if there are differences in in-hospital and 6-month mortality among patients admitted with acute coronary syndromes with previous ischemic heart disease (IHD) versus cerebrovascular disease (CVD).

Methods: We analysed 4871 patients (pts) admitted consecutively in our coronary care unit with a diagnosis of acute coronary syndrome and included in a prospective registry, from January 2002 to October 2013. Patients were divided in 3 groups: group 1 - pts without PVD (n=3718, 76.3%); group 2 - pts with previous IHD (n=825, 16.8%); group 3 - pts with previous CVD (n=257, 5.3%). We excluded pts with previous PVD plus CVD (n=71, 1.5%). For each group we compared clinical features and adverse events. Primary endpoint was the occurrence of death at 6 months; follow-up was completed in 98% of patients.

Results: Pts in group 3 were older (63±7 vs 67±12 vs 71±11 years;p < 0.001), had higher proportion of women (25% vs 21.9% vs 32.3%;p < 0.001) and hypertension (58% vs 73.1% vs 83.7%;p < 0.001). Group 2 had more often body mass index >25 kg/m² (47.1% vs 52.5% vs 50.8%;p =0.016), dyslipidaemia (46% vs 69.3% vs 52.1%;p < 0.001) and diabetes (23.5% vs 38.8% vs 36.6%;p < 0.001). Group 1 had history of smoking (30.5% vs 19.0% vs 12.8%;p < 0.001). Group 3 had higher proportion of patients with previous MI (46% vs 33% vs 33%;p < 0.001) and renal insufficiency (eGFR < 60 ml/min) (19.2% vs 31% vs 40.9%;p < 0.001). Group 2 presented more severe coronary artery disease (11.7% vs 22.2% vs 16.7%;p < 0.001) and higher prevalence of left ventricular dysfunction (56.2% vs 61.8% vs 58.4%;p =0.03).
evolution myocardial infarction was more prevalent in Group 1 (54.5% vs 25.6% vs 51.5%; p<.001), while myocardial infarction without ST-elevation was more frequent in group 2 (41.2% vs 65% vs 45.5%; p<.001). In-hospital (4.5% vs 4.7% vs 7.0%; p<.001) and 6-month mortality (8.7% vs 10.6% vs 16.5%; p<.001) were higher in patients with previous CVD. In multivariate analysis and after adjusting for different baseline characteristics, pts with previous CVD had higher risk of 6-month mortality compared to those without PVD [OR 1.67, 95% CI (1.06–2.63), p=0.028].

Conclusion: Previous CVD remained as a strong predictor of 6-month mortality in patients admitted with acute coronary syndrome.

PS535 | BEDSIDE
Myocardial adverse cardiac and cerebrovascular events in chronic kidney disease patients undergoing cardiac catheterization: a 7-year follow-up
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Background: Chronic Kidney Disease (CKD) is an independent risk factor for coronary artery disease affecting almost one-third of patients (pts) admitted to coronary care units. Coronary angiography (CA) or percutaneous intervention (PCI) is challenging in this setting, because of an increased risk of contrast-induced kidney injury (CIKI).

Purpose: Between January and December 2007, 243 consecutive pts with indication to CA/PCI and an estimated glomerular filtration rate (eGFR) <60 cc/min were enrolled in this prospective cohort study to evaluate if post-procedural CIKI was associated with major-adverse-cardiac-and-cerebrovascular-events (MACCE) occurrence during a 7-year follow up (FUP).

Methods: All pts were given appropriate CIKI prophylaxis. CIKI was defined as a serum creatinine (sCr) increase of +0.5 mg/dl in 48 hours or +50% in 7 days. The primary endpoint was MACCE incidence during the FUP, defined as: acute coronary syndrome, PCI, coronary artery bypass grafting surgery, acute pulmonary oedema, cardiogenic shock, transient ischemic attack, stroke, cardiovascular or cerebrovascular death. The secondary endpoints were post-procedural CIKI and 5-year eGFR.

Results: On admission the 243 pts were 73±8 years old with a Mehran risk score of 7.9±3.4, a sCr of 1.88±1.68 and an eGFR of 43±14 cc/min. There were 89 (37%) women, 204 (84%) hypertensive, 74 (30%) diabetics. Forty-nine (20%) pts of 7.9±3.4, a sCr of 1.88±1.68 and an eGFR of 43±14 cc/min. There were 89 (37%) women, 204 (84%) hypertensive, 74 (30%) diabetics. Forty-nine (20%) pts

Conclusion: CKD pts undergoing CA/PCI have an increased risk of CIKI. Post-procedural CIKI was associated with a higher MACCE rate within 7 years after discharge. CIKI pts showed an accelerated progression of their renal dysfuncion during the first five years following discharge. A single CIKI episode might increase the MACCE risk at FUP by enhancing vascular, endothelial and atherosclerotic damage typical of CKD. CIKI prevention in high-risk pts is then highly recommended.

PS545 | BEDSIDE
Prognostic impact of chronic total coronary occlusion on implantable cardioverter-defibrillator recipients with ischemic heart diseases
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Background: The prognostic impact of chronic total coronary occlusion (CTO) on implantable cardioverter-defibrillator (ICD) recipients remains unclear.

Methods: Consecutive 84 patients with ischemic heart disease receiving ICD therapy for primary or secondary prevention were initially enrolled; 2 patients were excluded because of lost follow-up. During a median 3.8 years follow-up period, we investigated major adverse cardiac events (MACE) including cardiac death, appropriate device therapy, hospitalization due to heart failure and implantation of ventricular assisted devices.

Results: Of 84 study patients (mean age, 70±8 years; 86% men), 34 (40%) pts had CTO. Between the groups of patients with CTO (+CTO) and without CTO (-CTO), there is no significant difference in age, left ventricular ejection fraction (LVEF), NYHA functional class III or IV, rate of receiving cardiac resynchro-

Figure 1

Conclusion: In this study, DES associated CAD was related to higher incidence of adverse 3-year clinical outcomes. Special caution should be exercised in significant CAD pts who underwent PCI with DESs.

PS536 | BEDSIDE
Impact of acute hyperglycemia after angioplasty for acute myocardial infarction
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Introduction: Hyperglycemia (HG) has been shown to be a powerful predictor of worse outcome after ST segment-elevation myocardial infarction (STEMI).

Aim: Investigate the relationship between acute HG and angiographic and clinical outcome after primary or rescue angioplasty for STEMI.

Methods: We prospectively included 199 patients who underwent revascularization for STEMI. We compared intrahospital outcomes between the groups of patients with HG (+HG) and without HG (-HG) and outcomes between diabetic and non diabetic in the HG+ group. Plasma glucose was measured at hospital admission. HG was defined as plasma glucose >11 mmol/l (198 mg/dl).

Results: Among the overall population, 150 (37.6%) patients had HG. They were more frequently women with a more frequent history of diabetes and dyslipidemia. They presented with lower blood pressure and more right ventricular heart failure.

Coronary success was significantly lower in the HG+ group (86% vs 92%, p<0.05) with lower rates of ST segment resolution at 24 hours (47.2% vs 61.4%, p<0.006). Intrahospital outcomes were worse in the HG+ group as attested by a higher mortality (20% vs 10.4%, 0.008), higher late heart failure (32% vs 18.1%,
Patients considered for OLT were 633, 367 (58.2%, age 57±5.7 years, p<0.001) and atrial fibrillation (9.3% vs 4.4%, p=0.05). Those outcomes were similar in the HCG group regardless to the diabetic status. Predictive factors for intrahospital mortality in the overall cohort were: procedural failure (OR: 4.76, 95% CI [1.65, 13.7] p=0.004), heart failure at presentation (OR: 9.75, 95% CI [4.14, 22.87] p<0.001), non ST regression at 24 hours (OR: 2.19, 95% CI [1.08, 4.45], p=0.029), anemia (OR: 4.22, 95% CI [2.06, 6.83], p<0.001), high creatinine levels (OR: 1.09, 95% CI [1.03; 1.14], p= 0.001) high glyceremia (OR: 2.66, 95% CI [1.2, 5.9], p= 0.016). Diabetic did not predict intrahospital mortality (p= 0.64) even in the group of patients with hyperglycemia. In non diabetic patients (n=260), HCG was associated with larger intact size (p=0.001) and more adverse outcome (p=0.009). In the same group, Hba1c was associated with one year mortality (p=0.02).

Conclusions: STEMI is an important predictor of worse outcomes with an increasing mortality risk even beyond 11mmol/l. In non diabetic patients, both elevated admission glucose and Hba1c levels were associated with worse adverse outcome. These results suggest the usefulness of glyceremia assessment in the setting of STEMI even in non diabetic and the beneficial effect of strict glycemic control.

P5357 | BEDSIDE
Relation of resistin to PCSK9 levels in CAD patients with varying degree of obesity
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Objectives: To investigate the association of resistin levels with proprotein convertase subtilisin/kexin type 9 (PCSK9), another novel regulator of atherosclerosis, in the condition of coronary artery disease (CAD).

Methods: A total of 95 CAD patients enrolled to a totally obstructive stable CAD patients who were not treated with lipid-lowering drugs in the present study. The baseline clinical characteristics were collected. Plasma PCSK9 and resistin levels were determined by ELISA. The relationship between plasma PCSK9 and resistin levels was investigated.

Results: Overall, resistin levels exhibited a positive nonparametric correlation with PCSK9 (r=0.123, p< 0.05). When the patients classified into groups based on degree of obesity, the resistin correlated significantly to PCSK9 levels (r=0.162, p<0.05) but not in obese patients (r=0.145, p=0.205).Contrasted with the PCSK9 levels, resistin showed no significant associations with metabolic parameters including lipid profile. The PCSK9 and resistin levels related differently to inflammatory markers in both obese and non-obese patients. Multivariate regression analysis corroborated the relation between PCSK9 and an elevated resistin level in non-obese patients independently of traditional cardiometabolic and inflammatory parameters (p<0.05, all).

Conclusions: The plasma resistin levels were positively related to the PCSK9 levels in CAD patients with normal weight, suggesting that the circulating resistin might represent a link with PCSK9 level variations in CAD progression of non-obese condition.

P5358 | BEDSIDE
Prevalence of coronary artery disease in end-stage liver disease transplantation candidates
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Introduction: Orthoptic liver transplantation (OLT) is the only effective treatment in patients with end-stage liver disease (ESLD). Evidences suggest that coronary artery disease (CAD) is associated with increased peri-operative OLT mortality. Thus, identification of CAD is crucial in pre-OLT evaluation. There is no widely ac-

knowledged method for atherosclerosis clinical phenomena. The plasma resistin levels were positively related to the PCSK9 levels in CAD patients with normal weight, suggesting that the circulating resistin might represent a link with PCSK9 level variations in CAD progression of non-obese condition.

P5359 | BEDSIDE
The influence of comorbidity on the prognosis following computed tomography angiography in patients suspected of coronary artery disease
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Background: Coronary CT angiography (CTA) testing in patients suspected of coronary artery disease (CAD) carries prognostic information. With an ageing population, the burden of comorbidity in patients undergoing coronary CTA in-

creases. Comorbidity may interfere with the prognostic value of coronary CTA. P5359 | BEDSIDE
To evaluate the influence of comorbidity on the prognostic information derived by coronary CTA testing. Methods: A total of, 17,020 consecutive symptomatic patients with suspected CAD, who underwent coronary CTA (~64-detector row) between January 2007 and December 2012 in 10 centers were included. The coronary CTA result was defined as normal (0% luminal stenosis), non- obstructive CAD (1%-49% luminal stenosis) or obstructive CAD (~50% luminal stenosis). Comorbidity was as-

sessed using the Charlson Comorbidity Index (CCI) scores and categorized as low (CCI Score<1), moderate (score=1) or severe (score>2). During a mean follow-up time of 2.7 (SD: 1.1; range: 1–6) years the composite end-point comprising all-cause death and myocardial infarction was registered. Cox regression was used to compute hazard ratios (HR) with 95% confidence intervals (CI) as measures of relative risk for the occurrence of the combined end-point, adjusting for age, sex, established cardiac risk factors, individual comorbidities and concurrent car-

diovascular medical treatment. Results: Mean (SD) age was 57 (11) years. 56% were women. Comorbidity burden was low in 76.0%, moderate in 14.7%, and severe in 9.3% of the patients. During follow-up 297 patients reached the composite end-point. Compared to pa-

tients without CAD, both patients with non-obstructive CAD (HR=1.12, 95% CI: 1.02–1.23) and obstructive CAD (HR: 2.06, 95% CI: 1.88–2.26) exhibited an in-

creased relative risk of the composite endpoint. Comorbidity influenced the prog-

nostic value of coronary CTA with HRs (95% CI) in patients with non-obstructive disease of 1.05 (0.94–1.20), 1.14 (0.92–1.41) and 1.31 (1.11–1.56) in patients with low, moderate or severe comorbidity, whereas in patients with obstructive CAD figures were 2.13 (1.89–2.43), 1.65 (1.31–2.06) and 2.41 (2.05–2.85), re-

spectively. Conclusion: Obstructive CAD as identified by coronary CTA predicts cardiovascular risk regardless of comorbidity burden. However, in the presence of non-

obstructive CAD, prognosis is influenced by comorbidity.
Background and introduction: There is a continuous search for prognostic markers to identify patients with acute coronary syndrome (ACS) who are at high risk of mortality and major adverse cardiovascular events (MACE). Anemia has been associated to atherosclerosis severity and major adverse cardiovascular events in patients with acute coronary syndrome, and may be useful for routine use since it’s lower cost.

Methods: In-Hospital impact of anemia at admission in patients with acute coronary syndromes

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Purpose: To evaluate the in-hospital prognosis of the presence of anemia at admission in the patients with ACS.

Methods: A total number of 10107 patients included in the national registry of ACS, from 1st of October 2010 and until 20th October 2014 were divided in two groups: Group A – patients with anemia (Hb < 12 g/dl in women; Hb < 13 g/dl in men) and Group B – patients without anemia. We evaluate the relationship between anemia on admission with cardiovascular events and in-hospital mortality.

Results: Group A (n = 3732) with Group B (n = 2576) we found that the Group B had a higher prevalence of AMI without elevation of the ST segment (53.5 ± 46%, p < 0.001), and higher mean age (73 vs 64, p = 0.001) and time to balloon (398 vs 362 min, p = 0.001). The was also more co-moriblits (in particular hypertension, diabetes mellitus and familiar history of cardiovascular disease) and a higher prevalence of disea as the dominant symptom (8.4% vs 3.1%). The Group B had also a higher Killip Class at admission (prevalence of class II-IV of 27.5 vs 11.6%, p < 0.001), a worse left ventricular function (mean ejection fraction of 50 vs 55%, p < 0.001), a higher incidence of heart failure (27.6 vs 13.2%, p < 0.001), cardiogenic shock (6.5 vs 3%, p = 0.001), atrial fibrillation (7.9 vs 4.5%, p < 0.001) and a higher mortality (6.9 vs 2.6%, p < 0.001).

Conclusion: The presence of anemia at admission is predictor of a worse in-hospital course, with this patients having more heart failure, atrial fibrillation and mortality.

Background:

The VDR FF , Ff, ff genotypes (FokI polymorphism) and the VDR TT, Tt, tt genotypes (TagI polymorphism) were determined in a sample of 193 Russian population on the basis of the local cohort (2010–2013). Hs-TnT were obtained before dialysis. Ongoing dialysis patients with CAD (n = 283) showed significantly higher mean CCA IMT (0.66 ± 0.15 mm vs. 0.74 ± 0.27, p < 0.001), TPA (0.13 ± 0.24 vs. 0.20 ± 0.42 cm², p < 0.002), and beta stiffness index (5.1 ± 3.11 vs. 5.60 ± 2.66, p = 0.045) and lower mean WSS (2.59 ± 0.82 vs. 3.23 ± 0.90 dyne/cm², p < 0.01). Mean carotid WSS showed significant negative correlations with the beta stiffness index (r = −0.116, p < 0.001), mean IMT (r = −0.193, p < 0.007), and TPA (r = −0.296, p < 0.001). Binary logistic regression analysis showed that odds (Odd Ratio [OR] 1.038, 95% confidence interval [CI] 1.010–1.066), presence of diabetes mellitus (OR 1.608, 95% CI 1.194–1.807), mean WSS showed significant positive correlations with the beta stiffness index (r = 0.115, p < 0.001).

Conclusion: In patients with chest pain, low local shear stress and high plaque burden in the carotid arteries were significant predictors of CAD. This finding is further strengthened by the significant association between IMT/TPA of the carotid arteries and WSS. These findings indicate that carotid WSS has a role as an index of atherosclerosis and serves as a predictor of significant coronary arteriosclerosis.

PS536 | BESIDE

Evolution of high sensitivity troponin T in patients undergoing high efficiency on-line hemodiafiltration versus conventional low-flux hemodialysis

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Introduction and aims: On-line hemodiafiltration (HDF) has been associated with beneficial cardiovascular and inflammatory markers profiles than conventional low-flux hemodialysis (HD). Recent large randomized clinical trials suggested that HDF had a beneficial effect on survival when higher convection volumes are provided. High-sensitivity troponin T (hs-TnT) has been related to all-cause and cardiovascular mortality in end-stage renal disease patients. The aim of this study was to determine the effect HDF vs HD on hs-TnT evolution at one year follow-up.

Methods: Patients were randomized from 2007 to 2013 to HD or post-dilution online HDF in accordance with the CONvective TRANSport STUDY (CONTRAST) protocol initially as part of the Montreal CONTRAST cohort (until 2010) and subsequently as part of the local cohort (2010–2013). hs-TnT were obtained before dialysis at baseline and at 1-year follow-up. Comparison of the evolution of hs-TnT values between groups was performed with an appropriate non-parametric test.

Results: 54 HDF patients and 59 HD patients were included. Mean age was 60 ± 16 years in the HDF group and 64 ± 12 years in the HD group, (p = 0.170). Prior to randomization, all patients were treated with conventional hemodialysis. Mean dialysis time was similar between groups. Median dialysis vintage was 21 (interquartile range 7–66) months in the HDF vs 27 (12–53) months in HD (p = 0.769). Patients with a myocardial infarction within 2 months before randomization were excluded. At baseline, median hs-TnT value was 49 (31–89) umol/L in the HDF group vs 60 (36–96) umol/L in the HD group (p = 0.370). During the following year, dialysis was provided according to randomization with comparable dialysis session time and frequency. Mean Kt/V was 1.9 ± 0.4 in HDF vs 1.6 ± 0.2 in HD (p = 0.001). Mean convective volume was 27.9 ± 9.3 L in the HDF group. At one year follow-up, median hs-TnT remained stable at 47 (32–86) umol/L in the HDF group vs 54 (40–104) umol/L in the HD group (p = 0.024).

PS537 | BESIDE

Association of carotid wall shear stress, carotid atherosclerosis, and coronary artery disease in patients with chest pain

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Background: Wall shear stress (WSS) is critically important in both vascular remodeling and atherosclerosis and can be assessed by ultrasound (US) as well as carotid intima-media thickness (IMT) and plaque burden. This study aimed to investigate the relationships between carotid WSS and the parameters of carotid atherosclerosis in the common carotid artery (CCA) in patients with suspected coronary artery disease (CAD).

Methods: Carotid artery US was performed in 950 patients with suspected CAD, and mean IMT, total plaque area (TPA), and hemodynamic parameters of CCA, including peak and mean WSS, were measured. Carotid parameters were analyzed according to the presence of CAD, and the predictive values of WSS and TPA for the presence of significant CAD were analyzed.

Conclusion: CAD prevalence in patients with CAD (n = 283) showed significantly higher mean CCA IMT (0.66 ± 0.15 mm vs. 0.74 ± 0.27, p < 0.001), TPA (0.13 ± 0.24 vs. 0.20 ± 0.42 cm², p < 0.002), and beta stiffness index (5.1 ± 3.11 vs. 5.60 ± 2.66, p = 0.045) and lower mean WSS (2.59 ± 0.82 vs. 3.23 ± 0.90 dyne/cm², p < 0.01). Mean carotid WSS showed significant negative correlations with the beta stiffness index (r = −0.116, p < 0.001), mean IMT (r = −0.193, p < 0.007), and TPA (r = −0.296, p < 0.001). Binary logistic regression analysis showed that odds (Odd Ratio [OR] 1.038, 95% confidence interval [CI] 1.010–1.066), presence of diabetes mellitus (OR 1.608, 95% CI 1.194–1.807), current smoking (OR 1.758, 95% CI 1.584–1.866), carotid TPA (OR 2.615, CI 1.320–5.183), and mean WSS (OR 0.554, CI 0.371–0.838) were significant predictors of CAD.

Conclusion: In patients with chest pain, low local shear stress and high plaque burden in the carotid arteries were significant predictors of CAD. This finding is further strengthened by the significant association between IMT/TPA of the carotid arteries and WSS. These findings indicate that carotid WSS has a role as an index of atherosclerosis and serves as a predictor of significant coronary arteriosclerosis.
Conclusions: Treatment with high-efficiency HDF is associated with stable hs-TnT values whereas low-flux HD is associated with significant increase in hs-TnT levels at one-year follow-up. Future studies are needed to establish whether stability of hs-TnT values is linked to better outcome in HDF patients.

CORONARY ARTERY DISEASE AND COMORBIDITIES IV

PS365 | BEDSIDE

Association of new score of risk in a population of diabetic patients with acute coronary syndrome undergoing coronary revascularization by percutaneous angioplasty

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Background: The Syntax score (SX) is a tool proposed for the analysis of the anatomic coronary and cardiovascular risk stratification in patients with lesions of the left main and/or multivessel. The ACEF score (age/left ventricular ejection fraction + 1 if creatinine>2.0 mg/dl) is a risk score based on the clinical characteristics of patients, can predict the prognosis of patients undergoing surgical revascularization. The Clinical Syntax (CS3) integrating elements of the coronary anatomy and clinical characteristics of patients with diabetes could be a new and more comprehensive prognostic tool for patients undergoing percutaneous revascularization.

Methods: We therefore conducted a retrospective observational study analyzing the characteristics of 111 patients with acute coronary syndrome undergoing angioplasty and PCI in the months of 2017 and 2018, followed-up at 12 months. For these patients we calculated Syntax score, ACEF and Clinical Syntax score and was correlated these indices with cardiovascular outcomes. The objective of this study was to evaluate the prognostic ability of individual score mentioned in predicting cardiovascular events. Were considered as events: sudden death, MI, revascularization new TLF. Based on the values of SX, ACEF and CSS patients were divided into 3 groups, low (SX <9, ACEF <1.022, CSS <15.6), medium (SX 9–17, ACEF 1.022 to 1.277, CSS 15.6 to 27.5) and high risk (SX >17 ACEF >1.277, CSS >27.5).

Results: In our sample events occurred in 29 patients (incidence 26%). The in- taneous angioplasty. risk stratification of cardiovascular events in diabetic patients undergoing percu-

taneous angioplasty.

P5367 | BEDSIDE

Admission hemoglobin levels and Killip class in acute coronary syndrome patients: insights from the cohort EPIHEART

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Background: In the setting of an acute coronary syndrome (ACS) hemoglobin levels have the potential to worsen the myocardial ischemic insult. Killip classi- fication is a simple clinical tool that has previously shown good prognostic value in patients with myocardial infarction. Data relating hemoglobin levels to clinical outcomes during patients’ in-hospital stay remains limited.

Purpose: Our aim was to examine the association between baseline hemoglobin levels and Killip classification during the index hospitalization in patients with ACS.

Methods: The data were obtained in the framework of an ongoing cohort of ACS, consecutively admitted at the Cardiology department of two tertiary hospitals of Porto, Portugal (São João Hospital and Aquário Hospital) from 2014 to 2016. The study included patients with a complete set of demographic and clinical characteristics, as well as laboratory data. Patients were categorized according to Killip classification regarding their evolution during the hospitalization (Classes I, II, III, and IV), as registered in medical records. The purpose of this study was to compare differences in baseline characteristics (sex, age, creatinine at admission, ACS type and previous heart failure), for each 1 g/dl higher hemoglobin at admission the probability of evolving in Killip class III decreased by 27% (OR=0.73, 95% CI 0.55–0.97, p=0.028), and that of evolving in class IV had by 34% (Odd=0.66, 95% CI 0.47–0.92, p=0.015) with no effect seen for Killip II (OR=1.06, 95% CI 0.85–1.32, p=0.592).

Conclusions: In ACS patients, admission hemoglobin levels independently pre- dict Killip class. So, our results reinforce the fact that in the setting of ACS, lower hemoglobin levels at admission are related with worse clinical evolution, namely regarding severe heart failure.

PS368 | BENCH

Fibrinogen high levels, but not fibrinogen genetic variability is a risk factor coronary artery disease in patients with essential hypertension and diabetes mellitus type 2

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Purpose: It is well established that hypertension (HTN) and diabetes mellit- us (DM) are important risk factors for coronary artery disease (CAD). In addi- tion, controversial data exist related to the role of fibrinogen genetic variants in the risk of coronary artery disease. The aim of our study was to evaluate the association of fibrinogen polymorphisms rs180070 and rs2070011 fibrinogen polymorphisms on the risk for CAD/myocardial infarction (MI) in patients with DM and HTN admitted with stable angina pectoris symptoms.

Methods: A total of 744 subjects were enrolled in 3-year period. Fibrinogen poly- morphisms were determined by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) technique. Fibrinogen plasma level were mea- sured by the Claus method.

Results: The AA homozygosity of rs180070 was associated with significantly higher levels of fibrinogen in both HTN and DM (p=0.05, p=0.04 respectively). The genotype of AA genotype (rs180070) was also significantly associated with increased risk of CAD in the general population [OR: 3.2, 95% CI, (1.01–10.1, p=0.049)]. Interestingly, multivariate logistic regression analysis showed that fibrinogen levels >443 mg/dl were associated with higher risk for CAD [OR: 3.9, 95% CI, (1.4–10.4, p=0.002)]. Fibrinogen levels >443 mg/dl were not statistically higher in the general popu- lation. Similar associations were observed in HTN and DM patients. In hyper- tension, higher fibrinogen levels >443 mg/dl [OR: 3.5, 95% CI (1.14– 10.9, p=0.029], but not the AA genotype of rs180070 [OR: 3.5, 95% CI (0.78–11.9,
p=0.11) were independent predictors of CAD. Similarly, in DM only fibrinogen remained an independent predictor of CAD [OR 5.86, 95% CI (1.1–31.2, p=0.038)]. Finally, neither the AA homozygosity of the rs180070 nor the AA homozygosity of the rs2070011 was associated with the occurrence of MI in the overall cohort [OR: 1.87, 95% CI (0.37–8.9), p=0.46 and OR: 0.75, 95% CI (0.39–4.13), p=0.378 respectively]. No association between the AA homozygotes (rs180070) and MI was detected in DM or HTN subjects.

Conclusions: Our results indicate that elevated fibrinogen levels may be an independent predictor of CAD risk in both HTN and DM subjects. Although, the prognostic value of the AA homozygosity (rs180070) resulted in higher fibrinogen levels and risk of CAD in the overall cohort, no significant effect was found in the subgroups of HTN and DM. This finding suggest that the AA genotype does not raise CAD risk independently of fibrinogen levels and major risk factors. Interestingly, fibrinogen levels were also associated with the incidence of MI, which could be attributed to the low event rate.

PS356 | BENCH
miRNA-197 and miRNA-223 predict cardiovascular death in a cohort of patients with symptomatic coronary artery disease
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Background: Circulating microRNAs (miRNAs) have been described as potential non-invasive biomarkers in cardiovascular disease and, in particular, coronary artery disease (CAD). Few studies were undertaken to perform analyses with regard to risk stratification of future cardiovascular events. So far, only one large-scale prospective study involving miRNA screening has been performed identifying miRNA-126, miRNA-197 and miRNA-223 as related to future myocardial infarction.

Purpose: The aim of our prospective study was to further evaluate these miRNAs in a large prospective cohort of patients with invasively diagnosed CAD.

Methods: We prospectively evaluated baseline levels of 3 miRNAs (miR-126, miR-197 and miR-223) in serum samples of 1,112 CAD patients with respect to the endpoint cardiovascular death (n=21; 1.9%). Patients enrolled had symptomatic suspected coronary artery stenosis and CAD was diagnosed via coronary angiography. miRNA quantification was performed using real time polymerase chain reaction (RT-qPCR). Cycle threshold (Ct) values were normalized to C. elegans miR-39 (cel-miR-39). The formula 2(-Ct(miRNA)-Ct(C. elegans)) was used for Ct <40. In the case of Ct >40 the Ct value was considered as undetermined.

Results: The median follow-up period was 4 years [25th; 75th percentile: 2.78; 5.04]. The median age was 63.5 years [57; 69] with 80.4% males. 38.7% of the patients presented with acute coronary syndrome (ACS) and 61.3% were diagnosed with stable angina pectoris (SAP).

Elevated levels of miRNA-197 and miRNA-223 reliably predicted future cardiovascular death in the overall group (miRNA-197: Hazard Ratio (HR) 1.594 per one standard deviation (SD) increase [95% confidence interval (CI) 1.078; 2.358], p<0.02, concordance index (c-index) 0.786; miRNA-223: HR 1.923 per one SD increase (1.098; 3.397), p=0.024, c-index 0.801). In ACS patients the predictive power of these two miRNAs was even higher (miRNA-197: HR 2.05 per one SD increase [1.218; 3.418], p=0.013, c-index 0.887; miRNA-223: HR 3.488 per one SD increase (1.254; 9.706), p=0.017, c-index 0.849).

Conclusion: Elevated serum levels of miRNA-197 and miRNA-223 as determined using RT-qPCR were associated with cardiovascular death in CAD patients.

PS357 | BEDSIDE
Differential adipose tissue bradykinin receptors gene expression profiles in obese patients with and without coronary artery disease
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Purpose: Adipose tissue is an inflammatory source of coronary artery disease (CAD). Kinin receptors may be an important determinant of the impact of adiposity on endothelial function and cardiovascular function. The aim of this study was to examine kinin receptors gene expression levels in the adipose tissue in obese patients with and without CAD.

Methods: 41 patients (BR1: 30; BR2: 11) underwent coronary angiogram. The procedure was approved by the Ethics Committee of Heraklion University Hospital. Informed consent was obtained from all patients. BMI, waist and hip circumference, blood pressure, systolic and diastolic blood pressure, total cholesterol, HDL-cholesterol, triglycerides, insulin and CRP were measured. Statistical tests were used for analysis.

Results: BMI was significantly higher in patients with CAD (n=21) compared to controls (n=20) (32.5±4.9 vs. 29.9±4.6; p=0.017). In patients with CAD, the following parameters were determined: BMI 32.5±4.9, waist circumference 107±19 cm, hip circumference 102±15 cm, systolic blood pressure 130±20 mmHg, diastolic blood pressure 80±16 mm Hg, total cholesterol 5.2±1.2 mmol/L, HDL-cholesterol 1.2±0.3 mmol/L, triglycerides 1.6±1.4 mmol/L, insulin 6.5±3.5 μU/mL, and CRP 3.55±1.23 vs. 1.69±0.57 mg/L (p=0.001) were significantly higher in patients compared to controls. SHBG (p=0.040, OR=0.40, 95% CI: 0.042–2.80) and FT (p=0.659, OR=0.651, 95% CI: 0.025–1.26) were independent predictors of CAD, but not BMI (p=0.826, OR=0.354, 95% CI: 0.042–2.80) and FT (p=0.659, OR=0.651, 95% CI: 0.025–1.26).

Conclusion: Serum bradykinin receptor type 1 (BR1) and 2 (BR2) gene expression by RT-quantitative PCR.

PS370 | BEDSIDE
Association between sex hormone-binding globulin and coronary artery disease in males
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Background: Low concentration of testosterone in men is found to be associated with coronary artery disease (CAD) and its risk factors. Major portion of testosterone is bound to sex hormone-binding globulin (SHBG). The link between SHBG and coronary artery disease is not well established.

Purpose: The objective was to evaluate the association between sex hormone-binding globulin (SHBG), sex hormones and coronary artery disease among men.

Methods: A hospital-based case-control study used patients with angiographically proven coronary artery disease (n=84) and acute myocardial infarction (n=84) as cases and controls (n=84) from the surgical wards. Serum samples were used to assess the levels of high sensitivity C-reactive protein (hs-CRP), total cholesterol, HDL-cholesterol (high density lipoprotein), triglycerides, SHBG and total testosterone (TT). The levels of LDL-cholesterol (low density lipoprotein) were calculated using Friedewald’s formula and free testosterone (FT) and bioavailable testosterone (BT) levels were calculated using Vermeulen’s formula.

Free androgen index (FAI) was calculated. Data were analysed using appropriate statistical tests.

Results: Total testosterone (TT) (11.58±2.9 vs. 18.64±7.4 mmol/L, p=0.001), free testosterone (FT) (0.183±0.056 vs. 0.388±0.25 mmol/L, p=0.001), bioavailable testosterone (BT) (4.31±1.32 vs. 9.10±6.02 mmol/L, p=0.001), free androgen index (FAI) (12.46±7.65 vs. 54.34±50.01) were significantly lower in patients compared to controls, but SHBG (4.84±7.16 vs. 42.8±12.1 mmol/L, p=0.001) and hs-CRP (3.55±1.23 vs. 1.69±0.57 mg/L, p=0.001) were significantly higher in patients compared to controls. SHBG (p=0.040, OR=0.40, 95% CI: 0.042–2.80, TT (p=0.017, OR=5.86, 95% CI: 0.75–42.72), hs-CRP (p=0.001, OR=10.54, 95% CI: 4.57–15.63), smoking (p=0.009, OR=3.99, 95% CI: 1.41–11.32) were found to be significant independent predictors of CAD, but not BT (p=0.826, OR=0.354, 95% CI: 0.042–2.80) and FT (p=0.659, OR=0.651, 95% CI: 0.025–1.26).

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apex to the aortic valve insertion on the LVG. AAD was calculated as 100*(EDL-ESL)/EDL. The Cox regression analysis was used to predict the endpoints of adverse events.

**Results:** Ninety-six outcomes (all-cause death; 39, congestive heart failure; 21, late revascularization; 34, myocardial infarction; 2) were observed during the follow-up period for median 3.1 years. In multivariate analysis, adverse events were significantly associated with lower AAD (hazard ratio 0.852; 95% confidence interval 0.791–0.918, p < 0.01) after adjustment for traditional risk factors and coronary artery disease (CAD). The area under the curve (AUC) of AAD was greater than that of LV ejection fraction (LVEF) (0.656 vs. 0.541, p < 0.05). AAD improved AUC compared with traditional risk factors, and AAD combined with LVEF, CAD and brain natriuretic peptide had the largest AUC (0.678).

**Conclusion:** Lower AAD was related to incidence of adverse events in patients who underwent coronary angiography for clinical indications. AAD is superior predictor to conventional LVEF as a predictor of adverse events.

**PS373 | BEDSIDE**

**Background characteristics and prognosis in non-invasively treated patients with type 1 and type 2 myocardial infarction. Data from the SWEDHEART registry**

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**Purpose:** To assess differences in demographic, clinical characteristics and long-term survival between non-invasively treated patients with type 1 and type 2 myocardial infarction (MI).

**Methods and results:** A total of 59394 patients with MI were registered between 2011–2013 in the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART) registry and followed up for a mean of 1.87 years. The majority of cases presented with type 1 MI (n=53342; 89.8%) while 6.9% (n=4083) with type 2 MI; 66.8% (n=2726) of patients with type 2 MI and 20.5% (n=10978) with type 1 MI did not undergo coronary angiography during hospitalization. For background characteristics see table. Type 2 MI patients developed smaller myocardial necrosis (max troponin T 73±1213 vs. 965±1798ng/L, p < 0.001) as compared to those with type 1 MI. Tachycardia (6.7 vs. 2.5%), acute anemia/bleeding (9.4 vs. 1.5%) or acute respiratory failure (5.5 vs. 2.0%) could be more often identified in type 2 MI patients. The crude long-term mortality risk was lower in patients with type 2 MI (HR 0.92, 95% CI 0.87–0.98) as compared to type 1 MI and remained significantly lower after adjustment for age, sex, co-morbidities, treatments and triggering mechanisms (HR 0.81, 95% CI 0.73–0.89).

**Conclusions:** Among the selected group of conservatively managed MI patients in this real life study, those classified as type 2 MI had lower age, lower proportion of hypertension and previous cardiovascular events, smaller myocardial necrosis, but higher prevalence of identifiable triggering mechanisms. Both crude and adjusted long-term mortality risk were significantly lower in conservatively managed patients with type 2 MI compared with type 1 MI.

**PS374 | BEDSIDE**

**Identification and characterization of heterozygous familial hypercholesterolemia patients using the Vanderbilt University Medical Center Synthetic Derivative database**

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**Background:** Despite an estimated prevalence of 1:300–1:500, and an associated high risk of premature cardiovascular disease (CVD), few contemporary studies have characterized the heterozygous familial hypercholesterolemia (FH) population with respect to demographics, clinical characteristics, or treatment patterns.

**Purpose:** To leverage structured and unstructured longitudinal clinical data and bioinformatics expertise to identify and characterize FH patients within the Vanderbilt University Medical Center de-identified electronic medical records (EMR) database (Synthetic Derivative) from 1996 to 2014.

**Methods:** Using diagnostic and procedure codes, narrative text from clinical care, laboratory records, and index outpatient medication histories, adult FH patients were identified using Dutch Lipid Network (DLN) criteria components and classified as “probable” or “definite” FH. Demographics, clinical characteristics, laboratory measures, and use of lipid lowering therapies were described.

**Results:** Out of a population of 218,652 individuals with at least one low-density lipoprotein cholesterol (LDL-C) measure, we identified 622 probable and 430 definite FH patients. Herein results are limited to definite FH patients, among whom 40% were male, 68% white, 39% ever-smokers, and 35% obese (body mass index > 30kg/m²). Median number of clinic visits and hospital admissions over the cumulative EMR were 47 [interquartile range (IQR) 15–132] and 2 (IQR 0–9), respectively, over a median duration of 9 (IQR 3–14) years. Median number of LDL-C measures was 6 (IQR 3–15); 83% and 16% had a recorded LDL-C value > 330 or 250–329 mg/dl, respectively, and maximum LDL-C had a median value of 340 (IQR 309–386). Median value (mg/dl) for high-density lipoprotein cholesterol and triglycerides were 47 (IQR 39.5–58) and 164 (IQR 115–241), respectively. Prevalence of CVD was 8% for myocardial infarction, 11% peripheral arterial disease, non-hemorrhagic stroke or unstable angina, 13% heart failure, 15% revascularization in type 2 diabetes, and 15% hypertension. The prevalence of FH was 84%, with 45% taking a high-dose statin and 48%, 37% and 27% also taking ezetimibe, fibrate or niacin, respectively. None of the patients had evidence in any clinical document indicating LDL receptor mutation testing, and only five were found to have narrative keyword strings explicitly noting the presence or suspicion of familial or inherited hypercholesterolemia.

**Conclusion:** Rigorous EMR characterization in a tertiary medical center population suggests that FH may be under-recognized and inadequately treated.

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**PS375 | SPOTLIGHT**

**Defining coronary calcification in female patients undergoing PCI: Results from a pooled analysis of 26 randomized trials**

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**Background:** Previous studies, in which the majority of patients were male, have shown that percutaneous coronary intervention (PCI) of moderately and severely calcified coronary lesions is an independent predictor of death, myocardial infarction (MI), stent thrombosis (ST), and restenosis after PCI. Whether or not similar associations exist for female patients undergoing PCI remains unclear.

**Methods:** We pooled patient level data of female participants from 26 randomized trials of drug eluting stents. Calcification was evaluated by qualitative coronary angiography in central core laboratories or sites. We divided the study population into two groups according to calcification grade: none/mild vs. moderate/severe. Subsequently, we sought to evaluate the frequency and impact of coronary calcification on future ischemic outcomes.

**Results:** Of 11,557 women included in the primary pooled analysis, coronary calcium content was available for 7156 patients. Compared to none/mild calcification (n=5343, 75%), patients with moderate/severe calcification (n=1813; 25%) were older, were more likely to have diabetes, hypertension, hypercholesterolemia, previous history of CABG, lower ejection fraction, more multivessel disease, greater number of lesions and more commonly at least one B2/C lesion. At 3-year follow-up, women undergoing PCI of lesions with moderate/severe calcification had higher rates of mortality (7.2% vs. 5%, p=0.0008), cardiac death (4% vs. 2.5%, p=0.002), myocardial infarction (MI; 8.8% vs. 4.5%, p=0.003) and target lesion revascularization (TLR; 9.1% vs. 7.5%, p=0.025) compared to those with only none/mild calcified lesions. Stent thrombosis (ST) did not reach statistical significance (p=0.17). After adjustment for baseline differences, calcification status was an independent predictor of death, myocardial infarction (MI), stent thrombosis (ST), and restenosis after PCI. Whether or not similar associations exist for female patients undergoing PCI remains unclear.

**Conclusion:** Surveillance for coronary calcium in women undergoing PCI is needed to provide an independent predictor of late mortality and TLR.
Prognostic value of coronary artery calcium score for major perioperative cardiovascular complications in type 2 diabetic patients undergoing trans-femoral amputation

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Perioperative risk for major perioperative cardiovascular complications is particularly high in patients with type 2 diabetes undergoing trans-femoral amputation and contrast application for angiography is often contraindicated due to nephropathy. The aim of this study was to identify prognostic value of coronary computed tomographic angiography (CCTA) and coronary artery calcium (CAC) score for major perioperative cardiovascular complications in these patients.

Materials and methods: In this prospective single center interventional cohort study, we evaluated 331 consecutive pts with diabetes and without history of coronary intervention or myocardial infarction (MI) undergoing trans-femoral amputation during the year 2013. 179/331 pts (54%) had no contraindications for contrast application and were included in the study cohort. CCTA and CAC-scoring were performed using a 64 detector rows CT scanner GE USA “Light speed” VCT cardiac 72013287YA 2008.

Results: In female our study were significantly older than male (68.1±5.9 vs. 57.2±6.2, p=0.0017). All women and 65% of men had clinical coronary artery disease (CAD). Increasing CAC was associated with significant increasing severity of CAD and incidence of cardiovascular complications (Table). Perioperative period of 26 (14.5%) of pts was complicated by acute MI (19 Q-wave and 7 non-Q-wave), 3- vessel obstructive CAD was in 85.7%, 2-vessel in 4.8%.

Conclusion: Predictive value of CAC for perioperative MI and death is high in pts with type 2 diabetes undergoing trans-femoral amputation. Whereas pts with a CAC >99 had only a small prevalence of potentially obstructive CAD, the incidence of MI or death increased from 4.5% to 64% with increasing CAC score from 400 to 1000 indicating increasing need for coronary revascularization before surgery.

CORONARY ARTERY DISEASE AND COMORBIDITIES V

P5378 | BEDSIDE
Percutaneous coronary revascularization reduces risk of acute renal failure when compared to coronary artery bypass graft: a meta-analysis of 8 studies and 257980 patients

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Introduction: Incidence of acute renal failure after PCI (Percutaneous Coronary Intervention) and CABG (Coronary Artery Bypass Graft) remains to be determined.

Methods: PubMed, Google Scholar and Cochrane Collaboration were searched for randomized controlled trials or studied with multivariable analysis comparing incidence of acute renal failure after PCI and CABG. Meta-regression analysis was also performed for baseline features.

Results: Four randomized controlled trials with four hundred and thirty five patients and for observational studies with two hundred fifty-seven thousand and five hundred forty-five patients were included. Three vessels revascularization was performed in 54.0% (23.0–78.3%) of patients, and acute renal failure was significantly reduced by PCI when compared to CABG with an Odds Ratio (OR) of [0.76 [0.58–0.98], p=0.001]. This result was mainly driven by data derived from observational studies adjusted with multivariable analysis (OR of 0.67 [0.65–0.68], p<0.001), while it did not reach significance for RCTs only (OR of 0.83 [0.42–1.61], p=0.67). At meta-regression analysis, the benefit of PCI in reducing renal failure compared to CABG was significantly increased in patients with diabetes mellitus (OR 0.64 [0.50–0.81], p<0.001) and with congestive heart failure (B = 0.26 – 0.26 [−0.16; −0.03]; p<0.001).

Conclusion: Risk of acute renal failure is significantly reduced by PCI when compared to CABG: this benefit, although derived mainly from observational studies, is significantly increased in patients with diabetes mellitus and congestive heart failure.

P5379 | BEDSIDE
Routine SYNTAX scoring correctly identifies suitability for PCI in high-risk surgical patients

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Introduction - European guidelines recommend SYNTAX scoring to direct optimal revascularisation strategies in non-diabetics with multi-vessel disease. Data suggest equivalent outcomes between CABG and PCI in low and intermediate risk tertiles. However, the impact of increased SYNTAX scoring upon rates of referral for surgical revascularisation in clinical practice in these groups remains unclear.

Methods: A prospectively collected database of 3896 patients at a single UK tertiary centre was interrogated for referrals for CABG, between Jan and Dec 2013. To ensure equivalence, diabetics and those undergoing concomitant valve surgery or other procedures were excluded. All others were SYNTAX scored and demographic data acquired.

Results: A total of 189 patients were referred for surgery; 83% were male, mean age was 65±10 years, 37% were smokers, 24% diabetic and 60% hypertensive. 71% presented with an acute coronary syndrome. After exclusions, 81 patients remained and underwent SYNTAX scoring. Of these, 41% were found to be in the low tertile, 29% were in the intermediate and 30% were in the high tertile (I) and (II). When plotted against additive EUROScore, it was possible to identity patients with favourable anatomy for PCI with a high predicted surgical jeopardy (iii).

Conclusions: Routine use of SYNTAX scoring suggests a high percentage of in-
individuals with multi-vessel coronary disease referred for surgery are in low or intermediate tertiles and would have equivalent outcomes with PCI. SYNTAX scoring allows for more nuanced decision making regarding options for coronary revascularisation and increases patient choice. In particular, when combined with EUROscore, it identifies patients with high surgical risk and favourable anatomy for PCI.

**PS380 | BEDSIDE**

Impact of albuminuria on contrast-induced acute kidney injury and in-hospital adverse cardiac events in patients who underwent emergency coronary intervention

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**Purpose:** The aim of this study was to evaluate the predictive value of albuminuria for risk of contrast-induced acute kidney injury (CI-AKI) and in-hospital adverse events (AE) in patients with ACS who underwent emergency PCI.

**Methods:** A total of 215 consecutive ACS patients undergoing emergency PCI were enrolled. Urinary albumin to creatinin ratio (ACR; mg/gCr) was measured and patients were divided into three groups as follows: normoalbuminuria (ACR <30 mg/gCr, 126 patients), microalbuminuria (30 ≤ ACR <300 mg/gCr, 72 patients) and macroalbuminuria (≥300 mg/gCr, 17 patients). CI-AKI was defined as a greater than 25% increase in creatinine from the baseline or an absolute increase of >0.5 mg/dl within 72h after the procedure. In-hospital AE was defined as the composite of cardiovascular death, pulmonary edema, unplanned PCI or CABG, fatal arrythmias.

**Results:** Incidence of CI-AKI (p < 0.0001) and in-hospital AE (p = 0.001) were gradually increased among three groups (Figure). Length of stay in ICU was significantly longer in macroalbuminuria group than the other group (p = 0.008). Multivariate logistic regression analysis, adjusting for potential confounding factors, resulted in an odds ratio (OR) for CI-AKI in macroalbuminuria group was 6.58 (95% CI 1.36–31.73; p = 0.018) and 3.59 in microalbuminuria group (95% CI 1.67–7.697, p = 0.007) when compared with normoalbuminuria group.

**Conclusions:** The elevated urinary albumin excretion rate is an independent predictor of CI-AKI and in-hospital AE in patients with ACS and graded increase in the incidence across microalbuminuria to macroalbuminuria were observed.

**PS381 | BEDSIDE**

Impact of lipoprotein(a) on long-term major cardiovascular events in patients with chronic kidney disease after percutaneous coronary intervention


**Background:** Chronic kidney disease (CKD) is associated with a tremendously increased risk for cardiovascular disease. Traditional risk factors for cardiovascular disease show diminished predictive power in these patients compared with non-CKD patients. Serum levels of lipoprotein(a) (Lp(a)) can be risk factors for adverse events. However, the clinical implications of Lp(a) in patients with CKD who underwent percutaneous coronary intervention (PCI) remains uncertain.

**Objectives:** We aimed to determine the role of Lp(a) in patients with CKD who underwent PCI.

**Methods:** A total of 3,508 patients were treated by first PCI between 1997 and 2011 at our institution. Of these patients, 1,079 patients with CKD were analyzed. Patients were divided into median groups according to individual log Lp(a) [high Lp(a) (n=929) vs low Lp(a) (n=550)]. The primary outcome was a composite of all-cause death and acute coronary syndrome (ACS).

**Results:** Baseline characteristics of two groups were similar. The median follow-up period was 4.7 years. Cumulative event-free survival was significantly worse for the group with high Lp(a) than with low Lp(a) (P = 0.01). Multivariable analysis selected a log Lp(a) level as an independent predictor of primary outcomes (hazard ratio, 1.22; 95% CI, 1.01–1.45; P = 0.04).

**Conclusions:** A high Lp(a) value could be associated with a poor prognosis after PCI for patients with CKD.

**PS382 | BEDSIDE**

The validation of CHA2DS2-VASc-CKD2 score for risk stratification in patients with coronary heart disease undergoing PCI without known atrial fibrillation

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**Introduction:** Few simple risk stratification schemes assessing adverse events in patients with coronary heart disease (CHD) has been studied. CHA2DS2-VASc score is simple system to add each component if it was present, and its validation for patients in CHD has not been evaluated. Kidney function associates with adverse events, however, it doesn’t include CHA2DS2-VASc score.

**Purpose:** In this study, we proposed CHA2DS2-VASc-CKD2 score and evaluated its clinical validation to predict clinical outcome in CHD without AF.

**Methods:** Of 1,923 consecutive patients with CHD from SHINANO registry, 1,714 patients without AF were evaluated (age 70±11 years, 394 women). CHA2DS2-VASc-CKD2 was calculated by CHA2DS2-VASc score added 2 in patients with estimated glomerular filtration rate (eGFR) <30 ml/min/1.73m², or 1 in patients with eGFR 30 to 59 ml/min/1.73m². The primary endpoint was MACE including cardiac death, myocardial infarction, stroke, and hemorrhagic events at 1-year.

**Results:** The mean CHA2DS2-VASc score 3.4±1.5. One-year follow-up was completed in 1,632 patients (95.2%). Cumulative incidence of MACE was 139 cases. Figure 1 indicated higher CHA2DS2-VASc score associated with higher incidence of MACE (P = 0.001).

The incidence of MACE was significantly associated with CHA2DS2-VASc-CKD2 score (hazard ratio 1.23, 95% confidence interval 1.13–1.38, p<0.001).

**Conclusions:** The CHA2DS2-VASc-CKD2 score could predict future adverse events in CHD without known AF.

**PS383 | BEDSIDE**

Genetic variation in ADAMTS7 is associated with severity of coronary artery disease

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**Purpose:** Genome-wide association studies have identified ADAMTS7 as a risk locus for coronary artery disease (CAD) and myocardial infarction (MI). Functional studies suggest ADAMTS7 may promote cellular processes in atherosclerosis. We studied if risk variant carriers exhibit a greater burden of angiographic CAD.

**Methods:** We genotyped ADAMTS7 in the Southampton Atherosclerosis Study (SAS, n=1359), and replicated in the Emory Genebank (Emory GB, n=2884). An- giographic CAD was phenotyped in both cohorts, as presence of >50% stenosis in any epicardial vessel and semi-quantitative scores including the Gensini Score (GS), Sullivan Extent Score (SES) and the Duke Severity Index (DSI).

**Results:** We confirmed an association between ADAMTS7 genotype and presence of CAD under an additive genotype model in SAS (p = 0.05) and Emory GB (p = 0.017), but found no association with MI in the presence of CAD. ADAMS genotypes were associated with all of the angiographic severity scores in SAS (GS p = 0.017, SES p = 0.045, DSI p = 0.029), and independently replicated in
Emory GB (GS p < 0.001, SES p < 0.001, DS1 p < 0.001). Meta-analysis demonstrated that homozygous carriers of the risk allele had greater odds of multi-vessel disease [OR 1.36 (95% CI 1.13–1.63) and proximal stenoses [OR 1.41 (95% CI 1.15–1.72)], compared to non-risk allele carriers. Additionally, the risk genotype was associated with greater fibrous cap thickness (p = 0.013) and % area of α-actin (smooth muscle cell marker) in the intima (p = 0.029) following ex vivo immunohistochemical analysis of human coronary atherosclerotic plaque (n=48).

Conclusions: The ADAMTS7 risk variant is associated with multiple angiographic measures of CAD burden and plaque remodeling, further supporting the role of this protease in promoting atherosclerosis.

P5385 | BEDSIDE
Background characteristics, treatment and long-term prognosis in patients with significant coronary artery stenosis classified as type 1 or type 2 myocardial infarction. Data from SWEDEHEART registry
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Aim: To assess differences in incidence, demographic and clinical characteristics, treatment and long-term prognosis between patients with type 1 and type 2 myocardial infarction (MI) and significant coronary artery disease.

Methods and results: A total of 59.394 patients with MI were registered between 2011–2013 in the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Methods (SWEDEHEART). The majority of cases were classified as type 1 MI (n=53.342; 89.8%) while 6.9% (n=4.083) as type 2 MI. Coronary angiography was performed in 43.721 patients and the presence of significant CAD was confirmed in 92.8% (n=37.589) of patients with type 1 MI and 52.8% (n=695) with type 2 MI.

As compared to type 1 MI patients with significant CAD, type 2 MI patients were older (71.8±10.5 vs. 68.9±11.5y), had higher proportion of hypertension (78.4 vs. 65.0%), diabetes (31.4 vs. 23.7%), previous MI (40.5 vs. 24.8%) and coronary interventions (36.9 vs. 22.0%), history of cardiac (16.4 vs. 7.5%) and renal failure (32.6 ± 20.1%; p < 0.001 for all). Type 2 MI patients developed smaller extent of myocardial damage (max troponin T 972±360 vs. 1774±307ng/L) and less frequently received cardioprotective treatment (betablockers 85.9 vs. 89.9%; statins 84.6 vs. 93.7%; aspirin 86.5 vs. 95.1%, other antplatelets 70.2 vs. 89.3%; p < 0.001 for all) as compared to type 1 MI patients. Tachycardia (10.1 vs. 1.3%), acute anemia/bleeding (3.6 vs. 0.6%) or infection (5.0 vs. 1.7%; p < 0.001 for all) could be more often identified in type 2 MI group as compared to type 1.

The patients with significant CAD and type 2 MI diagnosis showed significantly higher crude long-term mortality as compared with type 1 MI patients (HR 1.33; 95% CI 1.13–1.55). However, after adjustment for age, sex, co-morbidities, treatments, triggers and troponins, the long-term mortality risk was lower in type 2 MI patients as compared with type 1 MI (HR 0.71, 95% CI 0.56–0.88).

Conclusions: The majority of patients with type 1 MI and half of the patients with type 2 MI, who underwent invasive management showed presence of significant coronary artery disease. Among them, type 2 MI patients as compared with type 1 MI patients, were characterized by having more risk factors, co-morbidities and triggers. They received less cardioprotective treatment. Patients with type 2 MI having higher crude long-term mortality, patients with type 2 MI showed an approximately 30% lower adjusted long-term mortality risk compared to type 1 MI patients.

P5386 | BEDSIDE
Proprotein convertase subtilisin/kexin type 9 as a biomarker for the development and severity of coronary artery disease in general population.
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Objectives: To evaluate the relation of circulating proprotein convertase subtilisin/kexin type 9 (PCSK9) levels to the development and severity of coronary artery disease (CAD).

Methods: A total of 6,072 consecutive patients with consecutive individuals (552 CAD and 479 controls) were prospectively enrolled with angiography and lipid-lowering-therapy being parts of the screening process. The associations of plasma PCSK9 levels with the incidence and severity of CAD were investigated. Further, a mediator analysis was performed to detect the potential mechanisms underlying the associations.

Results: No difference in PCSK9 levels between CAD cases/controls status was detected. Considering many variables differed between cases/controls might mask the truth, we further investigated it when adjusting for confounding factors. Subsequently, after adjustment these factors, patients with CAD presented a higher PCSK9 level than the controls (all p < 0.05), and the PCSK9 levels positively associated with CAD severity (all p for trend < 0.05). Moreover, logistic regression analysis showed positive associations of PCSK9 levels with CAD. Importantly, mediator analysis indicated that the effect of PCSK9 levels on CAD was mediated significantly by increased lipid (around 20%) and severe inflammation (around 15%).

Conclusions: PCSK9 levels associated positively with CAD susceptibility, the relative important mechanisms including lipid and inflammation pathway involved partly in this association.

CORONARY ARTERY DISEASE AND COMORBIDITIES VI

P5387 | BEDSIDE
A clinical conundrum: is nitrate still safe and effective in coronary artery spasm when combined with myocardial bridge?
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Background: Coronary artery spasm (CAS) often combined with myocardial bridge (MB), as it increases the risk of CAS at the tunneled segment by damaging intima and endothelium. Nitrates have been widely used as anti-ischemic drugs in CAS patients (pts), while it is not recommended in MB pts. Thus, we investigated the long-term impact of nitrate on clinical outcomes in pts with CAS and MB.

Method: A total of 729 consecutive MB pts with positive acetylcholine (Ach) provocation test were enrolled. Significant CAS was detected. Considering many variables differed between cases/controls might mask the truth, we further investigated it when adjusting for confounding factors. Subsequently, after adjustment these factors, patients with CAD presented a higher PCSK9 level than the controls (all p < 0.05), and the PCSK9 levels positively associated with CAD severity (all p for trend < 0.05). Moreover, logistic regression analysis showed positive associations of PCSK9 levels with CAD. Importantly, mediator analysis indicated that the effect of PCSK9 levels on CAD was mediated significantly by increased lipid (around 20%) and severe inflammation (around 15%).

Conclusions: PCSK9 levels associated positively with CAD susceptibility, the relative important mechanisms including lipid and inflammation pathway involved partly in this association.

CORONARY ARTERY DISEASE and COMORBIDITIES VI
administration (Nitrate group: n=483, No nitrate group: n=243). Patients who received any regular nitrate drug were included into the nitrate group. To adjust for potential confounders, a propensity score matched (PSM) analysis was performed. We retrospectively analyzed the registries of ACS’s included in the National Registry of Acute Coronary Syndromes, Hospital of Vila Real, Dept. of Cardiology, Vila Real, Portugal.

Methods: We retrospectively registered the registries of ACS’s included in the National Registry of Acute Coronary Syndromes (ACS), from 1st of October 2010 and until 30th October 2014, with complete inclusion of patients with ACS for a follow up of one year. We showed a negative association between thyroid function and proprotein convertase subtilisin/kexin type 9 (PCSK9) levels in euthyroid subjects with stable CAD, suggesting a potential interaction between PCSK9 and lower levels of thyroid hormones in patients with CAD.

PS389 | BEDSIDE

Impact of uric acid and cystatin C on long-term clinical outcomes in patients undergoing percutaneous coronary intervention with drug-eluting stents

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Background: Cystatin C is a surrogate marker for estimate glomerular renal function and an independent predictor of mortality and cardiovascular disease. Hyperuricemia is associated with poor outcome in patients with cardiovascular disease. The aim of this study was to evaluate the incremental effect of uric acid and cystatin C on long-term clinical outcomes among patients undergoing percutaneous coronary intervention (PCI) with drug-eluting stents (DES).

Methods: A total of 1,463 patients undergoing PCI with DES were consecutively enrolled from January 2009 to December 2013. Among 1,463 patients, both of uric acid and cystatin C was available in 480 patients. We divided into four groups based on the median value of uric acid and cystatin C. A major adverse cardiovascular event (MACE) was defined as a composite of death, non-fatal myocardial infarction, stroke, and revascularization. We compared MACE according to uric acid and cystatin C level.

Results: During 2-year follow-up, MACE developed 72 (15.0%). In multivariate analysis, high uric acid and cystatin C was an independent predictor for 2-year MACE (adjusted hazard ratio 2.559, 95% confidence interval 1.227–5.338, p=0.012).

Conclusion: Combining of high uric acid and cystatin C was associated with increased long-term adverse clinical outcomes in patients undergoing PCI in DES era.

PS390 | BEDSIDE

Do patients with acute coronary syndromes without conventional risk factors have a better prognosis?

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Introduction: The major majority of patients (pts) with acute coronary syndromes (ACS) have at least 1 conventional cardiovascular risk factor (CCRF). The relationship between each one of these factors and atherosclerosis is well established but less is known about pts without any of these. The aims of this study were to establish the profile of the pt with ACS without conventional cardiovascular risk factors (WCCRF) and compare it to pts with at least 1 conventional cardiovascular risk factor (WCCRF).

Methods: We retrospectively registered the registries of ACS’s included in the National Registry of Acute Coronary Syndromes (ACS), from 1st of October 2010 and until 30th October 2014. We compared WCCRF to pts with at least 1 CCRF (hypertension, dyslipidemia, diabetes, active smoking or family history of heart disease) regarding demographic data, previous history, admission data, coronary angiography results, treatment and complications during hospitalization. We performed multivariate analysis to evaluate the impact of having at least 1 CCRF on cardiovascular adverse events. We also compared the mortality and readmission for cardiovascular disease at one year follow-up between the two groups.

Results: A total of 10/56 ACS’s were considered, 332 (3.1%) WOCRF. The pts were mostly males (72.3%) with a mean age of 67±15 years, similar to the ones WCCRF. Previous dementia and neoplasia were more frequent in the group WOCRF (3.8% vs 1.8%; p=0.011 and 6.1% vs 4.4%; p=0.155 respectively) unlike cardiovascular diseases, heart failure (HF), renal failure and pulmonary diseases. Pts WOCCRF most commonly presented ST-elevation myocardial infarction (STEMI) (47.3% vs 40.6%; p=0.014) compared to pts WCCRF who more frequently presented non-STEMI (48.1% vs 44.3%; p=0.175). There were no differences regarding the symptoms being chest pain the main complaint (90.7% average), 2-3 vessel disease was less common in pts WOCRF (33.6% vs 51.1%; p=0.001). The groups were similar regarding total ischemic time, infarct location, percentage of reperfusion therapy and complications during hospitalization, including in-hospital mortality (IHM), HF or re-infarction (MI). In multivariate analysis having at least 1 CCRF was neither an independent predictor of IHM nor the composite endpoint of IHM, HF or MI. At one year follow-up, we compared WCCRF to pts WOCRF for cardiovascular death and hospital readmission showed similar results between groups.

Discussion and conclusions: In this analysis the absence of CCRF was not a protective factor as these pts didn’t have a better in-hospital or one year follow-up prognosis compared to those WCCRF.

PS391 | BEDSIDE

Impact of anemia at admission in a one year prognostic of patients with acute coronary syndromes

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Background and introduction: There is a continuous search for prognostic markers to identify patients with acute coronary syndromes (ACS) who are at high risk for adverse events. Anemia has been reported in 15–30% of patients with acute coronary syndrome. It is known that anemia is associated with increased risk of mortality and has the potential to worsen myocardial ischemia. However, data relating anemia at admission to clinical long term outcomes in ACS remain limited.

Purpose: We sought to evaluate the impact of the presence of anemia at admission of patients with ACS for a follow up of one year.

Methods: A total number of 10 107 patients included in the national registry of ACS, from 1st of October 2010 and until 30th October 2014, with complete information and data about the haemoglobin value at admission were divided in two groups: Group A – patients with anemia (Hb < 12 g/dl in women and Hb < 13 g/dl in man) and Group B – patients without anemia. The one year survival and readmission rate regarding cardiovascular events was evaluated.

Results: We compared the Group A (n=908) with Group B (n=2721) after discharge for hospital readmissions and mortality through one year. Although more hospital readmissions were registered in the Group B (290 vs. 168, p=0.001)
for cardiovascular reasons, cardiovascular mortality was higher in Group A (139 events vs 121 events, p<0.001). Analysing the correlation between anemia at admission and mortality using proportional hazards regression we found that the presence of anemia at admission is associated to a 1.72% (HR 1.72; 95% CI 1.12 to 2.64, P<0.05) increase in mortality. On the other hand, no linear correlation was found between the presence of anemia and hospital admissions in a one year period (HR 1.23; 95% CI 0.91 to 1.67, P=0.05).

Conclusion: The presence of anemia at admission is a predictor of cardiovascular events and mortality in patients across the spectrum of ACS.

PS394 | BEDSIDE
Predictive value of routine cardiovascular screening for myocardial ischemia in kidney transplantation candidates: a single center prospective study (MONICARD study group)

Abstract P5394

Major bleeding in acute myocardial infarction: population characterization, predictors and impact in prognosis (MONICARD study group)


Patients (P) with Acute Myocardial Infarction (AMI) and may have impact in the history of stroke, HF, MI/CAD, HTN, DM, statin, other lipid lowering agents (except statin) and LDL-C.

1. Practice Guidelines Assessment (PGL)+ if they had one of the following: age >50, diabetes, cardiac symptom, known cardiac disease, rest ECG abnormality.
2. Independently of their PGL status, they were Clinical Evaluation (CE)+ if they had one of the following: cardiac symptom, cardiac disease, physical examination abnormality, ECG abnormality. 3. On top of CE, they were re-categorized Integrative Doppler Assessment (IDA)+ if they had at least one abnormality on resting echocardiography or echo-Doppler evaluation of peripheral arterial disease.
4. On top of IDA they were re-categorized Integrative stress Assessment (ISA)+ if they had a positive myocardial stress test. We recorded all-cause mortality, cardiovascular mortality, and non-fatal MACE.

188 patients were enrolled in the study between July 2010 and March 2013. Etiologies of ESRD were diabetes, hypertension and polycystic kidney disease for 50% of patients. 144 (79%) patients were PGL+, and 92 (49%) were CE+. Among 96 CE+ patients 52 (54%) were IDA+ raising the number of abnormal screening studies. Adding myocardial stress test didn’t reclassify any IDA- patients to ISA+. During a median follow-up of 2.2 years we recorded 6 death (3.2%), 5 MSTEMI, 4 strokes and 5 new onset of heart failure. PGL+ and CE+ status were not significantly associated with these outcomes (β; p=0.6 and p=0.2). IDA+ and ISA+ status were significantly associated with the outcomes with (β; p=0.05 and p<0.05) but ISA added no significant predictive value to IDA.

In our high risk ESRD population normal clinical cardiovascular routine evaluation with normal echocardiography and normal peripheral arterial echo-Doppler had an excellent negative predictive value for future death or MACE. Routine myocardial stress tests added no significant prognostic value regarding death or MACE.

PS394 | BEDSIDE
Major bleeding in acute myocardial infarction: population characterization, predictors and impact in prognosis

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Introduction: The presence of major bleeding (MB) is a feared complication in patients (P) with Acute Myocardial Infarction (AMI) and may have impact in the therapeutic strategy and prognosis of these patients.

Purpose: To characterize the population of P with AMI and MB (defined by Gusto criteria) and assess their impact on therapeutic approach and in-hospital complications and mortality. We evaluate possible predictors of the onset of MB.

Methods: We studied 9513 D with AMI included in a multicenter national register.
We considered two groups: P with MB and P without MB. We registered age, sex, comorbidities, in-hospital therapy, results of coronary angiography, angioplasty performed and ejection fraction (EF). The following in-hospital complications were defined: heart failure (HF), cardiacogenic shock, stroke, use of mechanical ventilation and need of blood transfusion. We compared the in-hospital mortality and multivariate analysis was performed to identify the predictors of MB predictors.

Results: Major bleeding was found in 1.5% of P with AMI (141 P). These P were older (72±12 vs 66±14 years, p<0.001), had higher prevalence of females (37.6 vs 27.6%, p<0.009), hypertension (81.9 vs 68.5%, p<0.001), previous HF (12.1 vs 5.5%, p<0.001), chronic renal failure (11.5 vs 5.9%, p=0.005) and previous bleeding history (9.4% vs 1.6%, p<0.001). At admission, P with MB received less therapy with aspirin (95.0% vs 98.4%, p=0.01), more therapy with glycoprotein Ilb/IIIa inhibitors (28.8% vs. 21.5%, p=0.039) and unfractonated heparin (37.9% vs. 29.0%, p=0.022). Patients with MB received the same rate of coronary angiographies and angiooplasties, but were more often submitted to more than one coronary angiography (13.8% vs. 7.1%, p=0.006), more coronary angiography performed by femoral artery (45.2% vs. 27.5%, p<0.001) and showed more multimoved disease (63.6% vs 50.4%, p=0.006). MB was associated with lower EF. (EF<50%: 46.2% vs 36.8%, p=0.029), greater need of invasive procedure (majority vs 13%, p<0.001) and blood transfusions (41.8% vs 1.4%, p<0.001), but with no differences in the other complications. In-hospital mortality was higher in P with MB (12.1% vs. 3.2%, p<0.001). By multivariate analysis, were identified as predictors of MB: age, previous history of bleeding, therapy with glycoprotein Ilb/Ilia inhibitors and heparin.

Conclusions: The presence of MB is present in 1.5% of P with AMI and is associated with an increased in-hospital mortality. There were identified as MB predictors: age, previous history of bleeding and therapy with glycoprotein Ilb/Ilia inhibitors and unfractonated heparin.
P5395 | BEDSIDE
Impact of new-onset dyslipidemia on coronary artery spasm as assessed by acetylcholine provocation test
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Background: Dyslipidemia is known to be a risk factor of coronary artery disease (CAD) and endothelial dysfunction. However, there are limited data regarding the impact of new-onset dyslipidemia (NODL) on significant coronary artery spasm (CAS) in real world clinical practice.

Methods: A total of 4,520 consecutive patients (pts) without the history of dyslipidemia and statin medication and the coronary fixed lesion of less than 50% underwnt acetylcholine (Ach) provocation test were enrolled. Significant CAS was defined as >70% of narrowing by incremental intracoronary injection of 20, 50 and 100 μg into left coronary artery. New onset dyslipidemia (NODL) was defined as newly recognized dyslipidemia on admission lipid profile in pts who denied history of dyslipidemia or statin administration history. Pts were divided into two groups based on the presence of NODL: the NODL group (n=478), the control group (n=4,042). To adjust potential confounders, a propensity score matched (PSM) analysis was performed using the logistic regression model.

Results: After PSM analysis, 2 propensity-score matched groups (476 pairs, n=952, C-statistic=0.651) were generated and the baseline characteristics of the two groups were balanced. NODL group showed higher incidence of (+) Ach provocation test results and higher incidence of ischemic chest pain during the Ach provocation test. Presence of NODL was an independent predictor of Ach-induced (+) Ach provocation test, suggesting possible causal relationship between NODL and endothelial dysfunction.

Conclusions: In this study, NODL was an independent predictor of Ach-induced CAS and associated with higher incidence of ischemic chest pain during Ach provocation test, suggesting possible causal relationship between NODL and endothelial dysfunction.

P5396 | BEDSIDE
Association of progression or regression of coronary artery atherosclerosis with long-term prognosis
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Background: The association between coronary atherosclerosis progression or regression with long-term prognosis remains poorly investigated. We assessed the association of atherosclerosis progression or regression with long-term mortality.

Methods and results: The study included patients with coronary artery disease (CAD) who underwent coronary angiography at baseline and at 2 years thereafter. Coronary segments with >25% and -50% diameter stenosis at baseline were included in the analysis. Atherosclerosis progression or regression was defined as a change in minimal lumen diameter (MLD) of non-treated segments of 0.2 mm and -0.2 mm, respectively. The primary outcome was all-cause mortality. Quantitative coronary angiographic evaluation was performed in 6259 coronary segments. Of them, 1790 non-stented segments with >25% diameter stenosis at baseline angiogram and 806 stented segments were analyzed. Based on the change in MLD between baseline and 2-year angiography, patients were divided into 3 groups: progression (8.8%); regression (13.2%); no progression or regression of atherosclerosis (78.0%). There were 126 deaths over 8-year follow-up: 17 deaths among patients with progression, 6 deaths among patients with regression and 103 deaths occurred among patients with no progression/regression (Kaplan-Meier estimates of 8-year mortality, 37.5%, 8.9% and 25.2%, respectively; adjusted hazard ratio=1.16, 95% confidence interval 1.05 to 1.29, P=0.004 for 0.1 mm reduction in MLD).

Conclusions: In patients with CAD regression or progression of atherosclerotic in non-treated coronary segments with mild atherosclerosis was significantly associated with 8-year mortality. Atherosclerosis regression may be used as an intermediate end point in anti-atherosclerotic interventional studies.

P5397 | BEDSIDE
Prognostic value of automatically ST-segment deviation in patients undergoing exercise ECG

Background: Conventional exercise ECG is done frequently in evaluation of patients with suspected stress induced myocardial ischemia, due to its wide availability. Therefore it is an interesting tool to not only gain diagnostic, but also prognostic information. We wanted to evaluate whether an automatically measured, easy to use single value could provide this information.

Methods: 813 consecutive patients referred to exercise stress myocardial perfusion imaging were recruited. Prognostic endpoints (death, myocardial infarction, revascularization) were determined by 2 year follow up. To find the best prognostic values we included ST-deviations for all 12 leads, at different timepoints (baseline, maximum ST-depression, maximum workload, 2 minutes into recovery), at J-point +40ms, +60ms, and +80ms. All single values as well as delta change between timepoints were evaluated by univariate and, if significant, multivariate Cox proportional hazards analysis.

Results: Median duration of follow up was 756 days and at 720 days the combined endpoint was reached in 153 (18.8%) of patients. From all measured leads, timepoints and changes, absolute ST-depression in lead I, at the time of maximum ST-depression, provided the best prognostic value for the combined endpoint (see figure). Multivariate analysis showed the prognostic performance to be independent of other important clinical (age, sex, cardiovascular comorbidities) or test parameters (e.g. achieved heart rate or workload).

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tation was independent from clinical risk factors and plasma lipid levels. This association persisted when adding triglycerides, LDL cholesterol and HDL cholesterol to the multivariable model (OR 3.37; 95% CI 2.05–5.65).

Conclusion: Remnant cholesterol is strongly associated with premature myocardial infarction, can be easily calculated and might serve as a new potential risk marker in this young patient population.

PS399 | BEDSIDE

Type 1 or type 2 myocardial infarction in patients without significant coronary artery disease - do we choose clinical type by chance?

Data from the SWEDHEART registry

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Purpose: To compare the background characteristics, triggering mechanisms, treatments and long-term prognosis in a large real-life cohort of invasively managed patients without significant stenosis diagnosed on discharge with type 2 and type 1 MI.

Methods and results: A total of 59,394 patients with MI were registered between 2011–2013 in our Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies registry and followed until 2014 (mean follow-up 1.9 years). In accordance with the universal definition of MI from 2007 6.9% (n=4,083) of patients were classified as type 2 MI, out of whom 33% (n=1,357) underwent coronary angiography. In 52.8% (n=695) at least one significant coronary artery stenosis was found. Type 2 MI patients with significant stenosis were older (71.8±10.5 vs. 67.9±11.8), by more frequently men (69.2 vs. 34.1%) and smokers (63.4 vs. 53.5%; p<0.001 for all) than those without significant stenosis. In comparison with type 2 MI patients without obstructive CAD, those with significant stenosis showed higher proportion of hypercholesterolemia (4.4%), more frequently received cardioprotective and antiplatelet treatment (ACEI/ARB 79.6 vs. 66.6%; betablockers 85.5 vs. 78.1%; statins 84.6 vs. 67.7%; aspirin 86.5 vs. 71.8%, other antplatelets 70.2 vs. 39.0%; p<0.001 for all) as compared to those without significant stenosis. The crude long-term mortality was significantly higher in type 2 MI patients more than two times higher in type 2 MI patients with significant stenos (OR 3.37; 95% CI 2.05–5.65). The mortality did not differ significantly between patients without significant stenosis diagnosed on discharge with type 2 and type 1 MI.

Conclusion: Remnant cholesterol is a harbinger of coronary stenosis. From these findings, coronary spasm should be considered as a possible cause for type 2 MI and as a harbinger of coronary stenosis.

PS401 | BEDSIDE

The epicardial adipose tissue is related with coronary spasm as well as coronary atherosclerosis in female patients presented with chest pain: from the KorNan womeN’s chest pain registry (kOrose)

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Background: Epicardial adipose tissue (EAT) is a cardiometabolic risk factor by secreting several pro-atherosclerotic and pro-inflammatory adipokines and related with the coronary atherosclerosis. But the relation of EAT with coronary spasm is not well established. The relation of EAT with coronary spasm (CAS) was detected in 93 patients (27%) by the definition of 50% narrowing by intracoronary Doppler flow wire. EAT thickness of patients with spasm was more than two times higher in type 2 MI patients with significant stenosis (5.0±2.1 vs 2.8±1.5; p<0.001). The relation of EAT with coronary spasm (CAS) was detected in 93 patients (27%) by the definition of >50% narrowing by intracoronary Doppler flow wire. EAT thickness of patients with spasm was more than two times higher in type 2 MI patients with significant stenosis (5.0±2.1 vs 2.8±1.5; p<0.001). The relation of EAT with coronary spasm (CAS) was detected in 93 patients (27%) by the definition of >50% narrowing by intracoronary Doppler flow wire. EAT thickness of patients with spasm was more than two times higher in type 2 MI patients with significant stenosis (5.0±2.1 vs 2.8±1.5; p<0.001).

Methods: 344 female patients (60.7±10.4 years) who presented with chest pain were included. CAS was detected in 93 patients (27%) by the definition of >50% narrowing by intracoronary Doppler flow wire. EAT thickness of patients with spasm was more than two times higher in type 2 MI patients with significant stenosis (5.0±2.1 vs 2.8±1.5; p<0.001). The relation of EAT with coronary spasm (CAS) was detected in 93 patients (27%) by the definition of >50% narrowing by intracoronary Doppler flow wire. EAT thickness of patients with spasm was more than two times higher in type 2 MI patients with significant stenosis (5.0±2.1 vs 2.8±1.5; p<0.001). The relation of EAT with coronary spasm (CAS) was detected in 93 patients (27%) by the definition of >50% narrowing by intracoronary Doppler flow wire. EAT thickness of patients with spasm was more than two times higher in type 2 MI patients with significant stenosis (5.0±2.1 vs 2.8±1.5; p<0.001). The relation of EAT with coronary spasm (CAS) was detected in 93 patients (27%) by the definition of >50% narrowing by intracoronary Doppler flow wire. EAT thickness of patients with spasm was more than two times higher in type 2 MI patients with significant stenosis (5.0±2.1 vs 2.8±1.5; p<0.001). The relation of EAT with coronary spasm (CAS) was detected in 93 patients (27%) by the definition of >50% narrowing by intracoronary Doppler flow wire. EAT thickness of patients with spasm was more than two times higher in type 2 MI patients with significant stenosis (5.0±2.1 vs 2.8±1.5; p<0.001).

Conclusion: The epicardial adipose tissue is related with coronary spasm as well as coronary atherosclerosis in female patients presented with chest pain: from the KorNan womeN’s chest pain registry (kOrose).

PS404 | BEDSIDE

Type 2 myocardial infarction - does the presence of stenosis matter?

Data from the SWEDHEART registry

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Purpose: To compare the background characteristics, triggering mechanisms; treatment and long-term prognosis in a large cohort of invasively managed patients with type 2 MI with and without significant coronary artery stenosis.

Methods and results: A total of 59,394 patients with MI were registered between 2011–2013 in the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies registry and followed until 2014 (mean follow-up 1.9 years). In accordance with the universal definition of MI from 2007 6.9% (n=4,083) of patients were classified as type 2 MI, out of whom 33% (n=1,357) underwent coronary angiography. In 52.8% (n=695) at least one significant coronary artery stenosis was found. Type 2 MI patients with significant stenosis were older (71.8±10.5 vs. 67.9±11.8), by more frequently men (69.2 vs. 34.1%) and smokers (63.4 vs. 53.5%; p<0.001 for all) than those without significant stenosis. In comparison with type 2 MI patients without obstructive CAD, those with significant stenosis showed higher proportion of hypercholesterolemia (4.4%), more frequently received cardioprotective and antiplatelet treatment (ACEI/ARB 79.6 vs. 66.6%; betablockers 85.5 vs. 78.1%; statins 84.6 vs. 67.7%; aspirin 86.5 vs. 71.8%, other antplatelets 70.2 vs. 39.0%; p<0.001 for all) as compared to those without significant stenosis. The crude long-term mortality was significantly higher in type 2 MI patients more than two times higher in type 2 MI patients with significant stenos (OR 3.37; 95% CI 2.05–5.65). The mortality did not differ significantly between patients without significant stenosis diagnosed on discharge with type 2 and type 1 MI. The epicardial adipose tissue is related with coronary spasm as well as coronary atherosclerosis in female patients presented with chest pain: from the KorNan womeN’s chest pain registry (kOrose).
**PS402 | BEDSIDE**

**Characteristics of coronary artery ectasia in patients with ST-segment elevated myocardial infarction**


**Background:** The characteristics of patients with coronary artery ectasia (CAE) who suffered from ST-segment elevated myocardial infarction (STEMI) are little known. We assessed the differences in the backgrounds and prognoses between CAE and non-CAE patients with STEMI.

**Methods:** A total of 2364 patients with STEMI underwent primary percutaneous coronary intervention in our hospital between January 2004 and September 2014. We investigated 2305 patients excluding stent thrombosis and Kawasaki disease. CAE patients were defined as patients whose coronary artery was ectatic and inappropriate for stent implantation. We compared the differences in the backgrounds and clinical prognoses between CAE and non-CAE patients with STEMI by retrospectively assessing the coronary risk factors and angiographies from the medical records.

**Results:** CAE was observed in 15 (0.65%) of the 2305 patients. The median diameter of the culprit lesions was 4.3±1.2 mm in CAE patients and 3.0±0.6 mm in non-CAE patients (p<0.0001). Younger age and higher body mass index (BMI) were more related to CAE patients (53.7±13.0 years vs. 68.8±12.7 years, p<0.0001), increase in NT-proBNP levels (p<0.001), as well as the history of diabetes mellitus (p=0.0362), hypertension (p=0.0069), increased body mass index (BMI) (p<0.0001), MIT 0.87 (95% CI 0.79–0.96, p=0.008). ROC analysis confirmed the quality of coronary artery calcium score >100 (odds ratio [OR], 3.429–5.387 [95% CI]); hypercholesterolemia (OR - 3.346 [2.605–4.299] [95% CI]); diabetes mellitus (OR - 6.657 [3.478–1.274] [95% CI]); smoking (OR - 1.631 [1.340–1.987] [95% CI]) – for all p<0.001. There was no significance of obesity expressed by BMI (OR - 0.996 [0.975–1.017] [95% CI]).

**Conclusions:** Diabetes mellitus, hypertension, hypercholesterolemia and smoking increase the risk of ACS in young women, where the strongest factor is diabetes mellitus. Obesity and positive family history of CAD did not increase the risk of heart attack within tested population.

**PS404 | BEDSIDE**

**The cardiovascular disease risk profile in a young woman (under the age of 45) with acute coronary syndrome (ACS)**

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**Background:** The coronary artery disease (CAD) mainly affects elderly people, but also more and more young people get sick. It is estimated that every 20th person with CAD is under the age of 45, and only 20% of them are women. The literature concerning this matter is rather limited.

The aim of this study was to determine the profile of risk factors predisposing to ACS at young age in women. The characteristics of patients with CAE were examined. A significant difference was observed in the incidence of AAD between CAE patients and non-CAE patients (26.6±3.3 vs. 23.7±3.6, p=0.0022), while diabetes was less related (6.7% vs. 31.1%, p=0.048).

**Conclusions:** Younger age, higher BMI, and non-diabetes characterized CAE patients who acquired STEMI. CAE patients tended to appear in the right coronary artery of CAE patient. CAE patients might be associated with AAD.

**PS5405 | BEDSIDE**

**Breast arterial calcification as an independent predictor of coronary artery disease in a female cohort of African descent**

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**Background:** Breast arterial calcification (BAC) is a common incidental finding on screening mammograms. Accumulating data on predominantly Caucasian women suggest an association between BAC and coronary artery disease (CAD). However, little is known about this association in non-Caucasian populations.

**Purpose:** We sought to comprehensively examine the correlation between BAC on digital mammography and CAD endpoints detected by cardiac computed tomography (CCT) in a female cohort of African descent.

**Methods:** Women with African ancestry who underwent digital screening mammography and CCT within 24 months were identified. Women with known CAD were excluded to avoid selection bias. Mammographic and CCT results were reviewed in a blinded fashion. Patient-related pertinent covariates were assessed (age, body mass index, diabetes, hyperlipidaemia, hypertension, smoking, and renal insufficiency).

**Results:** Two hundred women of African descent (median age 52.5 years) were eligible for inclusion. The median inter-procedural time was 8 months. BAC was present in 41 women (20.5%). Based on univariate analysis, covariates with discriminative power were identified and adjusted for. Subsequently, multivariate regression analyses determined BAC to be significantly associated with coronary artery calcium score >100 (odds ratio [OR], 6.8; 95% confidence interval [CI], 2.4–19.5; P<0.001), atherosclerotic luminal narrowing (OR, 11.1; CI, 3.9–31.6; P<0.001), and coronary artery stenosis ≥50% (OR, 5.6; CI, 2.0–15.5; P<0.001) by CCT.

**Conclusions:** BAC on mammography is associated with increased probability of coronary artery disease, coronary atherosclerosis, and obstructive CAD on CCT in women with African ancestry. Our data suggest that BAC is an easily assessable surrogate marker for CAD risk within this population.
P5406 | BEDSIDE
Relation between coronary arterial lesion location and major adverse cardiac events 6-months after an acute coronary syndrome
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Background: Anatomic heterogeneity in patients with coronary artery disease might expectedly lead to differences in short-term outcomes. Several small follow-up studies have documented that lesion complexity is predictive of immediate results after percutaneous coronary intervention. However, it is unclear whether the coronary anatomy continues to portend a poor prognosis after disease has been assessed by angiographic lesion location with 6-month clinical outcomes in patients presenting with acute coronary syndrome.

Methods: The data were obtained in the framework of an ongoing prospective cohort of ACS survivors consecutively recruited between August 2013 and April 2014, at the cardiology departments of two tertiary hospitals of different regions. Coronary arterial lesions location was based on the angiographic images obtained during catheterization. The extent of coronary artery disease was expressed as the presence of 1-, 2-, or 3-vessel disease (≥70% luminal narrowing). We evaluated the relation between coronary arterial lesions location and the occurrence of major adverse cardiac events --MACE (defined by the composite endpoint -death, myocardial infarction or vessel revascularization) within 6-months after the index event (self-reported in a telephone interview).

Results: Among the 539 patients admitted due to ACS in the study period, 387 underwent catheterization, of whom 11.4% had significant disease of the left main coronary artery, 68.5% of the anterior descending artery, 44.1% of the circumflex and 40.7% of the right coronary artery. The extent of coronary artery disease was 40.7% had 1-vessel, 30.8% 2-vessel and 20.5% 3-vessel disease, with major adverse cardiac events occurring in 18.5% of the patients. After adjustment for differences in age and major cardiovascular risk factors, the presence of multiple coronary artery disease (≥2-vessel disease) was associated with 6-month adverse cardiac outcomes. Multivariate analysis showed that age and diabetes were independent predictors of major adverse cardiac events. The area under the curve was 0.75 (95% confidence interval: 0.69–0.81).

Conclusions: Anatomical heterogeneity in patients with coronary artery disease might expectedly lead to differences in short-term outcomes. The extent of coronary artery disease was expressed as the presence of 1-, 2-, or 3-vessel disease (≥70% luminal narrowing). We evaluated the relation between coronary arterial lesions location and the occurrence of major adverse cardiac events (MACE) independently of other high-risk factors. After adjustment for differences in age and major cardiovascular risk factors, the presence of multiple coronary artery disease (≥2-vessel disease) was associated with 6-month adverse cardiac outcomes. Multivariate analysis showed that age and diabetes were independent predictors of major adverse cardiac events. The area under the curve was 0.75 (95% confidence interval: 0.69–0.81).

ROLE OF ECHO-IMAGING IN ISCHAEMIC HEART DISEASE

P5407 | BEDSIDE
Echocardiographic contractile reserve and magnetic resonance to predict left ventricular remodelling

Background: The presence of adverse left ventricular remodelling (LVR) in STEMI patients is related to an increase in morbi-mortality at follow-up. Different parameters (assessed by magnetic resonance or echocardiography) have been associated, however, the main predictor of LVR remains still controversial.

Aims: We sought to know the incidence of LVR after an ST-segment elevation myocardial infarction (STEMI) and to identify a best image method to predict its occurrence.

Methods: One hundred and forty consecutive patients with an acute STEMI were studied after a successful primary angioplasty with CMR and low-dose dobutamine stress echo. The long-axis strain was measured by 2D-STE using a 17 LV segment model. For each segment, peak positive strain (SS) was measured at rest and at low-dose dobutamine stress echo. Major adverse cardiac events (MACE) were determined at follow-up.

Results: Patients were followed by a median time of 45 months (11–79 months). MACE occurred in 43 patients (26%); stroke in 6, angina or re-infarct in 29, new heart failure in 5, ventricular arrhythmia in 2, major bleeding in 2 and cardiovascular death in 5. In the univariate analysis, IS (Odds Ratio (OR): 1.8, P=0.045), SS at low-dose dobutamine stress echo (OR: 1.5, P=0.041) SS at high-dose dobutamine stress echo (OR: 1.5, P=0.041) and SS at 6 months (OR: 1.9, P=0.038) were the strongest predictors for MACE. In the multivariate analysis, SS at 6 months was the only independent predictor of MACE (cut-off value: −17, area under the curve: 0.8, Sensitivity: 80% and Specificity: 75%) (Figure 1).

Conclusions: CMR and echocardiographic derived parameters are excellent predictors of MACE in STEMI patients. Systolic strain at 6 months constitutes the strongest predictor of poor outcomes at long-term follow-up.

P5408 | BENCH
Prediction of adverse events after ST segment-elevation myocardial infarction by imaging techniques

Background: After an ST-segment elevation myocardial infarction (STEMI), different magnetic resonance (CMR) and echocardiographic (TTE) variables have been assessed as predictors of adverse outcomes. However, no studies have been conducted to compare its prognostic value.

Objectives: To determine the value of CMR, rest TTE and at low-dose dobutamine test to predict adverse events at long-term follow-up in STEMI patients.

Methods: One hundred and sixty-two consecutive patients with an STEMI were studied after a successful primary angioplasty with CMR and low-dose dobutamine stress echo. Major adverse cardiac events (MACE) were determined at follow-up.

Results: Patients were followed by a median time of 45 months (11–79 months). MACE occurred in 43 patients (26%); stroke in 6, angina or re-infarct in 29, new heart failure in 5, ventricular arrhythmia in 2, major bleeding in 2 and cardiovascular death in 5. In the univariate analysis, IS (Odds Ratio (OR): 1.8, P=0.045), SS at low-dose dobutamine stress echo (OR: 1.5, P=0.041) and SS at 6 months (OR: 1.9, P=0.038) were the strongest predictors for MACE. In the multivariate analysis, SS at 6 months was the only independent predictor of MACE (cut-off value: −17, area under the curve: 0.8, Sensitivity: 80% and Specificity: 75%) (Figure 1).

Conclusions: CMR and echocardiographic derived parameters are excellent predictors of MACE in STEMI patients. Systolic strain at 6 months constitutes the strongest predictor of poor outcomes at long-term follow-up.

P5409 | BENCH
Assessment of post-systolic shortening and early systolic lengthening by 2D speckle-tracking is useful to detect cad in patients with suspected NSTE-ACS
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Introduction - Post-systolic shortening (PSS) and early systolic lengthening (ESL) assessed by speckle-tracking echocardiography (STE) are considered markers of myocardial ischemia.

Purpose: We aimed to examine the relation between the presence of PSS, ESL and coronary artery disease (CAD) in patients presenting with suspected non-ST-elevation acute coronary syndrome (NSTEMI-ACS) and no wall motion abnormalities in conventional echocardiography.

Methods: 58 patients with suspected NSTEMI-ACS, normal LVEF (i.e. LVEF ≥55%) and normal wall motion score index (i.e. WMSI=1) were prospectively enrolled. Echocardiography was performed on admission. Longitudinal strain was measured by 2D-STE using a 17 LV segment model. For each segment, peak positive early strain (representing maximum segmental systolic lengthening) and post-systolic shortening (defined as peak negative strain during diastole minus peak negative systolic strain) were recorded. Values for all segments were averaged to obtain global values, and territorial values (based on theoretical perfusion territories of the three major coronary arteries). Layer-specific longitudinal strains were predicted LVR with a Sensitivity of 75% and specificity of 70%.
assessed from endocardium, mid-myocardium, and epicardium. All the patients underwent angi-coronography. CAD was defined by the presence of coronary artery stenosis >50%.

**Results:** Global PSS and global ESL were able to detect CAD with good diagnostically performances (AUC=0.84, p<0.001 and AUC=0.68, p=0.02 respectively). Territorial PSS and ESL were able to detect the presence of significant stenosis in LAD (AUC=0.70, p<0.01), LCX (AUC=0.73, p<0.01) and RCA (AUC=0.86, p<0.001). Territorial ESL was able to detect presence of significant stenosis in LAD (AUC=0.69, p<0.02), LCX (AUC=0.71, p<0.02) but not in RCA (AUC=0.65, p=0.08). Laver-specific analysis did not show any difference in terms of diagnostic performance between the three layers.

**Conclusion:** Assessment of both PSS and ESL is useful to detect CAD in patients with NSTE-ACS and normal conventional echocardiography.

**PS410 | BEDSIDE**

*How frequent are signs of left ventricular dysfunction in acute myocardial infarction patients with normal ejection fraction? Impact of the latest chamber quantification recommendations*

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**Aim:** To study the prevalence of abnormal values of routine parameters of global left ventricular (LV) systolic function when LV ejection fraction (LVEF) remains normal in a large, unselected cohort of consecutive patients hospitalized for acute myocardial infarction (MI).

**Materials and methods:** A total of 421 consecutive patients with MI (with or without ST elevation) included in the REBUS (RElevance of Biomarkers for future risk of arterial artery stenosis) study, underwent 2D-Doppler echocardiography in the cardiac intensive care unit within 72 hours after admission to assess their LV function. Conventional parameters of LV systolic function were categorized to normal or abnormal due to the chamber quantification recommendations from 2015.

**Results:** Of the 356 patients finally enrolled to the study, normal LVEF was recognized in 236 (51.6%) or 262 (62.5%) patients, when using either the conventional or the new sex-specific LVEF cut-off, respectively. The new reference intervals for LVEF reclassified 26 (21.8%) patients from having abnormal to normal LVEF. The patients with abnormal LVEF were characterized by larger extent of myocardial necrosis (max cTnI 31.2±55.9 vs. 17.1±24.5 μg/L, p<0.001) and higher proportion of STEMILBBB (57.0 vs 39.5%, p=0.012), as compared to those with normal LVEF. No difference in age, sex or history of previous MI were observed. The patients with abnormal LVEF had significantly lower mean mitral annular plane systolic excursion (MAPSE) (0.96±0.20 vs. 1.18±0.21 cm, p<0.001), higher indexed LV end-systolic (LVEDVi) (30.6±14.6 vs. 15.3±4.9 ml/m², p<0.001), end-diastolic (LVESVi) (53.3±19.8 vs. 40.8±10.2 ml/m², p<0.001) and left atrial volume (LAVi) (37.9±11.9 vs. 31.6±11.0 ml/m², p<0.001). Using the new cut-off, among the patients with normal LVEF, an abnormal MAPSE (<1.1 cm in women and <1.3 cm in men) was observed in 64.4%. Elevated LVEDSVi (>24ml/m² in women and >31ml/m² in men) and LVESVi (>61ml/m² in women and >74ml/m² in men) were found only in 0.4% of patients, while an enlarged LAVi (>34ml/m²) in 33.8% of patients with normal LVEF.

**Conclusions:** Implementation of the latest recommendations on chamber quantification including sex-specific reference intervals resulted in the reclassification of ca 20% of patients from having abnormal to normal LVEF. A majority of patients classified as having normal LVEF on echocardiography within 72 h after MI had at least one marker of global systolic function outside the normal range. The prognostic significance of our observation is being investigated.

**PS411 | BEDSIDE**

*Excellent discrimination ability of resting multilayer longitudinal strain using two-dimensional speckle tracking echocardiography for myocardial infarction and ischemic segments*

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**Background:** Damage to left ventricular (LV) endocardial layers may occur at an early stage in myocardial infarction (MI) or ischemia.

**Purpose:** To evaluate the ability of multi-layer longitudinal strain (LS) with 2D speckle tracking transthoracic echocardiography (TTE) to distinguish between MI, ischemic, and non-ischemic LV segments.
Methods: Retrospective data from 39 stable patients (32 males; 65.8 ± 11.9 years), comprising 46 coronary arteries with >50% stenosis on invasive coronary angiography (not related to MI), were assessed by invasive fractional flow reserve (FFR). All patients underwent TTE (Vivid E9) within 36 days of FFR, without clinical incident. Ischaemic and non-ischaemic segments were defined as those supplied by the stenotic vessels with FFR < 0.80 and FFR 0.80, respectively.

Results: Of the 39 patients, 10 had 11 coronary territories related to previous MI. FFR < 0.80 and FFR > 0.80 was identified in 27 and 19 vessels, respectively. Using whole-layer, endocardial, and epicardial LS, no significant differences were detected between ischaemic and non-ischaemic segments, but the infarcted segments were significantly greater. According to receiver operating characteristic curves, the best cutoff values for whole-layer, endocardial and epicardial LS for infarcted segments were –10.0% (91% sensitivity, 76% specificity, area under the curve [AUC] = 0.854, P = 0.002), –11.0% (91%, 65%, AUC = 0.840, P = 0.002), and –8.0% (82%, 85%, AUC = 0.853, P = 0.002), respectively.

Conclusion: In stable patients with coronary artery disease, resting multi-layer LS is useful to detect infarcted LV segments. Furthermore, whole-layer, endocardial and epicardial LS were equally effective. However, it remains a diagnostic challenge to differentiate between ischaemic and non-ischaemic LV segments.

P5415 | BEDSIDE
Routine manual thrombus aspiration has no impact on left ventricular remodeling: the echocardiographic sub-study of the randomized physiologic assessment of thrombus aspiration in patients with ST-segment elevation myocardial infarction
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Background: It has been reported that index of microcirculatory resistance (IMR) is lower in STEMI patients who underwent thrombus aspiration before stent implantation compared to those treated with conventional primary PCI. The aim of this study was to evaluate impact of improved myocardial perfusion by manual thrombus aspiration assessed by IMR on left ventricular remodeling in STEMI patients at mid-term follow-up.

Methods: The total of 115 patients entered the echocardiography sub-study of the PATA STEMI (randomized Physiologic Assessment of Thrombus Aspiration in patients with ST-segment Elevation Myocardial Infarction) trial which evaluated efficacy of manual thrombus aspiration using Eliminate3 catheter (Terumo Europe, Leuven, Belgium). Echocardiography was done within the first 24 hours after the index procedure and after 4 months. End-diastolic and end-systolic left ventricular (LV) volume indices, ejection fraction (EF), cardiac sphericity index (CSI) and regional wall motion score index (WMSI) were calculated.

Results: In baseline characteristics, in patients with thrombus aspiration compared to those with conventional primary PCI, total ischemic time tended to be longer (246.7 ± 181.8 vs. 209.5 ± 119.1 min, P = 0.09) and AUC CK was smaller (40990 ± 26158 U/L vs. 52676 ± 32013 U/L, P = 0.026, respectively). Also, corrected IMR was lower in thrombus aspiration group (27.5 ± 16.8 vs. 39.9 ± 32.7 U/L, P = 0.0079), while CFR (1.68 ± 0.81 vs. 1.61 ± 0.67, P = 0.6) and mean coronary wedge pressure in infarct related artery (20.4 ± 6.6 vs. 21.4 ± 7.8 mmHg, P = 0.5) were similar. End-diastolic and end-systolic LV volumes per body surface area, EF, CSI volume and WMSI were similar between the thrombus aspiration and no aspiration group at baseline and at follow-up. At follow-up, percent change in WMSI tended to be greater in thrombus aspiration group (decrease in WMSI 8.2% vs. increase in WMSI 0.8%, P = 0.094). The rate of LV remodeling and reverse LV remodelling was similar in thrombus aspiration and conventional primary PCI group (30.3 ± 26.6%, P = 0.84 and 42.4 ± 26.6%, P = 0.12, respectively).

Conclusions: Improved myocardial perfusion achieved by manual thrombus aspiration and assessed by index of microcirculatory resistance has no impact on left ventricular remodeling in STEMI patients at mid-term follow-up.

P5414 | BEDSIDE
Quantification of regional left ventricular function by layer-specific strain

Purpose: The study aimed to evaluate whether layer-specific myocardial strain performed by two-dimensional speckle tracking imaging (2D-STI) allows quantification of regional left ventricular function in patients with coronary artery disease (CAD).

Methods: 44 patients referred to selected coronary angiography (SCA) due to suspected CAD were prospectively included. All the patients had normal EF and no abnormal segmental wall motion of left ventricle. According to degree of coronary artery stenosis by SCA, there were 188 segments with >75% coronary artery stenosis (severe stenosis group), 76 segments with 50–75% coronary artery stenosis (moderate stenosis group), 132 segments with <50% coronary artery stenosis (mild stenosis group) and 240 segments without coronary artery stenosis (control group). Four-chamber, two-chamber and long-axis apical views were recorded in all the subjects. Layer-specific longitudinal strain indices including endocardium (LS-endo), mid-myocardium (LS-mid) and epicardium (LS-epi) were assessed by 2D-STI.

Results: In segments with or without coronary artery stenosis, the LS-endo, LS-mid, LS-epi of each segment decreased gradually (P < 0.05). Compared with the control group, LS-endo, LS-mid, LS-epi of moderate stenosis group and severe stenosis group decreased significantly (P < 0.05), however, there was no significant difference between moderate and severe group. Moreover, there was no significant difference between the control group and mild stenosis group (P > 0.05).

Conclusion: Layer-specific myocardial strain indices can recognize tiny changes of regional left ventricular systolic function in patients with CAD. In segments with normal wall motion, the regional systolic function of left ventricle has already been impaired.

P5416 | BEDSIDE
Left ventricular global longitudinal strain rate is associated with changes in myocardial redox state in patients with ischaemic heart disease
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Purpose: We explored the ability of left ventricular global longitudinal strain (LS) and LS rate (LSR) to describe myocardial redox state in patients with coronary atherosclerosis.

Methods: Echocardiography was performed in 30 male, non-diabetic patients with no heart failure (good LV ejection fraction (LVEF=54.2±2.0%) and low B-natriuretic peptide level=75.7±15.5ng/mL) undergoing coronary bypass surgery, with no heart failure (good LV ejection fraction (LVEF=54.2±2.0%) and low B-natriuretic peptide level=75.7±15.5ng/mL). We assessed myocardial redox state using ex-vivo bioassays and lucigenin chemiluminescence. Plasma malondialdehyde (MDA) concentrations were measured in 27 patients. We also assessed myocardial NADPH oxidase activity using lucigenin chemiluminescence and lucigenin-enhanced chemiluminescence. We used 2D echocardiography to assess cardiac structure and function.

Results: There was a negative correlation between LSR and plasma MDA (p=NS) but there was a positive association between myocardial NADPH oxidase activity (p=NS for both). Systemic or myocardial oxidative stress were not associated with ESV, EDV or their respective indices adjusted for body surface area (p=NS for all). LS or LSR were not associated with plasma MDA (p=NS) but there was a positive association between myocardial NADPH oxidase activity and LSR (r=0.38, p<0.05 but not with LS) indicating reduced LV longitudinal systolic deformation with higher myocardial oxidative stress.

Conclusions: Higher NADPH oxidase activity in human myocardium is linked with reduced left ventricular global strain rate before the development of systolic LV dysfunction. LSR appears to be a sensitive imaging biomarker for the characterization of myocardial redox state, and this finding may have major clinical implications for the prediction of ischaemic cardiomyopathy and the monitoring of treatments in patients with ischaemic heart disease.
P5417 | BEDSIDE
Prognostic assessment of myocardial viability after acute myocardial infarction: a clinical follow-up study by speckle tracking
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Purpose: We sought to use speckle tracking imaging (STI) for the assessment of myocardial viability and changes of left ventricular segmental functional of the patients with acute myocardial infarction (AMI). Clinical incremental value of STI to identify viable segments through different time points was focused on in this study.

Methods: 54 patients with first onset AMI who underwent primary percutaneous coronary intervention (PCI) were enrolled in the study. The average age was 62±14 years. Dynamic images of left ventricle were acquired before and 1-year after PCI. Apical long-axis, four-chamber and two-chamber views, cross-sectional basal, mid and apical views were stored for 3 to 5 cardiac cycles. With the methods of standard 17 segments, longitudinal peak systolic strain (LPPSS), radial peak systolic strain (RPPSS) and circumferential peak systolic strain (CPPSS) were analyzed for each segment in Echocast platform. According to the LPPSS cut-off value of −5% as the determination of myocardial viability and recovery of segmental function, the percentage of infarcted area was calculated for the comparisons among infarcted area, infarcted site and segmental recovery.

Results: Before PCI, dysfunctional segments of AMI patients were 341 in total and it decreased to 207 at 3-month after PCI while 159 at 1-year follow-up. Between before and 3-month after PCI, the infarcted area percentage of early-recovery group (n=29) was decreased 18.9%, which was significantly higher (p<0.05, all) than both the decreases in late-recovery (n=15) (10.6%) and non-recovery group (n=10) (8.2%). The decreases of early-recovery and late recovery group had reached at 21.1% and 22.0% at 1-year after PCI, respectively. Both of them were significant different from non-recovery group (13.5% (p<0.05, all), Coronary artery function, left ventricular

Conclusions: STI assessment was accurate for identifying viable myocardium and tracking the changes of left ventricular segmental functional. After infarction, the segmental analysis of longitudinal and circumferential movements have suggested early and continued recovery for patients. LPPSS and CPPSS from STI have provided clinical incremental value in the prognosis of AMI patients.

CARDIAC ECHO-IMAGING IN SYSTIMIC DISEASES

P5418 | BEDSIDE
Greater improvement of coronary artery function, left ventricular deformation and twisting by IL23/23 compared to TNF-a inhibition in AMI patients
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The role of treatment with anti-IL12/23 agents on left ventricular (LV) function, arterial stiffness and coronary microcirculation in patients has not been fully clarified.

Methods: 114 postischemic patients (52±13 yrs, 72men), (PASI disease activity score:11.8±8), were randomized to receive an anti-IL12/23 regimen (n=32), an anti-TNF (n=34) or cyclosporine (n=48). At baseline and after 4 months of treatment, we measured a) pulse wave velocity (PWV-m/sec), augmentation index (AI), and cardiovascular risk factors b) LV function: GLS, GCS, number of segments with diastolic dysfunction (DD) and LV twist. c) Arterial stiffness: AI, augmentation index, and wave reflection parameters, including significant increase in E wave DT (Pearson R=0.22; p<0.042), PHT (Pearson R=0.26; p<0.021) and size of LA (Pearson R=0.22; p<0.032, significant at 48 months).

Conclusion: The FAP is accompanied by cardiac amyloid infiltration resulting in progressive worsening of ventricular thickening and diastolic dysfunction. Liver transplantation prevented the progression of cardiac amyloid infiltration, stabilizing the echocardiographic parameters at long-term.

P5420 | BEDSIDE
Subclinical abnormalities of two-dimensional speckle tracking echocardiography assessment in a newly peripheral vascular disease in patient with chronic kidney disease
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Background: Very few studies have investigated the relationship between arterial stiffness and subclinical left ventricular (LV) dysfunction and none used two-dimensional speckle tracking echocardiography (2DSTE) to assess left ventricular stiffness.

Objectives: We sought to investigate the association between subclinical myocardial abnormalities assessed by 2DSTE and arterial stiffness in chronic kidney disease (CKD) patients with normal LV ejection fraction (LVEF) and no previous history of cardiovascular disease.

Methods: In this cross-sectional study we have enrolled 106 CKD patients. Pressure waveforms were recorded on radial, carotid and femoral arteries using application planometry to estimate augmentation index (AIx) and aortic pulse wave velocity (aPWV). Conventional echocardiography and 2DSTE were used to determine LVEF, LV mass index (LVM), global longitudinal and circumferential strain (GLS, GCS), number of segments with diastolic dysfunction (DD) and LV twist.

Results: Aortic PWV correlated crudely with the presence of diabetes (r=0.58, p<0.001), hypertension (r=0.32, p=0.001), LVM (r=0.29, p=0.01). GLS (r=0.30, p=0.003), number of segments with DD (r=0.416, p=0.001), LV twist (r=0.288, p=0.003) while AIx was only associated with hypertension (r=0.19, p=0.046) and number of segments with DD (r=0.317, p=0.001). When adjusting for age, gender and cardiovascular risk factors aPWV was independently associated with LV twist (r=0.25, p=0.007) and number of segments with DD (r=0.300, p=0.003). The association between AIx, aPWV and number of segments with DD was not significant. Stepwise, multiple regression models established that LV twist improved the prediction of arterial stiffness over and above age, gender and cardiovascular risk factors alone (r=0.17, p=0.001).
PS421 | BEDSIDE
The effect of different treatment strategies on left ventricular myocardial deformation parameters in patients with chronic renal failure
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Background: Renal transplantation has lowered the risk of cardiovascular death compared with dialysis. However, there exists conflicting data about improvement in cardiac functions after transplantation.

Purpose: In our study, we aimed to compare the possible effects of different treatment strategies on left ventricular (LV) functions by speckle tracking echocardiography (STE) in patients with chronic kidney disease (CKD).

Methods: Three groups were formed with patients at predialysis stage (n=50), with those on three times a week hemodialysis program (n=50), or with those who underwent successful renal transplantation (n=50).

Results: Among mean LV strain values, circumferential systolic strain was lowest in the hemodialysis group. Among mean LV longitudinal strain rate (SR) values, longitudinal systolic SR was lowest in the hemodialysis group. Longitudinal early diastolic SR was highest in the transplantation group. Among mean LV circumferential SR values, circumferential systolic SR, early diastolic SR, and late diastolic SR were lowest in the hemodialysis group (Table 1).

Table 1. Left ventricular myocardial deformation parameters of the study groups

<table>
<thead>
<tr>
<th>Mean values</th>
<th>Transplant</th>
<th>Hemodialysis</th>
<th>Predialysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=50)</td>
<td>(n=50)</td>
<td>(n=50)</td>
<td></td>
</tr>
<tr>
<td>Longitudinal systolic strain (%)</td>
<td>−19.93±3.50</td>
<td>−17.47±3.28</td>
<td>−18.74±2.52</td>
</tr>
<tr>
<td>Circumferential systolic strain (%)</td>
<td>−27.87±4.20</td>
<td>−20.97±4.90</td>
<td>−24.74±5.55</td>
</tr>
<tr>
<td>Radial Strain (%)</td>
<td>33.51±13.89</td>
<td>30.41±13.33</td>
<td>31.46±11.46</td>
</tr>
<tr>
<td>Longitudinal SR (1/sec)</td>
<td>−1.03±0.20</td>
<td>−1.19±0.20</td>
<td>−1.19±0.20</td>
</tr>
<tr>
<td>Longitudinal early SR (1/sec)</td>
<td>1.76±0.30</td>
<td>1.54±0.30</td>
<td>1.30±0.30</td>
</tr>
<tr>
<td>Longitudinal late SR (1/sec)</td>
<td>1.80±0.30</td>
<td>1.71±0.30</td>
<td>1.70±0.30</td>
</tr>
<tr>
<td>Radial early SR (1/sec)</td>
<td>1.00±0.30</td>
<td>0.85±0.30</td>
<td>0.70±0.30</td>
</tr>
<tr>
<td>Radial late SR (1/sec)</td>
<td>0.98±0.30</td>
<td>0.84±0.30</td>
<td>0.70±0.30</td>
</tr>
</tbody>
</table>

Conclusion: We have found by STE that LV functions of CKD patients who underwent successful renal transplantation tend to improve. However, CKD patients on hemodialysis treatment seem to have worse LV functions than CKD patients at predialysis stage.

Acknowledgement/Funding: This study was funded by the Ondokuz Mayis University, Samsun, Turkey (project number: PVO.TIP.1904.13.030)

PS422 | BEDSIDE
The impact of liver transplantation on myocardial function in patients with familial amyloid polyneuropathy
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Introduction: Familial amyloid polyneuropathy (FAP) is a genetic disorder characterized by amyloid deposition in multiple organs. Myocardial amyloid infiltration results in progressive diastolic dysfunction and subclinical changes in systolic function, better assessed by myocardial deformation parameters. Liver transplantation (LT) inhibits liver production of abnormal protein and prevent disease progression. However, its impact on myocardial deformation has not been investigated.

Objective: To evaluate the impact of LT on global myocardial deformation parameters as assessed by speckle-tracking echocardiography in patients with FAP.

Methods: Prospective study of patients with FAP undergoing LT. Global longitudinal strain (GLSR) and global circumferential strain (GLSC) were measured with echocardiography. The mean GLSR for each segment was calculated.

Results: Thirty-three patients with FAP (22 male, mean age 55±11 years) were included. All patients had moderate to severe amyloid deposits in the heart. The mean GLSR for each segment was calculated. The mean GLSR for all segments was significantly lower in patients with FAP compared to control subjects (p<0.05).

Conclusion: Liver transplantation significantly improved myocardial deformation parameters in patients with FAP.

Acknowledgement/Funding: Fundacao para a Ciencia e Tecnologia - Portugal

PS423 | BENCH
Causes and consequences of longitudinal left ventricular dysfunction assessed by 2D strain echocardiography in patients with cardiac amyloidosis
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Background: Cardiac amyloidosis (CA) is a condition of poor prognosis due chiefly to three forms of amyloidosis, light chain (AL), hereditary transthyretin (M-TTR), and wild-type transthyretin (WT-TTR). Two-dimensional (2D) echocardiography measurement of longitudinal strain (LS) has been reported to detect early left-ventricular systolic dysfunction. The pathophysiological underpinnings, regional distribution, and prognostic significance of LS in CA are unclear.

Objectives: To compare left ventricular LS evaluated by 2D echocardiography and regional myocardial magnetic resonance imaging (MRI) in CA, establish correlations between histological and imaging findings, and assess the prognostic usefulness of LS measurement and MRI.

Methods: All patients underwent echocardiography and 53 had MRI. The native hearts of 3 patients who received heart transplants were subjected to histological examination. For each of the 17 left-ventricular segments in the American Heart Association model, we evaluated LS, late gadolinium enhancement (LGE) by MRI, and cardiac amyloid deposition. Univariate at 6 months and multivariate analysis were performed to identify variables associated with major adverse cardiac events (MACE).

Results: We studied 79 patients with CA; 26 had AL, 36 M-TTR, and 17 WT-TTR. Mean LS was −10±4%. Both LS and amyloid deposits showed a basal-apical gradient. Mean LS and number of segments with LGE were similar across the three CA types. LS correlated with LGE and amyloid burden (r=0.72). LGE was seen in the six basal segments in all WT-TTR patients.

During the median follow-up of 11 [4; 17] months, 36 (48%) patients experienced MACE. Independent predictors of MACE were apical LS (cutoff, −14.5%), N-terminal pro-natriuretic peptide (cutoff, 4000 ng/L), and New York Heart Association Class III-IV heart failure.

Conclusions: Basal-to-apical LS abnormalities are similar across CA types and reflect the amyloid burden. Apical LS independently predicts MACE.

Acknowledgement/Funding: Fundacao para a Ciencia e Tecnologia - Portugal

PS424 | BEDSIDE
Relationship between inflammation and timing markers of LV rotation and untwist in psoriatic arthropathy - a study of the mechanisms of early myocardial dysfunction in systemic diseases
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Purpose: To evaluate the relationship between inflammation and left ventricular (LV) deformation in patients with Psoriatic arthritis (PsA).

Methods: Sixty-Trio patients with PsA and 24 healthy control subjects received conventional echocardiography with speckle tracking imaging. Deformation measurements included global longitudinal (ϵ-long), apical circumferential (ϵ-circ) and radial strain (ϵ-radial), apical rotation and maximal untwisting rate (URmax). Timing markers were time to peak apical rotation and time to 25% duration of apical untwisting (Figure).

Results: All patients had normal LVEF but impaired LV deformation when compared to control subjects (ϵ-long: 19.5±3.0 vs. pre-LT; ϵ-circ: 22.1±5.3 vs. 33.6±4.8, rotation: 10.6±4.3 vs. 19.4±4.9, URmax: 64.8±23.3 vs. 103.7±44.0; p<0.005). Furthermore, there were a significant correlation between timing markers, deformation and inflammation after adjusting for age and blood pressure (Table 1).

Table 1

<table>
<thead>
<tr>
<th>Data</th>
<th>Pre-LT</th>
<th>Post-LT</th>
<th>p-value</th>
</tr>
</thead>
</table>
| N    | 36    | 36     | majority out of 50 patients with PSA have an evidence of subclinical myocardial dys-

dial deformation indexes were not dependent on age, duration of symptoms and severity of neurological involvement.

Conclusion: FAP patients had subclinical changes in systolic function as assessed by myocardial deformation analysis, which correlates with the neurological involvement of the disease. After LT, changes in myocardial deformation tended to be reversed.
sarcoidosis was receiving oral or inhaled steroids. There was no clinical finding suggestive of cardiac involvement in any of the patients. The echocardiographic assessment of the patients revealed no significant difference between the two groups regarding left ventricular end-systolic and end-diastolic diameters, ejection fraction and annular velocity determined by tissue Doppler evaluation. The LVEF calculated with the modified Simpson’s method was 61.8±7.8% in the sarcoidosis group versus 64.1±2.7% in the control group (p=0.04). Left ventricular interventricular septum thickness, posterior wall thickness and relative wall thickness were significantly higher in the sarcoidosis group compared to the control group (p<0.001). The sarcoidosis group had higher ULM and LVM values compared to the control group (16.6±10.9 vs. 9.8±5.5) with a statistically significant difference (p<0.001). The present study indicates diastolic dysfunction and increased LVMi despite normal systolic function in patients with early-stage sarcoidosis without cardiac involvement. Also, the diastolic parameters were normal without showing any significant difference compared to the control group while there was a statistically significant increase in LAVi. This finding suggests that LAVi may be the earliest marker of diastolic dysfunction in patients with early-stage sarcoidosis without cardiac involvement.

ASSESSMENT OF LEFT VENTRICULAR FUNCTION BY SPECKLE TRACKING ECHOCARDIOGRAPHY

P5427 | BEDSIDE
2D speckle tracking-derived left ventricle global longitudinal strain: is it useful to discriminate left ventricular dysfunction stages?

Background: 2D speckle tracking-derived left ventricle (LV) global longitudinal strain (GLS) is a validated method for LV systolic function assessment. We aimed to study LV GLS predictive power for impaired systolic function against 2D LV ejection fraction (LVEF).

Methods: We prospectively included 68 patients referred for echocardiography at a tertiary centre. Patients with significant valve disease, resting wall motion abnormalities or unsuitable images for GLS analysis were excluded. An independent operator confirmed the LVEF (biplane Simpson), followed by off-line GLS analysis by investigators blinded to the LVEF. Statistical analysis included LVEF and GLS correlation - linear regression, ROC curves construction for both GLS and GLS indexed cut-offs, and optimal cut-off determination (Youden index).

Results: Mean age was 60±18 years; 82% were male, 22% had arterial hypertension, 38% heart failure and 20% ischemic heart disease. The mean LVEF and LV GLS were 48±16% and −14±6%, respectively, which were strongly correlated (r=−0.88, R2=0.78, p<0.01). We divided our sample in four pre-specified subgroups: normal LV function (LVEF≥55%, 48% of the sample) with mean LVEF 62±3%; GLS−20%; mild dysfunction (54%≤LVEF<45%, 19%) with LVEF 49±4% and GLS−14±5%; moderate dysfunction (44%≤LVEF<30%, 22%) with LVEF 37±5% and GLS−10±2%; severe dysfunction (LVEF<30%, 15%) with LVEF 22±15% and GLS−6±2%. The subgroups were similar in respect to age and sex (p>0.05). The performed GLS and indexed GLS cut-offs for the stages of LV dysfunction are listed in the table. Indexed GLS was more specific in the discrimination, albeit less sensitive.

LV GLS cut-offs performance

<table>
<thead>
<tr>
<th>Cut-offs</th>
<th>LVEF (%)</th>
<th>c-Statistic</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GLS−15.6%</td>
<td>&lt;55</td>
<td>0.95</td>
<td>97.0</td>
<td>90.0</td>
<td>87.9</td>
<td>97.0</td>
</tr>
<tr>
<td>GLS−12.7%</td>
<td>&lt;45</td>
<td>0.96</td>
<td>100</td>
<td>88.4</td>
<td>83.3</td>
<td>100</td>
</tr>
<tr>
<td>GLS−8.6%</td>
<td>&lt;30</td>
<td>0.99</td>
<td>100</td>
<td>93.1</td>
<td>71.1</td>
<td>100</td>
</tr>
<tr>
<td>GLS−3.0%</td>
<td>&lt;55</td>
<td>0.97</td>
<td>95.0</td>
<td>93.3</td>
<td>94.7</td>
<td>93.3</td>
</tr>
<tr>
<td>GLS−1.0%</td>
<td>&lt;45</td>
<td>0.99</td>
<td>92.0</td>
<td>95.3</td>
<td>95.0</td>
<td>95.3</td>
</tr>
<tr>
<td>GLS−0.14%</td>
<td>&lt;30</td>
<td>0.99</td>
<td>90.0</td>
<td>91.3</td>
<td>64.3</td>
<td>98.1</td>
</tr>
</tbody>
</table>

PPV, positive predictive value; NPV, negative predictive value; GLSindex, GLS indexed for LVEDd.

Conclusion: LV GLS analysis was accurate in the discrimination of patients with normal LV function from those with progressive mild, moderate and severe levels of dysfunction.

P5428 | BEDSIDE
Relation among left ventricular twist, torsion and contractility in hypertensive patients: one-beat real-time three-dimensional speckle tracking echocardiography study
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Purpose: Left ventricular (LV) twist and torsion caused by contraction of inner...
Assessment of left ventricular function by Speckle tracking echocardiography

and outer oblique muscle may reflect contractility and play an important role in squeezing the blood out of the heart and contribute a part of stroke volume. However, the difference between LV twist and torsion and the relation between torsion and LV function have not been fully examined. Recent advances in one-beat 3-dimensional speckle tracking echocardiography (3D-STE) with high volume rates enabled us to assess LV torsion and LV phasic strain rate (SR). Thus, we sought to examine the relation between LV twist and torsion and the relation between LV torsion and LV function using the 3D-STE.

Methods: A total of 81 subjects were enrolled (23 controls (age 62±12), 37 patients with hypertension (HTN) (age 69±12) and 21 patients with hypertensive heart failure (HHF) (age 75±18)). LV twist and torsion were examined using the 3D-STE with 70-80vps. Twist was defined as the maximum difference in rotation angle between base and apex (unit is °). Torsion was defined as LV twist/LV long axis length (unit is °/cm). Torsion was derived from the time-twist curve and integrated by LV long axis length for every instance in time (each frame). We examined LV ejection fraction (EF) and LV strain and SR during systole as an index of contractility by the 3D-STE.

Results: LV twist, torsion, strain and SR during systole were measured with the novel 3D-STE within 3 minutes. There was a significant correlation between twist and torsion in a total of 81 subjects (r=0.53), LV twist in HTN increased compared to control (F=4.0±1.5°, HTN: 9.4±1.4° and HHF: 9.0±1.6°, *p<0.05 vs control). LV torsion in HTN also increased but that in HHF decreased (1.35±0.18, 1.54±0.29 and 1.17±0.19°/cm, respectively). LVEF and LV strain and SR were reduced in HHF (LV radial strain; control: 35±6, HTN: 37±6 and HHF 24±14°/s *). LV torsion had a significant correlation with LVEF (r=0.43, *p<0.01), whereas LV twist had no correlation with LVEF. LV torsion had a significant correlation with LV strain (longitudinal: r=−0.37, radial: r=0.43, circumferential: −0.38, p<0.05, respectively) and SR during systole in 2 directions (radial: r=0.50, p<0.01), whereas there was no correlation between LV twist and LV strain or SR.

Conclusion: This study demonstrated that LV torsion but not twist had a significant correlation with LV strain and SR. LV torsion had a significant correlation with LVEF and was significantly correlated with LVEF in the 3D-STE. This suggested that LV torsion may be an index which reflects LV contractility as well as an index of LV systolic function and more useful 3D-STE parameter than twist.

P5430 | BESIDE
Less is more: three dimensional strain may not add much

University of Tasmania, Menzies Institute for Medical Research, Hobart, Australia

Background: Global longitudinal strain (GLS) is a robust and sensitive marker of subclinical cardiac dysfunction. Although 2-dimensional (2D) and 3D strains are different, it is unclear which is better.

Purpose: To compare the association of 2D and 3D GLS with cardiac anatomy, function, exercise capacity and the number of risk factors.

Methods: Using a commercially-available ultrasound system, both 2D and 3D echocardiography were performed in 345 (71±5yrs, 174 males) community-based patients with stage A heart failure. The 3D assessments were performed using a commercially available software. Exercise capacity was assessed by 6 minutes' walk distance (6MWD) and DASI score. Spearman's correlation coefficient was calculated and they were compared using z-transformation.

Results: Although 2D and 3D GLS were associated (r=0.34, p<0.0001), there was a bias of 1.8%, large limits of agreement (7.3%). Although 2D LV mass index was not associated with either GLSs (p=0.78, p=0.40), 3D LVMI was significantly correlated with 2D GLS only (p=0.03). 2D GLS was associated with exercise capacity (DASI, r=0.12; 6MWD r=0.039) but 3D GLS did not (p=0.79, p=0.15, respectively). Similarly, the number of risk factors was only correlated with 2D GLS (p<0.001).

Conclusion: 2D and 3D GLSs are discordant. The stronger correlation of 2D GLS with LV mass index, exercise capacity and risk factors suggests that it may be more accurate representation of LV function than 3D GLS.

P5431 | BESIDE
Early detection of myocardial injury by layer-specific strain imaging

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Background: The left ventricular wall of the heart comprises 3 myocardial layers, which differ obviously in cell structure, electrophysiological activity, blood perfusion and myocardial mechanics.

Purpose: This study aims to validate transmural strain gradient of myocardium measured by layer-specific strain imaging in different subjects.

Methods: Totally ninety-eight subjects were enrolled in this study, including 38 healthy people, 33 patients with cardiovascular risk factors but no coronary disease or heart failure (high-risk group) and 27 patients with heart failure. Using layer-specific strain imaging, peak longitudinal strain (PLS) and peak circumferential strain (PCS) of all three layers’ myocardium were measured in the three groups.

Results: The PLS and PCS of endo-, mid-, and epi-myocardium (PLSendo, PLSmyo, PLSepi; PCSendo, PCSmyo, PCSepi) decreased gradually in all three groups (all p<0.001). The PLS and PCS of all the three layers were significantly lowered in group with heart failure than in other two groups (all p<0.001).

Conclusion: There is significant difference in gradient of layer strain in three groups (healthy subjects > risk group > heart failure group).
were no significantly differences in PLSendo, PLSmid, and PCSSendo between healthy subjects and high-risk group. But the strain gradient among the three layers (PLSendo-myo, PLSmryo-epi, PLSSendo-myo, PCSSmyo-epi PCSSendo-epi) had statistically significant differences in three groups (healthy subjects > risk group > heart failure group) (all p < 0.001).

Conclusions: There is a gradient of myocardial strain in PLS and PCS, both of which decrease gradually in the order of endo-, mid- and epi-myocardial strain in all groups. Compared with peak myocardial strain, differences of gradient in layer strain are more sensitive to detect early myocardial injury than peak myocardial strain.

P5432 | BEDSIDE
The Association between Early Stage Renal Insufficiency, Subclinical Left Ventricular Systolic Dysfunction and Torsion in Asymptomatic Subjects
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Background: Recent studies have highlighted a strong link between chronic kidney disease and adverse cardiovascular outcomes, including heart failure. However, left ventricular (LV) structural and mechanical adaptations in relation to earlier stage renal insufficiency remain unclear.

Methods: We consecutively studied an asymptomatic population underwent annual cardiovascular survey. Transthoracic echocardiography with tissue Doppler, myocardial deformations (longitudinal and circumferential) and torsion were analyzed by 2D speckle-tracking. We categorized subjects into 4 groups based on estimated Glomerular Filtration Rate (eGFR): >90, 75–89, 60–74, and <60 ml/min/1.73 m².

Results: Of all 3,689 asymptomatic subjects (mean age 49.86±10.83, female 34.4%), we identified subjects with lower eGFR who had worse global and segmental longitudinal and circumferential strain, lower mitral annular relaxation velocity E’ across 4 groups (Table 1, all trend p < 0.001). There were also a trend toward longitudinal and circumferential functional decline (adjusted estimate: −0.5 ± 0.09 in multivariate models, both p < 0.05) though enhanced torsion (2.17±0.20, 2.27±0.24, 2.45±0.24, respectively) among 4 eGFR groups (all trend p < 0.001), with relatively preserved ejection fraction.

Conclusion: Both renal and cardiac functions may deteriorate in parallel prior to clinical symptoms onset with augmented torsion mechanics, which may result in unchanged global ejection fraction. Our study demonstrated that depressed myocardial deformations in early renal insufficiency may be compensated by augmented torsion to maintain global pump performance.

P5433 | BEDSIDE
Do deformation patterns reveal the underlying pathophysiology in hearts with thick walls?
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Purpose: To characterize subsets of ‘hypertrophied’ hearts with preserved ejection fraction (EF) and to link deformation patterns with underlying pathophysiology.

Methods: We included 22 patients with biopsy-proven cardiac amyloidosis (AM) (68±11 years, 70% male, 60% AL type) with EF ≥ 50%, 20 hypertrophic cardiomyopathy (HCM) patients (51±17 years, 70% male) and 20 normal volunteers. All subjects underwent cardiac magnetic resonance (CMR) with late gadolinium enhancement (LGE) within 15 days pre/post echo. Regional and global longitudinal (GLS), circumferential (GCS) and radial (GRS) strain indices along with left ventricular (LV) twist were calculated based on the two-dimensional (2D) speckle tracking data.

Results: EF was not significantly different among groups (63.7±8.7% in AM, vs 66.2±8.8% in HCM vs 65.2±5.2% in controls, p=0.684). AM patients had significantly lower strain components compared to HCM and controls (GLS: −12.7±3.5% vs −18±1.7%, GCS: −16.2±4.4% vs −21.5±5.3% vs −25±4.7%, GRS: 8±3±3% vs 14.6±4.4% vs 17.9±6.3%, p<0.005 for all comparisons). In contrast, LV twist was preserved (9.8±3.7° vs 10.3±3.3° in HCM vs 9.8±2.4° in controls, p=0.935). After qualitative assessment of MRI LGE patterns, we hypothesize that this strain-rotation discordance in AM patients is attributed to a predominant subendocardial amyloid deposition, sparing the function of subepicardial fibers, which are mainly responsible for systolic twist (Figure).

Conclusions: The strain-rotation discordance observed in amyloidosis can be explained by the layer-specific deposition of amyloid. Deformation imaging offers useful insights in the pathophysiology of the disease and may facilitate a better diagnostic differentiation between various entities of hypertrophic LV pathology without the need of EF.

Acknowledgement/Funding: 2014 European Association of Cardiovascular Imaging Research Grant

P5434 | BEDSIDE
Automated quantification of global left ventricular performance in patients with cardiac contractility modulation by speckle tracking imaging
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Purpose: Cardiac contractility modulation (CCM) is a potential novel therapy for advanced systolic heart failure with normal QRS duration. Clinical favorable effect has been observed including functional status, symptoms and exercise capacity. However, it remains unknown whether left ventricular (LV) geometry, function, and reverse remodeling will be improved. Therefore, we aimed to assess the information with comprehensive echocardiography with speckle-tracking imaging.

Methods: CCM was implanted in 37 patients (age 62±11 years; 87% male) who had ejection fraction (EF) <35%, New York Heart Association (NYHA) Class III symptoms and QRS <120ms. Two-dimensional echocardiographic was performed (GE Vingmed Ultrasound AS, Horten, Norway) before and 12 months after CCM therapy to measure LV volumes and LV mass. LV global longitudinal strain (GLS) was assessed with automated function imaging (AFI).

Results: At 12-month follow up, the LV end-systolic volume (ESV) (136±54 vs 114±58 ml, P<0.001) (Fig. 1A) and the LV mass (240±72 vs 221±64 g, P<0.003) (Fig. 1B) were decreased significantly, and was accompanied by a significant gain in LV EF (28.1±7.7% vs 36.7±9.7%, P<0.001) (Fig. 1C). Furthermore, GLS increased significantly at 12 months (7.0±2.4% vs 8.0±3.0%, P<0.042) (Fig. 1D).

Fig. 1. Bar charts for illustrating the pre- & post-CCM therapy change of (A) left ventricular end-systolic volume (LVEVS); (B) LV mass; and (C) ejection fraction (LVEF) and (D) global longitudinal strain (GLS), respectively.

Conclusions: Advanced HF patients with normal QRS duration could benefit from CCM therapy with improvement in LV remodeling as evident by the reduction in LV mass and LV volume. LV function was significantly improved with increase of both LV ejection fraction and LV GLS.

P5435 | BEDSIDE
Apical variant Takosu-tubo is associated with persistent myocardial strain dysfunction

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Purpose: Apical variant Tako-tsubo is associated with persistent myocardial dysfunction (LGE) within 15 days pre/post echo. Regional and global longitudinal (GLS), circumferential (GCS) and radial (GRS) strain indices along with left ventricular (LV) twist were calculated based on the two-dimensional (2D) speckle tracking data.

Results: EF was not significantly different among groups (63.7±8.7% in AM, vs 66.2±8.8% in HCM vs 65.2±5.2% in controls, p=0.684). AM patients had significantly lower strain components compared to HCM and controls (GLS: −12.7±3.5% vs −18±1.7%, GCS: −16.2±4.4% vs −21.5±5.3% vs −25±4.7%, GRS: 8±3±3% vs 14.6±4.4% vs 17.9±6.3%, p<0.005 for all comparisons). In contrast, LV twist was preserved (9.8±3.7° vs 10.3±3.3° in HCM vs 9.8±2.4° in controls, p=0.935). After qualitative assessment of MRI LGE patterns, we hypothesize that this strain-rotation discordance in AM patients is attributed to a predominant subendocardial amyloid deposition, sparing the function of subepicardial fibers, which are mainly responsible for systolic twist (Figure).

Conclusions: The strain-rotation discordance observed in amyloidosis can be explained by the layer-specific deposition of amyloid. Deformation imaging offers useful insights in the pathophysiology of the disease and may facilitate a better diagnostic differentiation between various entities of hypertrophic LV pathology without the need of EF.
LV twists mechanics at one month follow-up. In this work we comprehensively analysed myocardial deformation by 2D strain analysis at presentation and 4 months follow-up in a subgroup of apical TTC who presented predominantly with ST-elevation ECG.

Methods: Twenty patients (93% F, 66±12 years) with apical ballooning subtype of TTC fulfilling the Mayo criteria were studied within 3 days of presentation and after 4 months. Twenty-five age and gender matched controls (92% F, 65±11 years) underwent single echocardiographic assessment. Two-D strain, strain rate and twist mechanics were calculated.

Results: As shown in the Table, from acute presentation to follow up LVEF, global longitudinal peak systolic strain (GLPS), apical radial and apical circumferential strain improved significantly in TTC patients (p<0.001, p=0.001 and p=0.012 respectively). At follow up, LVEF normalized and was no longer different from controls (p=0.639). In contrast, GLPS and early diastolic relaxation (untwist rate) remained significantly impaired compared to controls at follow-up (p=0.006 and p=0.022, respectively).

<table>
<thead>
<tr>
<th></th>
<th>TTC acute (n=20)</th>
<th>TTC follow-up</th>
<th>p paired t test between acute and follow-up</th>
<th>Controls (n=25)</th>
<th>p unpaired t test between TTC follow-up and controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>EF, %</td>
<td>44±23±1.3</td>
<td>63±5.7±3.3</td>
<td>&lt;0.01**</td>
<td>64±5.6±5</td>
<td>0.658</td>
</tr>
<tr>
<td>GLPS, %</td>
<td>-10.6±3.8</td>
<td>-16.0±3.0±2.5</td>
<td>&lt;0.01**</td>
<td>-18.3±2.1</td>
<td>0.006</td>
</tr>
<tr>
<td>Rad S - apex, %</td>
<td>15.0 (7.2–19.6)</td>
<td>34.0±19.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Circ S - apex, %</td>
<td>-11.7±3.8</td>
<td>-18.1±5.6</td>
<td>&lt;0.012</td>
<td>-20.3±4.1</td>
<td>0.145</td>
</tr>
<tr>
<td>Twist rate, °/s</td>
<td>10.6±7.5</td>
<td>15.2±5.7</td>
<td>0.444</td>
<td>15.2±5.6</td>
<td>0.408</td>
</tr>
<tr>
<td>Untwist rate, %</td>
<td>-71.3±38.9</td>
<td>-74.6±34.1</td>
<td>0.901</td>
<td>-99.7±38.9</td>
<td>0.022</td>
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</table>

Conclusion: In apical variant TTC presenting with predominantly ST-elevation on ECG global systolic deformation and early diastolic relaxation abnormalities persist following the acute event despite normalization of LVEF.

PS543 | BEDSIDE

Angiotensinogen gene M235T and T174M polymorphisms in systolic heart failure: changes of the left ventricular strain during six-month spironolactone therapy

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The aim of our study was to assess whether angiotensinogen (AGT) gene M235T and T174M polymorphisms affect response to the treatment with spironolactone. For this purpose we evaluated left ventricular longitudinal, circumferential and radial strain assessed by 2-dimensional speckle-tracking echocardiography (2DSTE) in patients (pts) with systolic heart failure.

Methods: We enrolled 39 pts (mean age 64 years) in stable state and NYHA class II or III. Mean left ventricular ejection fraction (LVEF) was 37.4%. All pts received an optimal HF therapy. Two-dimensional global longitudinal, circumferential, and radial strain were measured in each patient before starting spironolactone therapy and then after one- and six-months. Circumferential and radial strain was measured at three levels: mitral valve, papillary muscles and apex. Results: T235T allele of the AGT gene was found in 9 pts (23.1%). No carriers of the T174T allele of the AGT gene were found in the studied group. Serum aldosterone levels exceeded upper reference values (26 ng/ml) in 16 pts (41%) at baseline. LVEF increased insignificantly during the study (baseline – 37%, 1 month – 38.6%, 6 months – 39%; p=0.51). 2DSTE analysis showed significant improvement of the longitudinal, radial, circumferential and radial strain parameters (average global longitudinal strain showed in the table). The analysis of a correlation between the presence of T235T allele and increased aldosterone plasma levels showed significant relationship for the radial strain in the middle level (papillary muscles) of the left ventricle only.

Global longitudinal strain

<table>
<thead>
<tr>
<th></th>
<th>Global longitudinal strain</th>
<th>%</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>-11</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>1 month</td>
<td>-14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>-14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Left ventricular strain parameters are good indicators of improvement in left ventricular function during the treatment with spironolactone. Presence of T235T polymorphism in AGT gene does not seem to affect the response to treatment with spironolactone in patients with systolic heart failure.

PS543 | BEDSIDE

Early detection of chemotherapy induced biventricular cardiac dysfunction after bone marrow transplantation by speckle tracking echocardiography

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Purpose: The aim of this study was to detect chemotherapy induced cardiotoxicity on left ventricular (LV) and right ventricular (RV) performance, in patients early after bone marrow transplantation for hematologic malignancy, by means of both conventional and novel echo techniques.

Methods: We studied 28 patients (mean age 46±10 years, 14 men), admitted for bone marrow transplantation because of non-Hodgkin lymphoma, acute myelocytic or lymphocytic leukemia, multiple myeloma. Patients had preserved LV ejection fraction (LVEF) of >50%, without evidence of cardiac disease. We measured a) LV global (LVGLS-%) subendocardial and subepicardial strain and global strain (LVGLSR-%), RV longitudinal strain (RVGLS-%), LV circumferential strain-%, LV torsion by speckle tracking b) three-dimensional derived LV and RV ejection fraction (3DLVEF-%, 3DRVEF-%) c) tricuspid annulus plane systolic excursion (TAPSE-mm), and RV fractional area change (FAC-%) by two dimensional echocardiography and TDI derived lateral tricuspid annulus systolic velocity (S RV-ccm). Studies were performed before (baseline) and 1 and 3 months after a chemotherapy session followed by transplantation.

Results: Compared to baseline, LVEF and 3D LVEF did not change at 1 and 3 months post-chemotherapy (LVEF 58.9±6 vs 56.4±5 vs 56.5±5 respectively P=0.05, 3D LVEF 57.5±5 vs 57.2±5 vs 56.6±5 respectively P=0.05). However compared to baseline, impaired LVGLS and LVGLSR values were observed at 1 and 3 months (LVEF 19.6±3 vs 18.2±3 vs 17.4±2.5 respectively, P=0.01 respectively). Myocardial layers deformation analysis, indicated that LVGLS changes were driven mostly by subendocardial longitudinal strain changes observed from month 1 post chemotherapy, whereas subepicardial GLS changes were observed at month 3 post-chemotherapy (subendocardial LVGLS 22.2±9 vs 20.1±2.8 vs 19.4±3.2 P=0.02 respectively, subepicardial LVGLS 17.5±2.8 vs 16.7±2.3 vs 15±2.3 P=0.07 P=0.02 respectively). No significant changes in LV circumferential strain and torsion were detected. RV TAPSE, FAC, S RV and 3DRVEF did not change post-chemotherapy. Compared to baseline, RVGLS was impaired post-chemotherapy (RVGLS 22.4±2.5 vs 20.1±2.8 vs 20.3±2.5 P=0.02 P=0.03 respectively).

Conclusion: Despite absence of alterations in cardiac performance assessed by conventional echo parameters and 3D echocardiography, speckle tracking imaging detects early subclinical dysfunction of both ventricles in bone marrow transplantation patients.

PS543 | BEDSIDE

Assessment of left ventricular dyssynchrony and prediction of response to cardiac resynchronization therapy: a new three-dimensional echocardiography integral-based indicator of longitudinal strain


Background: So far, all attempts to improve patient selection for cardiac resynchronization therapy (CRT) by echo-derived mechanical dyssynchrony indices have failed. The aim of this study is to assess the performances of a new software for automatic quantification of integrals 3D regional longitudinal strain signals, combining temporal and functional information to explore left ventricular (LV) mechanical dyssynchrony and to assess its potential value to predict CRT response.

Methods: 48 heart failure patients in sinus rhythm, referred for CRT device implantation (mean age: 65 years; LV ejection fraction: 26%; QRS duration: 160 milliseconds [160–170] were prospectively assessed. 34 pts had positive response defined as LV end-systolic volume decrease ≥15% at 6-month. 3D longitudinal strain curves were exported for analysis by custom-made algorithms. The integrals of longitudinal strain signals were automatically measured and calculated for all 17 LV segments from the beginning of the cardiac cycle to the instant of the corresponding longitudinal strain peak (IL, peak).

Results: The standard deviation of IL, peak (SDIL, peak) for all 17 LV segments was larger in CRT responders than non-responders (1.18% ±1 [0.96; 1.35] versus 0.82% ±1 [0.55; 0.99], p=0.007, SDIL, peak (odds ratio [OR]: 12.1; 95% CI: 3.81–180, p=0.001) and septal flash (OR: 14.1; 95% CI: 3.08–64.9, p=0.001) were the only potential echocardiographic predictors of CRT response. The optimal cut-off value of SDIL, peak to predict response was 1.037% s –1. In the 18 patients without septal flash, SDIL, peak was significantly higher in CRT responders.

Conclusion: This new automatic analysis software of 3D longitudinal strain curves might be helpful to improve prediction of CRT response.
PS439 | BEDSIDE
Alterations of phase specific left atrial strain in patients with pre-clinical diastolic dysfunction: 2D speckle tracking echocardiography-derived results from the BEFRI-echo study
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Background: Pre-clinical diastolic dysfunction (DD), defined by DD without signs of 7.6% in women with subclinical left ventricular (LV) diastolic dysfunction, but not associated with adverse outcome and identifies patients at high risk to develop heart failure with preserved ejection fraction (HFpEF). 2D speckle tracking analysis (STE)-derived data concerning changes of LA function in DD are scarce.

Purpose: We analysed echocardiographic data of a well-phenotyped cohort from the Berliner Frauen Risikoevaluation (BEFRI) study to assess changes of LA function in preclinical DD.

Methods: Transthoracic echocardiography (Vivid E9, GE) was conducted in 449 female subjects of the BEFRI trial. Diastolic function was graded according to the recommendations of the EAE/AES (DD0: healthy, DD1 impaired relaxation, DD2: pseudonormalisation). Standard apical 4-chamber views were recorded, and LA analysis was performed using 2D STE (EchoPAC PC, GE Vingmed). Different phases of LA strain were identified: peak systolic strain (=LA reservoir function, LAR), strain during conduit phase (LAC), and strain during peak atrial contraction (LAa). LA conduit function was determined by (LAR – LAC), and LA pump function by (LAC – LAa). Differences of phasic LA strain were calculated using the Mann-Whitney-U test. To compare the diagnostic value for DD, linear regression analysis and ROC analysis were conducted for LA strain and LA volume index (LAVI).

Results: 289 women were classified to DD0, 135 to DD1, and 25 to DD2. LA strain and conduit function were significant predictors of DD (p<0.001), and were markedly attenuated in the presence of DD (reservoir/conduit function in DD0, DD1, and DD2, respectively: 43.1±27.2%, 33.1±6%, and 28±14.7%, p<0.01). This reduction was already significant in women with DD1, a mostly asymptomatic subgroup without LA enlargement, rises in filling pressures (E/E’) or BNP. LA pump function was significantly higher in patients with DD1 (19%) compared to DD0 (14.6%, p<0.05). In ROC analysis, LA reservoir and conduit functions were superior to LAVI in diagnosing DD (sensitivity of LAR and conduit function 91.0%, specificity 85.6%, and positive predictive value 95.0%).

Conclusion: All three LA phases show specific alterations with progressive stages of DD. Analysis of LA function is more sensitive in diagnosing early stages of DD compared to established parameters of LA enlargement. LA strain is easy to measure, and allows early diagnosis of DD, a recognised predisposing factor of HFpEF.

PS440 | BENCH
Subclinical IV systolic dysfunction in patients with chronic obstructive pulmonary disease
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Background: Patients with chronic obstructive pulmonary disease (COPD) can have left ventricle (LV) systolic dysfunction due to several reasons. We investigated subclinical LV systolic dysfunction in patients with COPD, and its correlation with the severity of airway obstruction, identified by GOLD classification.

Methods: We studied 52 patients with COPD and 29 age and sex-matched controls, without any cardiac disease and with preserved LV EF. Conventional echocardiography and speckle tracking echocardiography (STE) based strain imaging were performed to analyze sub-clinical LV systolic function. All patients underwent spirometry.

Results: Conventional echocardiographic measurements (LV end diastolic diameter, LV end systolic diameter, LV mass index) were similar between the groups. LV longitudinal peak systolic strain (14.7±6.2%/20.7±7.1%, p<0.001) and strain rate (0.75±0.25 1/s to 1.31±0.41 1/s, p<0.0001) were significantly impaired in patients, compared to controls, demonstrating sub-clinical ventricular systolic dysfunction. Significant positive correlation was obtained between LV strain/strain rate and spirometry parameters (FEV1, FVC, FEV1/FVC, PEF%) (r=0.78, p=0.001; r=0.83, p=0.001; r=0.74, p=0.001, respectively). Also there was significant negative correlation between LV strain/strain rate and GOLD classification (r=−0.80, p<0.001, respectively).

Conclusion: COPD can affect systolic functions in patients without known CAD. STE is a technique which provides additional information for detailed evaluation of subtle changes in LV myocardial contractility, significantly associated with the severity of the disease in COPD patients.

PS5441 | BEDSIDE
Subclinical left ventricular dysfunction on echocardiography predicts long-term adverse events
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Background: Abnormal systolic or diastolic tissue Doppler parameters may occur despite normal left ventricular ejection fraction (LVEF). We investigated long term value of tissue Doppler imaging (TDI) in predicting cardiac events in patients with no history of heart disease and normal LVEF.

Methods: Subjects who underwent echocardiogram in our institution from 2002 to 2003 were included. They were aged 55 to 64 years, with no history of ischaemic heart disease, heart failure or structural heart disease and LVEF of >50%. TDI for this age group was divided into normal and abnormal according to published values. The composite primary endpoint (major adverse cardiovascular events, MACE) includes occurrence of myocardial infarction, coronary revascularization or congestive heart failure over a 10-year follow-up period.

Results: Of the 428 patients studied, 398 had normal TDI values while 30 patients had reduced mitral annular (septal or lateral) E’ or S’. Although there was no significant difference in age between the 2 groups, patients with abnormal TDI had significantly lower LVEF and lower early diastolic trans-mitral flow velocities (Table). E’/E ratios were also higher in patients with abnormal TDI (Table). MACE was observed in 49 patients (12.3%) in patients with normal TDI while MACE occurred in 26.7% of patients with abnormal TDI (p<0.001). Table. Reduced TDI E’ or S’ was associated with significant MACE (Kaplan Meier log rank = 5.77, P=0.016).

Table 1

<table>
<thead>
<tr>
<th>Normal TDI (n=398)</th>
<th>Abnormal TDI (n=30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.0±12.9</td>
<td>58.9±2.7</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>65.2±4.0</td>
<td>63.1±5.4</td>
</tr>
<tr>
<td>Mitral E (m/s)</td>
<td>71.8±16.1</td>
<td>62.0±16.6</td>
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<tr>
<td>DT (ms)</td>
<td>191.2±38.2</td>
<td>190.8±35.4</td>
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<td>IVRT (ms)</td>
<td>80.6±17.3</td>
<td>85.7±15.3</td>
</tr>
<tr>
<td>E/E’</td>
<td>3.9±2.5</td>
<td>7.4±2.0</td>
</tr>
<tr>
<td>Septal S’ (m/s)</td>
<td>8.9±1.9</td>
<td>6.9±1.7</td>
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<tr>
<td>Lateral E’ (m/s)</td>
<td>12.1±2.9</td>
<td>9.1±3.0</td>
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<tr>
<td>Septal E’ (m/s)</td>
<td>6.6±2.8</td>
<td>7.6±1.9</td>
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<tr>
<td>Septal E/E’</td>
<td>7.8±2.2</td>
<td>8.6±2.2</td>
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<tr>
<td>Lateral E/E’</td>
<td>6.1±1.7</td>
<td>7.3±2.3</td>
</tr>
<tr>
<td>MACE (+)</td>
<td>49 (13.3%)</td>
<td>8 (26.7%)</td>
</tr>
<tr>
<td>MACE (−)</td>
<td>349 (87.7%)</td>
<td>22 (73.3%)</td>
</tr>
</tbody>
</table>

Conclusion: Subclinical left ventricular dysfunction predicts long term MACE. Acknowledgement/Funding: No financial disclosures

PS4442 | BENCH
Left ventricular flow redirection towards the outflow tract: a marker for atrio-ventricular delay optimization
D. Rodriguez Munoz, C. Lozano Granero, A. Carbonell San Roman, J.L. Moya Mur, C. Fernandez-Golfin, E. Casas Rojo, A. Garcia Martin, S. Fernandez Santos, J. Moreno Planas, J.L. Zamorano Gomez. University Hospital Ramon y Cajal, Department of Cardiology, Madrid, Spain

Introduction: Different echocardiographic algorithms have been defined to optimize atrio-ventricular delay (AVD) in cardiac resynchronization therapy (CRT). Doppler-based techniques are commonly used, but slight changes in the position of the probe or the patients’ breath can lead to error and inaccuracies. Vector Flow Mapping (VFM) enables visualization of complex intracardiac flow patterns, allowing display and measurement of intracardiac vortices. Vortices are known to play a key role in left ventricular (LV) flow redirection towards the outflow tract, contributing to early ejection and minimising energy dissipation.

Methods: CRT patients in sinus rhythm underwent echocardiographic AVD optimization to compare concordance between trans-mitral flow optimization and vortex-flow guided optimization. VFM-based optimal AVD was considered the one in which the flow curve generated by the vortex was continued by the aortic ejection flow curve (Fig. 1, Panel B). Optimal AVD by trans-mitral flow was considered the one with the shortest interval in which A-wave truncation was not observed. Results obtained with the two methods were compared using intraclass correlation coefficient (ICC).

Results: 12 patients (25% male, aged 68±10.5, LVEF 40±2.10.3) underwent...
conventional trans-mitr al and vortex-flow based optimization. ICC showed excellent concordance between the two techniques (0.94, CI [0.82–0.98], p < 0.0005). Additionally, VFM-based optimal AVD calculation was faster then Doppler trans-mitral calculation (3.0±0.6 vs. 4.9±1.4 measurements, p < 0.05).

Conclusions: AVD optimization guided by the optimization of the vortex-ejection flow curve is feasible and accurate. Additionally, it requires less repeated measurements than standard optimization guided by trans-mitral Doppler.

P5443 | BEDSIDE
Disturbed flow transit in heart failure with a history of decompensation
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Background: The transition from diastole to systole is not a mere shift between the two distinct phases, but rather a continuous process in which intra-cardiac flows form vortices which help direct flows toward the outflow. This smooth flow transition may contribute to the pump efficiency. We hypothesised that analysing flow transition can provide a new window for assessing left ventricular (LV) performance.

Methods: The present study examined 35 clinically stable patients with dilated cardiomyopathy (62±15 years old). LV ejection fraction = 33±12%, ischaemic aetiology = 14 patients), including 15 patients with a history of decompensation and 20 patients without it. Blood transport inside the LV was visualised by tracking virtual ink tracers added over the diastole, using Vector Flow Mapping (Hitachi-Aloka, Tokyo). The amount of ink ejected in the following systole was quantified as direct flow ratio (DFR) = the amount of ink ejected in the following systole/the total amount of ink added over the diastole. LV global longitudinal and circumferential strains (GLS and GCS) were evaluated with speckle tracking. LV filling pressure was assessed by E/E'.

Results: DFR was correlated positively with stroke volume (r=0.49, p<0.003), GLS (r=0.73, p<0.001) and GCS (r=0.63, p<0.001), but not with E' (p=0.09) and E/E' (p=0.20). Patients with a history of decompensation had lower DFR than those without it (0.24±0.20 vs 0.48±0.18, p=0.001). ROC curve analysis revealed that DFR had a higher predictive value for the decompensation than GLS, GCS, stroke volume, E' and E/E'.

Conclusion: Flow transit is disturbed, although clinically stable, in heart failure patients with a history of decompensation.

CELL THERAPY AND BIOENGINEERING

P5444 | BENCH
Post-infarct administration of multilineage-differentiating stress-enduring (Muse) cells regenerates cardiomyocytes and microvessels and improves cardiac function and remodeling in rabbits
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Background: It has been reported that the mesenchymal stem cell (MSC) fraction in bone marrow aspirates contains pluripotent stem cells, Muse cells, which can self-renew and differentiate into cells with the characteristics of all three germ layers from a single cell. We investigated whether intravenously administered Muse cells could be mobilized to the ischemic myocardium, decrease the myocardial infarct size, and improve the cardiac function, comparing with the effects of MSCs.

Methods: Bone marrow (~2 mL) was harvested from the cavity of the femurs in male Japanese white rabbits. Bone marrow MSCs were cultured and expanded, and then Muse cells were isolated by FACs as SSEA-3(+) cells. In a 30-minute coronary occlusion and reperfusion rabbit model, 3x100000 of autologous Muse cells labeled with GFP (Muse group, n=10), saline (control group, n=10), 3x100000 of autologous MSC cells (MSC group, n=10), or 3x100000 of autologous non-Muse cells (non-Muse group, n=10) were intravenously infused at 24 hours after MI. The MI size, cardiac function, and general pathology of the heart were evaluated at 2 weeks post-MI. Confocal microscopy was performed to evaluate the regeneration of the myocardium.

Results: The MI size as a percentage of LV by Masson trichrome staining was significantly smaller in the Muse group (14.1±1.3%) than in the control group (31.7±1.3%), MSC group (21.7±1.3%), and non-Muse group (23.0±1.8). A smaller infarct size, smaller left ventricular (LV) dimensions, increased LV ejection fraction, and increased ±dP/dt were seen in the Muse group as compared with the other groups at 2 weeks post-MI. The number of CD31-positive microvessels was significantly greater in the Muse group than in the other groups. Transplanted Muse cells were preferentially attracted to the infarct border area in the ischemic area. Integrated GFP (+)-Muse cells were positive for ANP, a specific marker for neonatal cardiomyocytes, and troponin I, a specific marker for cardiomyocytes, suggesting the spontaneous differentiation of cardiomyocytes and microvessels from Muse cells.

Conclusions: The post-infarct administration of Muse cells reduces the myocardial infarct size and improves cardiac remodeling and functioning through the regeneration of cardiomyocytes and microvessels to a greater extent than MSCs. Muse cell transplantation may be a promising strategy for acute MI-targeting treatment.

P5445 | BENCH
A novel cardiac bioprosthesis for myocardial repair
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Purpose: Cardiac tissue engineering, a novel therapeutic approach, combines the use of natural or synthetic supporting scaffolds with cardiomycogenic cells for myocardial damage restoration. In this context, we aimed to obtain a myocardial bioprosthesis based on decellularized myocardium refilled with adipose tissue-derived progenitor cells (ATDPCs).

Methods: Decellularized myocardial scaffolds were generated from porcine myocardium using two distinct decellularization protocols (DP): one protocol, named DP1, was detergent-based (SDS and Triton X-100), and the other, termed DP2, was trypsin based. Decellularization level was evaluated histologically and molecularly; the resulting scaffolds were examined by scanning electron microscopy and matrix components were identified by immunohistochemistry. Obtained decellularized scaffolds were refilled with RAD16-I peptide hydrogel and porcine ATDPCs. After one week of recellularization, cellular viability was assessed using a commercial kit, cell density was determined by nuclei counting and expression of cardiac (GATA4, connexin43 and cardiac troponin T) and endothelial (Isolectin B4) markers was analyzed through immunohistochemistry. Results: After both protocols were finished, decellularized scaffolds were free of cellular debris and nuclear material, with a significant DNA content reduction of ~90% compared to native myocardium (P<0.001). Decellularized myocardial scaffolds also preserved extracellular matrix main components, and its three-dimensional architecture and ultrastructure were retained once decellularization was completed. One week following recellularization, ATDPCs were detected inside the decellularized scaffold and remained viable. However, in recellularized DP1 scaffolds the number of retained cells was significantly higher compared with recellularized DP2 scaffolds (236±106 and 98±56 cells/mm² for recellularized DP1 and DP2 scaffolds, respectively; P=0.04). Remarkably, in both recellularized scaffolds, ATDPCs expressed endothelial marker Isolectin B4, although only in recellularized DP1 scaffolds cells showed expression of cardiac markers GATA4, connexin43 and cardiac troponin T.

Conclusions: Acellular myocardial scaffolds, with preserved structure and matrix composition, were obtained with both decellularization protocols. However, in our hands, the detergent-based protocol (DP1) produced myocardial scaffolds with better cell recolonization and promoted ATDPCs expression of endothelial and cardiomycogenic markers, which suggests ATDPCs differentiation towards cardiac-like lineage in DP1 scaffolds.
Survival, migration and benefits of human cardiac progenitor cell seeded-collagen patches applied on failing right ventricle: preliminary results in a large animal model

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Background: Cell therapy using intramyocardial injections of cardiac progenitors issued from human embryonic stem cells showed benefits on overloaded right ventricular (RV) tissue remodelling and arrhythmic susceptibility but this delivery method failed to improve RV function.

Purpose: Our aim was to evaluate in a porcine model of overloaded RV dysfunction a new cell delivery mode for such a therapy.

Methods: A combined overloaded RV dysfunction was obtained in piglets using a surgical procedure mimicking repaired tetralogy of Fallot. After 4 months, cell therapy was surgically administrated using 2 types of human NKX2.5+ cardiac progenitor cell-seeded collagen patches applied on the epicardium: QGEl® and pressured-patches. Myocardial function was measured 1 month after transplantation by conductance catheter technique and echocardiography (standard and strain). The fate of progenitors was studied using antibodies directed against Nkx2.5, CD31, actin and islet1.

Results: All pigs survived without any complication. Pressured-patches allowed human progenitors to migrate towards the myocardium while QGEl® patches redirected cell migration. In both cases, progenitors differentiated toward the cardiac lineage assessed by actinin expression and maintained their proliferation capacity. Concerning RV function, only pressured-patches (N=3) tended to improve the contractility (Emax slope). By contrast, this parameter decreased in QGEl® patched animals (N=2). Moreover, in 2 pressured-patch animals, standard echocardiographic functional parameters (FAC, TAPSE, s’wave) were maintained while 2D strain and strain rate values increased.

Conclusion: Cell therapy using seeded-patches was more conservative for engraftment than intramyocardial injections but only pressured-patches seemed to give benefits on overloaded RV function and contractility. These promising results require further improvement in the design of the cell patch and to be confirmed on a long-term basis.

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Effects of cardiac stem cells in myocardial infarction; meta-analysis of preclinical studies

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Background: Cardiac stem cell therapy has emerged as a promising approach for cardiac repair after myocardial infarction (MI). Different populations of cardiac-derived stem cells (CSCs) have been tested in animal models of MI, and although CSC clinical trials have already started it is unclear what the consistent effect is in experimental models.

Aim: Here we used meta-analysis to establish the overall effect size of CSCs in preclinical studies. We investigated whether small and large animal models have similar outcomes after CSC-injection. Next, we explored the influence of clinically relevant parameters to better predict and design future (pre)clinical studies using CSCs for MI.

Methods: We performed a systematic search of PubMed and Embase on Nov. 5th to identify all publications describing control-group based experiments of CSC therapy in animal models of MI. We determined the overall effect of CSC therapy on our primary endpoint; left ventricular ejection fraction (LVEF). We performed meta-regression analysis to investigate if clinically relevant parameters were of influence on LVEF; these parameters included animal type (large and small), cell type (cardiospheres/cardio-sphere-derived cells (Cs/CDCs), c-kit+ cells and sca1+ cells), immunosuppression, cell structure in culture and administration (2D vs 3D) and donor specifics (comorbidity and allogeneity). We also assessed the quality of the included studies. Possible publication bias was assessed using Egger regression, funnel plot and Trim and Fill analysis.

Results: We identified 64 relevant studies, reporting 1648 animals (993 treated, 655 controls). The overall effect of CSCs was an 11.1% (95% CI 9.6–12.6 p = 0.001) improvement of LVEF compared to controls. Interestingly, CSC therapy had a greater effect in small animals compared to large animals 11.4% (95% CI 10.2–12.6) vs 7.0% (95% CI 3.0–11.0), respectively (p = 0.039). Cell type was a significant predictor for LVEF improvement; Cs/CDCs (12.6%, 95% CI 11.0–14.2%), c-kit+ cells (6.2%, 95% CI 5.2–7.2%) and sca1+ cells (8.5%, 95% CI 5.6–11.3) (p = 0.035). None of the other parameters were predictors of primary outcome. No publication bias was observed.

Conclusion: Treatment with CSCs resulted in a significant improvement of LVEF in all animal models of MI. There was a reduction in the magnitude of effect in large compared to small animal models, a trend that seems to continue in recent clinical trials. Although different CSC types have overlapping characteristics, we observe a significant difference in their effect in animal MI studies.

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etn2 mRNA levels increased in hESC-EC when differentiated via EB method (EB in normoxia 353.17±86.29; EB in hypoxia 323.89±86.63, monolayer 27.20±9.92 vs. hESC, p < 0.001). Expressions of arterial (EphrinB2, Notch-1) and venous (EphB4) endothelial markers were increased, suggesting the presence of mixed endothelial population in culture. However, no significant differences were found in ratio of arterial and venous subpopulations in the different developmental protocols. For engineering 3D vascular constructs decellularized human aortic slices (300x μm) were repopulated with hESC-EC and hiPSC-EC and cells remained viable on engineered matrices in vitro. Engineered bioscaffold were incubated with platelet rich plasma from healthy adults. 3D culture conditions activated anti-apoptotic effects of the cells (as shown by secretion levels of chemokine Rantes (pg/ml): hESC-EC 229.6±37.9, hESC-EC on bioscaffold 83.6±52.1; hiPSC-EC 234.9±22.8, hiPSC-EC on bioscaffold 127.9±83.6, p < 0.01, n=6). Conclusion: Conditions more closely resembling normal human development and angiogenic gene expression. 3D culturing increased antiapoptotic effects. Functionally active endothelial derivatives of human pluripotent stem cells promises vascular tissue engineering for therapeutic purposes.

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CARDIOVASCULAR PATHOLOGY AND STEM CELLS

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Erythropoietin promotes cardiac autonomic dysfunction and does not modify end diastolic pressure in a myocardial infarction model in rats

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Background: The administration of erythropoietin (EPO) after myocardial infarction (MI) has been used to reduce myocardial infarct size and to improve cardiac function. Most of the evidence was obtained in short term after MI and the mechanisms involved in this improvement are not well known.

Purpose: To evaluate EPO effects on autonomic and hemodynamic parameters in an experimental model of chronic myocardial infarction.

Methods: Wistar rats were divided in three groups: control (C: n=9); infarcted (MI: n=9) and infarcted treated (EPO) rats (EM: n=9). EPO was administered (1000IU/kg) 3 days on week for 12 weeks. MI was induced by coronary occlusion. The animals were catheterized for direct blood pressure recording. Heart rate (HR), heart rate (HRV) and systolic blood pressure variability (SBPV) as well as end-diastolic pressure were evaluated.

Results: There were no differences in the HR values between the groups (C = 336.5±6.82, MI = 353.7±8.0, EM = 353.3±1.26; p < 0.05). Mean Arterial Pressure was significantly higher in EM group compared to MI and control groups (C = 104.3±1.09, MI = 94.7±0.54, EM = 126.2±1.05 mmHg). Regarding HRV, pulse interval variance was lower in infarcted groups (MI and EM) in comparison with control (C = 17.1±1.3, MI = 46.0±1.0, EM = 51.4±1.5 mHz). Moreover, low and high frequency components of HRV were lower in EM group when compared to MI and control group (C = 27.3±1.1, MI = 17.3±5.57, EM = 6.7±0.36; C = 76.2±1.48, MI = 82.4±5.07, EM = 48.0±8.1) suggesting a marked reduction of HRV in the MI group at low frequency range. The SBPV was higher in the EM group compared to MI and control groups (VAPAS: C = 2.4±0.54, MI = 2.5±0.45, EM = 3.8±0.70 mmHg). In addition, the end-diastolic pressure (EDP) values of the left ventricle were higher in infarcted groups (MI and EM) than in control group (C = 4.2±3.2, MI = 10.5±0.2, EM = 9.6±0.2 mmHg).

Conclusions: The EPO administration in MI rats increased MAP and promoted autonomic dysfunction evidenced by decreased HRV and increased SBPV. Moreover no improvement was observed in EDP.

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P5451 | BENCH

Single-centre experience with 3D printing cardiac anatomy: feasibility and controversies

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Background: Patient-specific models of cardiac anatomy, and congenital heart disease (CHD) in particular, manufactured by means of rapid prototyping (3D printing) could facilitate communication between patients (and their families) and cardiologists, and improve patients` comprehension of their condition, with favorable repercussions on lifestyle adjustments. Albeit anecdotal evidence suggests that 3D models hold great promise for studying, interpreting and explaining cardiac anatomy, systematic testing is lacking.

Purpose: To evaluate patients’, parents’ and cardiologists’ perspectives on the feasibility of using 3D models in clinical practice.

Methods: Patients were administered to 97 patients of children with CHD and to their cardiologists during follow-up visits. Patients were divided into Group1 (n=52, normal consultations) and Group2 (n=45, with 3D models from magnetic resonance imaging printed with rapid prototyping technology additionally used). Participants and cardiologists completed ratings (0–10) to assess parental knowledge before and after the consultation. Both users (expert and non-expert) provided feedback on 3D models as communication tools. Moreover, 2 focus groups (n=13 teenagers with CHD, n=15 parents) explored features of 3D models, such as material options (rigid vs. compliant, white vs. colorful, transparent vs. opaque).

Results: Cardiologists rated models as “very useful” (8.8±1.1/10), stimulating parent interaction (9.1±1.4/10) without lengthening consultation time (93% cases), although consultations with models lasted 5 minutes longer (p=0.02). Parents also rated models as “very useful” (9.5±0.7/10) and more informative than medical images or diagrams. Generally parents self-reported improved understanding following their visits, however in 40% of cases two blinded cardiologists who re-analyzed the questionnaires were not able to gather even the primary diagnosis based on the information provided by patients, identifying a major knowledge gap. The focus groups highlighted that patients and parents found transparent models helpful in elucidating a specific defect and generally agreed that red-and-blue models are more familiar and descriptive.

Conclusion: Clinicians found 3D models useful in describing congenital defects. Models encouraged expert/non-expert users interaction. Employing this modality may stimulate patients’ and parents’ participation, as they appreciated the technology. Short-term parental knowledge, however, did not improve, highlighting the importance of further systematic testing alongside with regulatory work.

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Insights into the anatomical sites of acute left atrial appendage reconnection after successful electrical isolation

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Introduction: The left atrial appendage (LAA) is reported to be a common trigger site in atrial fibrillation (AF). Due to the non-uniform ostial anatomy, LAA electrical isolation is challenging.

Purpose: We sought to evaluate the anatomical sites of acute LAA reconnection following successful isolation to define areas that may require more consideration during ablation.

Methods: 22 patients with longstanding persistent AF (mean duration 25±15 months) underwent LAA isolation with irrigated radiofrequency ablation following a standard AF ablation. LAA entrance and exit block were confirmed with intravenous adenosine after 60 min. Where reconnection was identified, ablation was performed to re-isolate the LAA.

A group of cadaveric human hearts were then examined macroscopically and histologically to assess regional variations in LAA ostial thickness in order to correlate with the observed sites of acute reconnection.

Results: 20/22 (91%) LAAIs were electrically isolated. Acute LAA reconnection occurred in 17/22 (78%). In these cases, there were a total of 37 episodes of acute LAA reconnection, mean 2.2±1.2 episodes per case. All were successfully re-isolated. We studied the LAAIs of 4 human hearts without previous ablation for comparison. The thickest sites were at the anterior (2.0±0.2mm) and superior (1.8±0.2mm) LAA margins. This correlated with the recorded sites of acute reconnection.

Conclusions: The addition of LAA electrical isolation to a persistent AF ablation has the potential to improve arrhythmia free survival. However, there is a substantial acute LAA reconnection rate, sites of which correlate with regions of thicker ostial tissue. This novel finding may improve our ability to deliver effective ablation to achieve durable LAA isolation.

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Central dopenezil infusion prevents progression of cardiac remodeling and dysfunction in chronic heart failure rats with extensive myocardial infarction

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Introduction: Previous studies have proved that oral administration of donepezil has the potential to improve arrhythmia free survival. However, there is a substantial acute LAA reconnection rate, sites of which correlate with regions of thicker ostial tissue. This novel finding may improve our ability to deliver effective ablation to achieve durable LAA isolation.
improves prognosis in chronic heart failure (CHF) rats, but its mechanisms remain unclear. As a centrally acting reversible acetylcholinesterase inhibitor, donepezil may exert the beneficial effects through a central mechanism. The present study aimed to test whether central infusion of donepezil would effectively prevent cardiac remodeling in CHF rats after extensive myocardial infarction (MI).

Methods: Fifteen rats survived for one week after MI were implanted with a blood pressure transmitter and a micro-infusion pump which connected with a cerebroventricular cannula. Animals were randomly assigned to central saline (CST, n=14) or central donepezil (CDT, n=13) infusion group. Donepezil was administered at a dosage of 0.1 mg/kg/day (one fifth of an oral dose used in the previous studies) for 6 weeks.

Results: Although there was no significant difference in the MI size between the two groups, CDT significantly decreased the heart rate (300±12 vs. 341±10 beats/min, P<0.05; P<0.01). Biventricular weight and cardiac fibrosis (2.77±0.07 vs. 2.97±0.05 g/kg, P<0.05; 4.9±0.8 vs. 9.0±0.9%, P<0.05) were significantly lower in CDT than CST group (359±8 vs. 429±27 pg/ml, P<0.05). Plasma levels of BNP and norepinephrine were significantly lower in CDT than CST group (359±8 vs. 429±27 pg/ml, P<0.05).

Conclusion: The central mechanism plays an important role in the donepezil treatment which prevents the progression of cardiac remodeling and dysfunction in CHF rats.

P5454 | BENCH
Isolation, characterization and bio-grafting of perivascular progenitor cells from myocardial specimens of paediatric patients undergoing palliative surgical repair of congenital heart defects
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Background: Congenital heart disease (CHD) still represents the primary cause of death in young children in industrialized countries. Prostates currently used to reconstruct complex cardiac defects are unable to grow and deteriorate over time. As a consequence, young patients undergo repeated and risky operations to replace failed grafts. Biological scaffolds integrated with progenitor cells able to grow and renew the prosthetic matrix may provide a definitive correction of CHD.

Purpose: To optimize a protocol for the isolation and expansion of Cardiac Pericytes (CPs) from infants affected by CHD, and to study the feasibility to integrate CPs within a clinically certified prosthetic graft (CorMatrix).

Methods: CD34+ cell suspensions from small myocardial samples left-overs (n=10, weight <0.1g), expanded and characterized for surface antigens, secretome, cardiovascular plasticity, clonogenicity, pro-angiogenic potential and capacity to colonize a CorMatrix patch.

Results: We successfully expanded CPs in vitro for several passages to reach a high number of cells (>20 million at PS). At flow cytometry/fluorescent micro-scopy analysis, CPs at P4–5 express pericyte/mesenchymal antigens (NG2, PDGFRα, CD105, CD44, Vimentin) but are negative for endothelial markers (CD31, CD144); they also express stemness markers (OCT-4, SOX-2, NANOG). Cellular microscopy showed that, in situ, CD34+CD31−NG2+ CPs are localized around capillaries and the external layer of arterioles. By single-cell sorting, we demonstrated the clonogenic capacity of CPs. When cultured with differentiation media, CPs failed to acquire mature endothelial or cardiomyocyte proteins, while their specific immunocytological staining (human-specific) immunocytological staining, patch-clamp and optical mapping. CPs did not relate to the percentage of human nuclei (R2=0.05), suggesting phenotypical heterokaryons. We hypothesized such forced heterocellular fusion creating a new, cardiomyocyte-like cell type by forced fusion between fibroblasts and surrounding fibroblasts. We hypothesized such forced heterocellular fusion (FHF) transfers desirable electromagnetic properties to fibroblasts and thereby protects CPs from pro-arrhythmogenic effects on cardiac tissue. We observed a 4-fold increase in the rate of apoptosis was observed in CSs (p<0.005).

Acknowledgement/Funding: Our data indicate that PD is a key regulator of CP response to hypoxia and favors the conservation of their undifferentiated state. Exosomal secreted miR-27a-3p and miR-543 are critical modulator of PD activity.
Methods: c-kit+ CSCs were clonally expanded from single cell deposition. Clonal-derived CSCs were primed in a stage-specific cardiopoietic growth factor cocktail to obtain spontaneously contracting cells in vitro. Freshly isolated CMs from adult hearts were used as controls. RNA-Seq was employed to analyze and compare whole mRNA and microRNA profiles of cells collected at CSC, c-kit- and c-kit+ cardiomyocyte (CM) stages.

Results: In the comparison of c-kit-positive CSCs vs. c-kit-ICMs, more than 4000 genes were up-regulated which mainly function in mitochondrial, sarcoplasmic, sarcomere-specific and calcium regulating processes, among others. Several sarcomere-related genes highly expressed in adult CMs (i.e. Tnn1, Tpc1, Mym, Tnnl3, Tnnt1, Myh7, Myh6) were indeed significantly up-regulated in c-kit-ICMs vs. CSCs in vitro. On the other hand, we found that most of cell cycle regulators/genes and a number of RNA processing genes were consistently down-regulated during differentiation from CSCs to ICMs. Interestingly, during differentiation from c-kit-positive CSCs to ICMs, known myo-miRs were upregulated while microRNAs positively regulating stem cell expansion and self-renewal were downregulated. Bioinformatics analysis built specific networks of regulated during differentiation from c-kit-positive CSCs to ICMs.

Conclusions: c-kit-positive CSCs robustly differentiate into functional beating cardiomyocytes in vitro. c-kit-positive CSC myogenic specification follow known development cardiac myocyte differentiation pathways and c-kit-ICMs transcriptome profile closely resemble adult CMs.

Methods: c-kit+ CSC-derived cardiomyocytes exhibit the typical transcriptional gene signature of adult cardiomyocytes (CMs) generated from c-kit+ cardiomyogenic progenitors in all layers under in vitro maturation process that is characterized by development of sarcomeric structure, binucleation, increased metabolic demand, and permanent exit from the cell cycle. This process is transcriptionally regulated by specific MYC microRNA (miRs). Adult cardiomyogenesis is accompanied by repression of developmental genes (e.g., transgenic expression of c-kit are able to undergo cardiomyocyte commitment in vitro and in vivo. However, it is still unknown if adult CSC-cardiomyogenic specification recapitulates cardiac development and if CSC-derived cardiomyocytes closely overlap adult cardiomyocyte whole gene profile.

To elucidate whether CMs generated from c-kit+ CSC differentiation in vitro (c-kit+CM) have a similar pattern of gene expression of adult CMs with a focus on miRNA-mRNA networks of adult CMs. Of interest, genes were upregulated which mainly function in mitochondrial, sarcoplasmic, and adult cardiac myocyte (aCM) stages.

To obtain spontaneously contracting cells in vitro. c-kit+ CSC-derived cardiomyocytes exhibit the typical transcriptional gene profile of adult CMs with a focus on miRNA-mRNA networks of adult CMs. Of interest, genes were upregulated which mainly function in mitochondrial, sarcoplasmic, and adult cardiac myocyte (aCM) stages.

Background: Resident cardiac progenitor/stem cells in adult heart is a promising therapy that repair in cardiac damaged heart such as myocardial infarction. Its embryonic origin, however, remains unclear. Purpose: The aim of this study was to elucidate its embryonic origin by fate mapping study using embryonic stage-specific Cre-deleter lines. Materials: Rosa26 reporter-deleter mice were crossed with Mesp1-Cre, Nkx2.5-Cre, aMHC-Cre, Wnt1-Cre, Islet1-Cre, Vav-Cre, Mel2a-AHC-Cre, Flk1-Cre, Tie2-Cre, cGata5-Cre and Wnt1-CreERT2 strains. At 8 to 12 weeks old, hearts were excited, enzymatically digested and lineage MACS-depleted, followed by staining with Hoechst 33342 dye and antibodies for stem cell marker, Sca1, as well as the markers for its subpopulations, PDGFRα and CD31+. The cells derived by each Cre were determined as tdTomato positive whilst non-fated as tdTomato negative cells by flow cytometry. A part of sorted cells were seeded into a 96-well plate for a subsequent single cell qRT-PCR analysis to examine the difference in gene expression between subpopulations.

Results: Virtually all cardiac Sca1+ cells, whether SP or non-SP, PDGFRα+ or CD31+, were derived from Mesp1+ mesoderm. In contrast, neither SP nor non-SP cells were derived from neural crest, hematopoietic cells, or pre-existing cardiomyocytes, defined using Wnt1-Cre, Vav-Cre, and aMHC-Cre, respectively. More than half of the Lin+-Sca1+ cells were Nkx2.5+ with an equal contribution from Islet1-fated cells. Less than 20% of SP and Non-SP cells were labeled by second heart field Mef2c-AHC-Cre. A proepicardial origin was confirmed by cGata5-Cre and Wnt1-CreERT2 in 50% and 35% of cardiac SP cells, respectively. By contrast to the proepicardial Cre line, Non-SP cells showed a greater contribution from Flk1- and Tie2-Cre. Finally, gene expression profiles were compared between SP and Non-SP cells from Nkx2.5-Cre strain in combination with PDGFRα+ and CD31+-expressing cells. Although there was a clear difference in gene expression profile between PDGFRα+ and CD31+-expressing SP cells, showing mesenchymal and endothelial property, respectively, no such clear difference was confirmed between Nkx2.5-fated and non-fated SP cells, suggesting identical population split into tdTomato positive or negative cells possibly due to incomplete Cre recombination.

Conclusion: We identified embryonic origin of PDGFRα+SP cells in mesenchyme of Nkx2.5- and Islet1- and Wnt1-labeled population. There was, however, a limitation of the interpretation of the results.

Acknowledgement/Funding: British Heart Foundation

Methods: c-kit+ CSCs were clonally expanded from single cell deposition. Clonal-derived CSCs were primed in a stage-specific cardiopoietic growth factor cocktail to obtain spontaneously contracting cells in vitro. Freshly isolated CMs from adult hearts were used as controls. RNA-Seq was employed to analyze and compare whole mRNA and microRNA profiles of cells collected at CSC, c-kit- and c-kit+ cardiomyocyte (CM) stages.

Results: In the comparison of c-kit-positive CSCs vs. c-kit-ICMs, more than 4000 genes were up-regulated which mainly function in mitochondrial, sarcoplasmic, sarcomere-specific and calcium regulating processes, among others. Several sarcomere-related genes highly expressed in adult CMs (i.e. Tnn1, Tpc1, Mym, Tnnl3, Tnnt1, Myh7, Myh6) were indeed significantly up-regulated in c-kit-ICMs vs. CSCs in vitro. On the other hand, we found that most of cell cycle regulators/genes and a number of RNA processing genes were consistently downregulated during differentiation from CSCs to ICMs. Interestingly, during differentiation from c-kit-positive CSCs to ICMs, known myo-miRs were upregulated while microRNAs positively regulating stem cell expansion and self-renewal were downregulated. Bioinformatics analysis built specific networks of regulated during differentiation from c-kit-positive CSCs to ICMs.

Conclusions: c-kit-positive CSCs robustly differentiate into functional beating cardiomyocytes in vitro. c-kit-positive CSC myogenic specification follow known development cardiac myocyte differentiation pathways and c-kit-ICMs transcriptome profile closely resemble adult CMs.

The isobaric tags for relative and absolute quantification (iTRAQ) system, a newly developed proteomic analysis method, has enabled us to comprehensively compare the absolute protein levels among multiple samples. Although proteomic profiles of humans and dogs are highly conserved because of their physiological and anatomical similarities, proteomic analysis of canine heart failure models using iTRAQ has not been reported.

Purpose: We aimed to reveal the proteomic profile of canine failing myocardium using iTRAQ.

Methods: Dogs were subjected to sham (Sham, n=2) or right ventricular rapid pacing (220 beats/min) for 4 (4W, n=2) and 6 weeks (6W, n=4) to create the heart failure model. After echocardiographic examinations, dogs were sacrificed and isolated hearts were thoroughly perfused with phosphate buffered saline. Myocardial tissues from left ventricular (LV) free wall were subjected to iTRAQ system. The data were analyzed by Ingenuity Pathway Analysis (IPA).

Results: In echocardiogram, the larger LV diastolic diameter (LVdD) and the lower ejection fraction (EF) were observed in 4W and 6W compared with Sham (LVdD: 45.4 and 39.11 vs. 30.3mm, EF: 36.0 and 25.0 vs. 81.3%, 4W and 6W vs. Sham, respectively). First of all, of initially identified 2615 proteins, we excluded 1782 proteins which lacked consistent expression in any of the samples. And a total of 805 proteins were analyzed with 1.2 folds expression levels compared with Sham in 4W (163 proteins) and 6W (174 proteins). Secondarily, using IPA, we searched the most possible canonical pathways that involve these proteins which lack consistent expression in any of the samples. And a total of 805 proteins were analyzed with 1.2 folds expression levels compared with Sham in 4W (163 proteins) and 6W (174 proteins). Secondarily, using IPA, we searched the most possible canonical pathways that involve these proteins which lack consistent expression in any of the samples. And a total of 805 proteins were analyzed with 1.2 folds expression levels compared with Sham in 4W (163 proteins) and 6W (174 proteins). Secondarily, using IPA, we searched the most possible canonical pathways that involve these proteins which lack consistent expression in any of the samples. And a total of 805 proteins were analyzed with 1.2 folds expression levels compared with Sham in 4W (163 proteins) and 6W (174 proteins). Secondarily, using IPA, we searched the most possible canonical pathways that involve these proteins which lack consistent expression in any of the samples. And a total of 805 proteins were analyzed with 1.2 folds expression levels compared with Sham in 4W (163 proteins) and 6W (174 proteins). Secondarily, using IPA, we searched the most possible canonical pathways that involve these.
proteins. Among the indicated canonical pathways, mitochondrial dysfunction and acute phase response signaling pathways were commonly identified in both 4W and 6W. Interestingly, while the proteins of acute phase response signaling pathway were comparable between 4W and 6W (11 and 12 proteins, respectively), the number of proteins included in mitochondrial dysfunction was larger in 6W (27 proteins) than 4W (11 proteins), that is mainly caused by increase in subunits of complex I, which may contribute to generate proton motive force and to create reactive oxygen species in mitochondria.

Conclusion: In canine failing heart induced by rapid pacing, proteins regarding mitochondrial dysfunction or acute phase response signaling pathways were up-regulated; the proteins involved in mitochondrial dysfunction seemed to be more important for the progression of heart failure. These pathological pathway may play an important role by quantitative up-regulation of involving proteins.

CVDOROLOGICAL PATHOLOGY AND EMBRYOLOGY

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Wilm's tumor-1 expression in cardiac endothelial cells
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Background: Restoring the myocardial wall by cardiac progenitor cells is a promising therapy after myocardial infarction. Wilm's tumor-1 (WT1) is expressed in the embryonic and reactivated adult epicardium and is therefore used as a marker for epicardial progenitor cells. Recently, it is suggested that also other cell types, like cardiomyocytes, express WT1. Our goal is to determine the WT1 expressing cell types during development and after cardiac injury in the murine and human heart, and to study the role of WT1 in these cells.

Results: Immunohistochemical analysis revealed that WT1 is expressed by cardiac endothelial cells (ECs) of the mouse heart from E15.5 onwards. In the adult heart, the expression of WT1 is reduced, although a subset of coronary ECs remains positive for WT1. Interestingly, after myocardial infarction a temporal upregulation of WT1 in ECs is observed in the infarcted area and the border zone of the heart. In the human foetal heart, WT1 expression is similar to the broader then observed in the embryonic mouse heart. In addition to the ECs, WT1 expression is also observed in the endocardial cells of the ventricles. The expression of WT1 in the ECs suggests a role in angiogenesis. To test this hypothesis, we performed in vitro experiments and show that WT1 can be induced in ECs by hypoxia, an angiogenic inducer, and that WT1 enhances cell proliferation of ECs through increased mRNA expression of CyclinD1. In addition, ECs lacking WT1 were not capable to establish a proper vascular network.

Conclusion: Together, these results suggest a role for WT1 in cardiac vessel formation during development which is reactivated after cardiac injury.

P5462 | BENCH
Physiopathology of the ubiquitin ligase E3, PDZRN3, in the development of dilated cardiomyopathies
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Dilated cardiomyopathy (DCM) is a leading cause of sudden cardiac arrest. 20–48% of all cases are familial types, mainly due to mutations in cytoskeletal or sarcomeric proteins. But an important part of the DCM has still not known mechanisms. DCM can result from mitochondrial dysfunction, sarcomeric proteins. But an important part of the DCM has still not known mechanisms. Mitochondria, as the powerhouse of cells, is crucial for cell metabolism and energy production. Accumulated evidence supports the role of mitochondrial dysfunction in the etiology of DCM. Mitochondria are dynamic organelles, and their quality is an important determinant of cell health. Mitochondrial quality control (MQC) mechanisms are responsible for maintaining the integrity of mitochondria and ensuring cellular function. The ubiquitin-proteasome system (UPS) plays a key role in MQC, involving the degradation of misfolded or damaged proteins. The ubiquitin E3 ligases recognize the damaged proteins and tag them for degradation. PDZRN3, a member of the PDZ (protein–domain–binding) family, functions as a ubiquitin E3 ligase. There are accumulating evidences that PDZRN3 is involved in the development of DCM.

Objective: To investigate the role of PDZRN3 in DCM and to explore the potential therapeutic targets for DCM.

Methods: We examined the expression of PDZRN3 in DCM patients and compared it with healthy controls. We performed gene expression analyses to identify the potential targets for PDZRN3. We also studied the effects of PDZRN3 silencing on cell viability and mitochondrial function in DCM cell models.

Results: We found that PDZRN3 expression was significantly increased in DCM patients compared with healthy controls. Gene expression analyses revealed that PDZRN3 was associated with several pathways related to mitochondrial dysfunction, including the mitochondrial depolarization and the unfolded protein response. Silencing of PDZRN3 in DCM cell models resulted in an improvement of cell viability and mitochondrial function.

Conclusion: Our findings suggest that PDZRN3 plays a crucial role in the development of DCM and that targeting PDZRN3 may be a promising therapeutic strategy for DCM.

P5463 | BENCH
Reduced number of active cardiac mitochondria in a rat model for long-term kidney disease
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Introduction - Cardiorenal syndrome (CRS) type 4 is characterized by primary chronic kidney disease (CKD) leading to an impairment of cardiac function. Two major pathological pathways may be involved: myocardial ischemia–reperfusion injury and inappropriate up-regulation of the Renin Angiotensin Aldosterone System (RAAS). We recently showed a reduced expression of several cardiac mitochondrial genes in short-term CKD rat model. We, thus, hypothesized that cardiac mitochondrial function and activity of RAAS in CKD may contribute to mitochondrial damage in the heart. We aimed to evaluate whether cardiac mitochondrial structure and function is modified in the setting of long-term CKD and if so, to characterize the potential associated mechanisms.

Methods: Lewis rats underwent 5/6 nephrectomy for induction of CKD. Renal and cardiac functions were confirmed by creatinine clearance, echocardiography and blood pressure. Upon necropsy, eight months later, cardiac sections were fixed for histological and electron microscopy (EM) analyses. Total mitochondrial DNA content was determined by the mitochondrial gene, cytochrome B. Mitochondrial function was assessed by mitochondrial respiratory (CS) activity in tissue homogenate and respiratory chain function was determined by the activity of complexes I-IV in isolated mitochondria. The levels of PGC1a, a transcription factor for mitochondrial biogenesis, and cytosolic cytochrome C (CytC) were determined by western blot. Serum Angiotensin II (AngII) was measured by ELISA and cytokine serum profile was determined by microarray analysis.

Results: Long-term CKD model leads to significant cardiac hypertrophy and increased interstitial fibrosis. EM analysis revealed a massive spatial disarrangement accompanied by a considerably increased volume of swollen-damaged mitochondria in CKD hearts. A significant accumulation of cytosolic CytC confirmed the mitochondrial damage. While total mitochondrial function was extensively reduced in CKD hearts, the remaining mitochondria retained intact activity. Despite the marked decrease in cardiac mitochondrial content, no differences were observed in PGC1a expression. Interestingly, we documented negative correlation between increased levels of IL1a, INFγ, IL2 and CS activity in CKD. Likewise, AngII plasma levels were slightly increased and negatively correlated to CS activity.

Conclusion: Altogether, the data suggest that CKD setting results in a marked reduction of active mitochondria in the heart. Pro-inflammatory cytokines and RAAS, which are induced in CKD, may set a deleterious environment to the cardiac mitochondria.

P5464 | BENCH
Inhibition of aortic valve calcification by local delivery of zoledronic acid: An experimental study
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The aim of the present study was to evaluate the safety and effectiveness of zoledronic acid in the treatment of aortic valve calcification. Aortic valve calcification (AVC) is a common complication of long-term kidney disease and is associated with increased cardiovascular morbidity and mortality. The pathogenesis of AVC is multifactorial and involves the deposition of calcium in the extracellular matrix of the aortic valve. The use of bisphosphonates, which are known to inhibit bone resorption, has been investigated as a potential treatment for AVC. However, the safety and effectiveness of these drugs in the treatment of AVC has not been fully established.

Methods: In this study, we performed a randomized controlled trial to evaluate the safety and effectiveness of zoledronic acid in the treatment of AVC. A total of 60 patients with AVC were randomized to receive either zoledronic acid or placebo. The primary endpoint was the change in the degree of AVC over a 24-month period. Secondary endpoints included the occurrence of cardiovascular events and the need for aortic valve replacement.

Results: At the end of the 24-month follow-up period, the change in the degree of AVC was significantly lower in the zoledronic acid group compared to the placebo group. There was also a significant reduction in the occurrence of cardiovascular events and the need for aortic valve replacement in the zoledronic acid group.

Conclusion: The results of this study suggest that zoledronic acid is safe and effective in the treatment of aortic valve calcification. Further studies are needed to confirm these findings and to evaluate the long-term safety and effectiveness of this treatment in a larger patient population.

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Conclusion: The results of this study suggest that zoledronic acid is safe and effective in the treatment of aortic valve calcification. Further studies are needed to confirm these findings and to evaluate the long-term safety and effectiveness of this treatment in a larger patient population.
Results: At baseline, all animals developed aortic valve stenosis with severe calcification. No differences regarding AVA were recorded between both groups. (21.37±1.76 vs 21.98±3.12, p=0.53). In all animals the local delivery of zoledronate and placebo mixtures was successful and uncomplicated. A total of 24 cusps were histologically examined from each treated group. The cusps treated with zoledronate had significantly lower expression of calcium content compared to the controls (16.40±0.90 vs 26.92±1.60% of the area, p < 0.0001)

Conclusion: Inhibition of aortic valve calcification by local catheter-based delivery of zoledronate is effective without evident short-term complications. The potential clinical implications should be confirmed in human studies.

PS5465 | BENCH
Intraleaflet haemorrhages induce anti-inflammatory and osteoclastic cell phenotypes and are associated with osteogenic metaplasia in stenotic aortic valves

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Background: Calcific aortic valve degeneration is an active process similar to atherosclerosis. Involvement of intraleaflet (intraplaque) haemorrhages in promotion of both pathologies has been recently postulated. Intraplaque haemorrhages induce expression of anti-inflammatory factors such as heme oxygenase-1 (HO-1) and IL-10. It is hypothesized that similar mechanisms are involved in aortic valve degeneration (AVD) but little is known about the impact of intraleaflet haemorrhages on the mode of calcific valvoreal remodelling which is a hallmark of AVD.

Purpose: The aim of this study was to check whether the occurrence of intravacular haemorrhages is associated with phenotypic modifications of monocyte derived cells and modification of calcific remodelling profile in human stenotic aortic valves.

Methods: Aortic valve specimens were obtained from 63 patients undergoing routine valve replacement surgery due to severe stenosis. Areas of intraleaflet haemorrhages were detected by immunohistochemical and histochemical methods (glycoporphin C/fibrin/iron) and all cases have been divided into haemorrhagic group (HG, n=28) showing substantial, continuous intraleaflet haemorrhages and nonhaemorrhagic group (NHG, n=35) without or with very limited signs of previous haemorrhages. In the valves of both groups, the following parameters were assessed: overall macrophage infiltration, density of CD163+ macrophages and tartrate resistant acid phosphatase positive (TRAP+) cells, neovessel formation, heme oxygenase-1 (HO-1) protein expression and occurrence of chondro- and osteogenic differentiation.

Results: Areas of haemorrhages were mostly located in the vicinity of focal calcifications. The HG group revealed more intense neovascularization (% of assessed myocardium; mean values): basal 33; midlevel 41; apical level 43.

Midventricular short axis section: radial distribution (% of the overall fibrosis within the section, mean values): anterior LV:11.6; anterolateral LV:16.1; inferolateral LV:6.3; inferior LV:24.4; anterior septum:11.5; medium septum:10.0, posterior septum:11.6; anterior RV:3.6; inferior RV:4.9.

Midventricular short axis section: epicardial-endocardial distribution (% of the overall fibrosis within the section, mean values): trabecular 24.3; subendocardial 21.3; midwall 33.1; subepicardial 21.3. Four main patterns were identified: midwall and subendocardial 21.7% (5/23), midwall and subepicardial 17.4% (4/23), transmural 43.5% (10/23), midwall 17.4% (4/23). Type of fibrosis: in all patients both types of fibrosis were detectable, whereas fibrosis was mainly of replacement type in 17 patients, and mainly perimycotic type in 7 patients.

Conclusions: In hearts of ES-HCM undergoing heart transplantation the amount of myocardial fibrosis is very marked. Moreover both replacement and perimyocytic fibrosis extensively affects the LV myocardium with some differences between base, mid and apex. Fibrosis involves more frequently midventricular and subepicardial layers with a relative sparing of subendocardial (never exclusively involved). While the entire septum and the inferior and anterior portions of LV are maximally involved, the inferolateral wall tends to be spared. These observations have potential implications on the comprehension of the pathophysiology of HCM and on interpretation of imaging techniques.

PS5466 | BENCH
Proliferating myofibroblasts contribute to extracellular matrix remodeling in a porcine model of ischemic cardiomyopathy

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Background: Fibroblast (Fb) differentiation is involved in the development of fibrosis and contributes to collagen maturation and cross-linking. This leads to stiffening of myocardial tissue and ultimately deterioration of heart function.

Purpose: In this study we sought to determine the Fb phenotypes responsible for extracellular matrix remodeling in ischemic cardiomyopathy.

Methods: A copper-coated stent was implanted in the left anterior descending coronary artery (LAD) of porcine hearts leading to a reduction in perfusion and development of a myocardial infarction (MI, 10% of left ventricular mass). Biopsies

Conclusions: In conclusion, this study is the first to demonstrate usefulness of IMS combined with FMW to visualize regional metabolic flux of glucose oxidation, revealing compensatory responses of energy management in the marginal regions between the ischemic core and intact regions.

PS5467 | BENCH
Heterogeneity of patterns and distribution of myocardial fibrosis in end-stage hypertrophic cardiomyopathy (ES-HCM) undergoing heart transplant: a morphometric analysis of 24 explanted hearts

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Background: Myocardial fibrosis is frequently found by cardiac MRI in HCM, particularly in cases with left ventricular (LV) dysfunction, and has been shown to carry an ominous prognosis. Nonetheless, extension and distribution of fibrosis have never been extensively pathologically characterized.

Purpose: To assess overall extension, apex-to-base, radial and epicardial/endocardial distribution (histomorphometric analysis), and type of myocardial fibrosis in a group of transplanted ES-HCM.

Methods: For each heart the following sections have been considered: midventricular short axis, epicardial-endocardial cross section with analysis of radial and transmural distribution, as well as 3 samples from basal and 3 from apical level. Histomorphometric analysis was carried out with a dedicated software and graphics workstation.

Results: Twenty-four hearts were examined between 2005 and 2014. One patient with previous alcohol ablation was excluded.

LV base-to-apex distribution (% of assessed myocardium; mean values). Basal level: 33; medium level: 41; apical level: 43.

Midventricular short axis section: radial distribution (% of the overall fibrosis within the section, mean values): anterior LV:11.6; anterolateral LV:16.1; inferolateral LV:6.3; inferior LV:24.4; anterior septum:11.5; medium septum:10.0, posterior septum:11.6; anterior RV:3.6; inferior RV:4.9.

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Conclusions: In hearts of ES-HCM undergoing heart transplantation the amount of myocardial fibrosis is very marked. Moreover both replacement and perimyocytic fibrosis extensively affects the LV myocardium with some differences between base, mid and apex. Fibrosis involves more frequently midventricular and subepicardial layers with a relative sparing of subendocardial (never exclusively involved). While the entire septum and the inferior and anterior portions of LV are maximally involved, the inferolateral wall tends to be spared. These observations have potential implications on the comprehension of the pathophysiology of HCM and on interpretation of imaging techniques.
were collected from the myocardium adjacent to the MI (not from scar tissue) and remote to the MI and from corresponding regions in SHAM operated animals (N=6 SHAM, N=6 MI). Sirius red staining was used to assess fibrosis and polarization microscopy to quantify collagen subtypes in the interstitial and perivascular area. Fb were isolated via enzymatic digestion and cultured in DMEM culture medium with 10% fetal bovine serum for 4 days to determine fibroblast phenotypes and for 8 days to evaluate proliferation capacity. F-actin was assessed using immuno-fluorescent staining. Immunostaining and Western blotting were used to assess lysyl oxidase (LOX) as marker for collagen cross-linking activity.

Results: Overall interstitial fibrosis was not increased in the adjacent or remote myocardium. However, there was a 3 fold increase of cross-linked collagen type I within the interstitial area of the adjacent myocardium; presence of cross-linked collagen bundles was confirmed by electron microscopy. Concomitantly, arteriole perivascular fibrosis was increased (2-fold increase of perivascular collagen type I and III). Fb from MI hearts from both regions compared to SHAM were larger (27% increase in the adjacent and 20% in the remote myocardium) and the number of Fb with f-actin stress fibers was increased 2-fold. Immunostaining showed nuclear LOX accumulation. These myofibroblasts maintained proliferation capacity after 8 days in culture.

Conclusion: Proliferating myofibroblasts underlie increased collagen cross-linking in the MI-adjacent myocardium and may contribute to myocardial stiffening. Fb differentiation in the remote myocardium could be triggered through increased hemodynamic load.

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P5469 | BENCH
Toll-like receptor 7 is involved in adverse ventricle remodelling after myocardial infarction
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Introduction: Toll-like receptor 7 (TLR7) detects viral nucleic acids to fight against viral infection. TLR7 also recognizes endogenous single-strand RNA (ssRNA) shed from dying cells that induces an inflammatory response in autoimmune diseases. A role for TLR7 in Myocardial Infarction (MI) is unknown. We showed that TLR7 receptor 4 activation deficiency results in a decreased inflammatory response and improved heart function after MI. We hypothesize that TLR7 detects ssRNA released from the dying heart cells, increases the inflammatory response and deterioration of left ventricle function after MI.

Methods: C57BL/6J wild type (WT) and TLR7 null mice, 10–12 weeks old, were subjected to myocardial infarction via permanent ligation of the left anterior descending artery (LAD). Cardiac function was assessed by Vevo2100 echocardiography at baseline, 7 and 28 days after MI. Mixed ANOVA for repeated measures was used to compare Ejection Fraction (EF) between WT (N=15) and TLR7 null mice (N=26) that had echocardiography at all 3 timepoints. Log rank test was used to assess differences in survival between WT and TLR7 null mice.

Results: Despite similar infarct size, survival of TLR7 null mice after MI was better than WT (p=0.010). After MI, 3 out of 31 TLR7 null mice (10%) died while 12 out of 34 WT mice (35%) died of cardiac rupture. TLR7 deficiency reduced left ventricular remodeling and preserved cardiac function (EF/SEM: 32.5±1.8 vs 25.3±1.6, P<0.05 for WT and TLR7 null mice, p=0.001). TLR7 deficiency did not affect survival of MI and tertiles of TLR7 were not significantly different between WT and TLR7 null mice.

Conclusion: TLR7 is involved in cardiac remodeling after MI, independent from infarct size. Lack of TLR7 preserves cardiac function and survival after MI and identifies TLR7 as a potential therapeutic target for adverse ventricle remodeling.

P5470 | SPOTLIGHT
PEAR1: a novel link between IgE-mediated allergic and cardiovascular disease
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GWAS for platelet function and cardiovascular disease repeatedly identified polymorphisms linked to Platelet endothelium aggregation receptor 1 (PEAR1), a cell surface receptor involved in stabilizing platelet aggregates. We sought to identify the extracellular ligands of PEAR1.

We created a protein microarray representing the secretome and receptor repertoire of the human platelet. 173 Recombinant proteins were expressed. Using an avid soluble recombinant PEAR1 protein and a systematic screening assay designed to detect extracellular interactions, we identified the high-affinity IgE binding subunit FcRn1α, as a PEAR1 ligand. FcRn1α and PEAR1 interacted with a strong affinity (KD ~30nM). Pre-complexing FcRn1α with IgE potently inhibited the FcRn1α-PEAR1 interaction. Oligomeric FcRn1α potentiates platelet aggregation and protects against 125I-phosphorylation, an event that was abolished for FcRn1α (Figure 1). This provides a mechanistic basis for the initiation of PEAR1 signaling in aggregation. The identification of FcRn1α as an activating ligand for PEAR1 and the finding that IgE can inhibit this interaction suggests a link between IgE and platelet function. The in vivo prevention of IgE binding to FcRn1α by a clinical anti-IgE monoclonal antibody omalizumab, showed that omalizumab can relieve IgE-mediated inhibition of the FcRn1α-PEAR1 interaction and may provide an explanation for the increased risk of cardiovascular disease associated with omalizumab use.

Conclusion: We developed a platelet protein microarray resource to gain new insights into the function of platelet PEAR1 and identified, the FcRn1α-PEAR1 interaction and its regulation by endogenous IgE, which provides a mechanism to explain previously under-appreciated interactions between allergy and cardiovascular disease.

P5471 | BENCH
Aging impairs cardiac Akt activation leading to myocardial sarcopenia
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Background: Aging causes skeletal muscle atrophy (i.e. sarcopenia). In heart, aging is also known to cause cardiac dysfunction such as diastolic dysfunction; however, the impact of aging on myocardial cell growth remains uncertain.

Aims: Because of the pivotal role of protein kinase Akt in cellular aging and growth of cardiomyocytes, the purpose of this study was to elucidate whether #1 aging may impair cardiac Akt activation leading to myocardial remodeling (including atrophy) in aged heart and #2 regular exercise may restore the aging-induced cardiac remodeling and Akt activation of Akt signaling.

Methods: Cohort-1: Male aged (40 week-old) C57BL6 mice, age-matched Akt knockout mice (C57BL6-background, heterozygotes; AkitoK), and young counterparts (14 w/o) were evaluated changes in each cardiac function by echocardiography, remodeling by pathology, and molecular signaling by biochemical procedure. Mice were randomly allocated to the regular exercise (EX, 60-min running by treadmill/day for 6 months).

Cohort-2: Male genetically senescence-accelerated ([SAM; senescence-accelerated prone (P10)]) and senescence-resistant counterpart (R1) were allocated to EX [45-min running by treadmill/every 2 day for 6 months].

Results: We first observed the impact of aging on cardiac Akt. In naturally aging mice, the cardiac Akt activity was decreased compared to those young counterpart, which was restored by EX. Aged C57BL6 exhibited systolic and diastolic dysfunction and reduced heart weight, all which were restored by EX. Independently of EX, the aged AkitoK exhibited reduced HW and systolic dysfunction. Interestingly, ERK activity was modestly increased by aging, however, it was unaffected by EX. In R1, EX promoted LV hypertrophy and enhanced cardiac Akt-mTOR-S6K activity. Of note, the baseline Akt activity was elevated in P10 heart, which was unaffected by EX. Because insulin-mediated autophagic regulation plays a pivotal role in skeletal muscle hypertrophy, we hypothesized the EX-induced increase in cardiac Akt-mTOR axis may modulate cardiac autophagy that restores aging-induced cardiac remodeling. Circulating insulin level remained unchanged by EX, however, the EX ameliorated cardiac insulin resistance (assessed by Ser307 phosphorylation of IRS-1) and subsequent autophagy (LC3 turnover and p62 level) observed in the aged mice.

Conclusion(s): Aging causes cardiac sarcopenia and systolic dysfunction via affecting cardiac Akt activity and subsequent insulin resistance. Exercise restored the cardiac insulin resistance induced by aging through the Akt/mTOR-dependent autophagy.

P5472 | BENCH
Genetic cardiomyopathy overlaps can modify phenotypic features in dilated cardiomyopathy patients - a comprehensive next-generation sequencing (NGS) study
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AORTIC VALVE DISEASE

P5473 | BENCH
Valvular heart disease and pulmonary hypertension in fawn-hooded rats: the role of SHT2B receptors
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Background: Patients with elevated serotonin levels are prone to develop valvular heart disease and also pulmonary hypertension (PH) via induction of pulmonary vasoconstriction and proliferation of pulmonary artery smooth muscle cells. In order to explore the role of SHT2B receptors, we treated Fawn Hooded rats by terguride, a 5-HT2B inhibitor.

Methods: Fawn Hooded rats (FH of age 1, 3, 6 and 9 months, n=6 rats/group) which genetically exhibit a platelet storage pool disease, hence are unable to store serotonin in platelets were compared with Brown Norway rats (BN of age 1, 3, 6 and 9 months, n=6 rats/group). Pulmonary artery systolic pressure (PAPs) was assessed by in vivo hemodynamic measurements (Millar catheter) and echocardiography. Cardiac fibrosis was evaluated by Masson's trichrome staining and aortic valve calcification by Von Kossa staining. Serotonin receptor expression was measured by qRT-PCR. Proliferation and serotonin receptor expression in cultured cardiac fibroblasts showed increased proliferation and upregulation of SHT2B receptor (RT-PCR), which was reversible with terguride.

Conclusions: Fawn Hooded rats developed both PH and valvular heart disease. Both PH and cardiac valvulopathy were attenuated by treatment with the 5-HT2B antagonist terguride.

P5474 | BEDSIDE
Scaling systolic volume to body surface area and its influence in the diagnosis of low-flow/low-gradient aortic stenosis

The definition of low-flow/low-gradient aortic stenosis (LFLGAS) is based on the scaling of systolic volume (SV) to body surface area (BSA). Assuming an isotropic relationship, the allometric coefficient (AC) should be 3/2 instead of 1 as generally applied. The aim of this study was to evaluate the correlations between measurements of body size and SV in order to calculate the precise AC (b) for a correct scaling.

Methods: Sixty-four individuals without evidence of heart disease were included. Mean age was 45±13 years, 35.9% males. The ranges of weight and height were 48–124 kg and 147–190 cm, SV was measured as the difference between end-diastolic and end-systolic left ventricular volumes. The b-value was calculated after a logarithmic transformation of the formula used to scale biological variables: \( Y = X^{b} \), where X is the variable to be scaled, Z is the body size and b the AC.

Results: SV was linearly correlated with all the variables that measure body size except body mass index: height \( r = 0.63; p < 0.0001 \); weight \( r = 0.52; p < 0.0001 \); BSA \( r = 0.60; p < 0.0001 \) and body mass index \( r = 0.19; p = 0.161 \). After the logarithmic transformation we found an allometric coefficient \( b = 1.3 \) for appropriate scaling to BSA \( (r = 0.59; p < 0.0001) \). The normal values obtained after scaling SV to BSA were 16.7 to 40.7 mL/m². However, scaling to the 1.3 exponent provided values ranging from 14.0 to 34.0 mL/m². When the difference between scaled SV were plotted against different values of BSA (Figure 1), we noted that an AC of 1.3 overestimates SV at low BSA and underestimates SV at high BSA values.

Conclusions: Scaling SV to BSA with an allometric coefficient of 1 incorrectly classifies patients low SV when BSA is either low or high. This finding has important clinical implications when the diagnosis of LFLGAS is considered.

P5475 | BEDSIDE
Transcatheter aortic valve implant vs surgical aortic valve replacement in low- to intermediate risk patients: a Meta-analysis
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Objectives: To test the hypothesis that Transcatheter aortic valve implant (TAVI), when compared with surgical aortic valve replacement (SAVR), have favourable clinical outcomes in patients with low or intermediate risk.

Methods and results: A PubMed, EMBASE and Medline search yielded 6 studies, of which 2 were abstracts. Over 2100 patients were randomised to TAVI vs SAVR. 30-day mortality was not different (Risk ratio was 1.4 (95% CI 0.88, 2.3). There was also no statistically significant difference in 1-year mortality, stroke, life-threatening bleeds, and major vascular complications. However, TAVI was associated with significantly shorter hospital stay.

Conclusions: Scaling SV to BSA with an allometric coefficient of 1 incorrectly classifies patients low SV when BSA is either low or high. This finding has important clinical implications when the diagnosis of LFLGAS is considered.

Outcomes | Risk ratio | 95% CI
--- | --- | ---
30-day mortality (primary outcome) | 1.4 | 0.88, 2.28
1-year mortality | 1.0 | 0.78, 1.27
Major stroke | 2.0 | 0.56, 7.42
Life-threatening bleeds | 1.8 | 1.00, 3.09
Major vascular complications | 8.6 | 0.57, 130

Conclusion: In low to intermediate risk patients, 30-day or 1-year mortality, risk of stroke, major vascular complications and life-threatening bleeds were not significantly different between patients treated by TAVI when compared with SAVR.
In conclusion, implantation depth under 4mm seems to have a positive impact on outcome of the procedure, has not been evaluated. Whether a higher implantation depth from 4 to 12 mm and Group II included those with implantation depth under 4mm (distance from either LCC or NCC to 0 mm) but without significant regurgitation requiring repositioning techniques.

Results: One hundred sixty four patients were evaluated. When Group I (81±4.5 years, 75 males (56%)) was compared with Group II (81±6.5 years, 16 males (53%)), peak gradient at discharge (17.7±5 vs. 14.7±7 mmHg, p=0.01) proved to be significantly higher in Group I. This remained significant after adjusting for the AR Core Valve. Discrimination was better for ES2 (AUC ROC 0.77) than GAV (AUC ROC 0.75). Comparing the 3 scores, NRI of ES2 was better than STS and GAV (ES2 x STS, NRI=+4.8%, p<0.0001) and STS (AUC ROC 0.75) than GAV (AUC ROC 0.73). Comparing the 3 scores, NRI of ES2 was better than STS and GAV (ES2 x STS, NRI=+4.8%, p<0.0001) and STS (AUC ROC 0.75) than GAV (AUC ROC 0.73). Comparing the 3 scores, NRI of ES2 was better than STS and GAV (ES2 x STS, NRI=+4.8%, p<0.0001) and STS (AUC ROC 0.75) than GAV (AUC ROC 0.73). Comparing the 3 scores, NRI of ES2 was better than STS and GAV (ES2 x STS, NRI=+4.8%, p<0.0001) and STS (AUC ROC 0.75) than GAV (AUC ROC 0.73).

Conclusions: ES2 and STS are accurate and well calibrated. ES2 showed the smallest NRI and Net Benefit. ES2 should be the risk model of choice for selection of AS pts for TAVI.

Background: Secondary mitral regurgitation (SMR) is generally reduced after isolated aortic valve replacement (AVR). Prosthesis-patient mismatch (PPM) may hinder normalization of left ventricular geometry and pressure overload following AVR. Purpose: We aimed to investigate the relationship between PPM and regression of SMR following AVR for aortic valve stenosis (AS).

Methods: A total of 578 patients with AS who underwent AVR at 2 institutions and presenting moderate SMR (mitral regurgitant volume (MRV) 30–45 ml/beat) not considered for surgical correction were included in this study. Clinical and echocardiographic follow-up were completed at a median follow-up of 72 months. PPM was defined as an indexed effective orifice area (EOA) <0.85 cm²/m².

Results: Aortic PPM and was found in 219/578 patients (37.9%). There were no significant differences in baseline and operative characteristics between patients with or without PPM. Patients with PPM had less regression of SMR following AVR compared to those with no PPM (change in MRV, -12±5 vs. -19±4 mL, respectively, p<0.0001). Variables significantly associated with postoperative change in MRV were also entered in a multivariable linear regression model which showed EOAi (p<0.0001) and LA diameter (p=0.006) to be independently associated with MRV improvement. Patients with PPM also had less postoperative improvement in 6-minute walking test distance (82±74 vs. 43±39m, p<0.0001).

Conclusions: PPM is associated with lesser regression of SMR following AVR. This unfavorable effect was associated with worse functional capacity. These findings emphasize the importance of operative strategies aiming to prevent PPM in patients with AS and concomitant SMR.

References:

P5479 | BEDSIDE
Study of mitral valve prolapse and chronic anxiety in patients with breast cancer

Background: Mitral valve prolapse (MVP) is more prevalent in females and is associated with chronic anxiety. We aimed to assess its prevalence in females with breast cancer before initiation of cancer specific therapy and to examine if anxiety as a part of MVP syndrome is a link between both conditions.

Methods: We included 110 females (Gpa) with recently diagnosed breast cancer, and 70 healthy females as control (Gpb). Group A was subdivided into sub A1 which included 25 patients with both breast cancer and MVP and suba2 which included 85 patients with breast cancer but no MVP/MVP was considered non classic if there is only leaflet sagging >2mm & classic if there is an increase in leaflet thickness >5mm. All patients underwent echocardiology & Hamilton anxiety scale (HAS) interrogation to detect anxiety and its degree.

Results: The prevalence of non classic & classic MVP in Gpa & Gpb was 27.7%,
Mitral regurgitation (MR) is a frequent valvular disorder primarily and secondarily accompanying various heart diseases. Significant MR initially decreases afterload. Increase in systemic vascular resistance (SVR) accelerates progression of MR severity and myocardial dysfunction. Determining SVR is helpful in management of significant MR, as well as various cardiac disorders. Pulmonary vascular resistance can be predicted non-invasively via a formula based on ratio of tricuspid valvular regurgitant flow maximal velocity (Vmax) to velocity time integral (VTI) obtained at right ventricular outflow tract. In this study, we aim to investigate whether this rationale would fit to the left side of the heart for determining SVR.

Methods: Patients undergoing cardiac catheterization for various reasons except for congenital heart diseases, who had moderate-severe MR were included in our study. Fick’s method was used for SVR calculation. Echocardiography was performed to patients just after cardiac catheterization. Mitral regurgitation Vmax and left ventricular outflow tract (LVOT) VTI were measured. Pearson correlation test was performed to determine the relationship between SVR and MR Vmax/LVOT VTI ratio.

Results: A total of 21 patients (12 female; 56.7±14.3 years) were included in our study. There was a very strong correlation between SVR values and MR Vmax/LVOT VTI ratios (r=0.833; p<0.001) (Figure 1). We generated a regression equation to predict SVR non-invasively as follows: SVR = 0.625 \* [MR Vmax/(cm/sec)/LVOT VTI] + 1.252. Our model calculated SVR values with a mean variation in MS patients demonstrated significantly elevated afterload (Ea: 3.0±1.3 mmHg/mL; p<0.001) and LV contractility (Ees: 4.1±1.6 vs. 2.4±0.5 mmHg/mL; p<0.001) as compared to controls, with higher Ea in subjects with smaller mitral valve area (MVA) <0.8 cm² and pronounced subvalvular fusion. Stroke volume (49±16 to 57±1.7 mL; p=0.001) and indexed LV end-diastolic volume (LVEDVindex: 57±16 to 64±16 mL/m²; p<0.001) increased following PTMC while Ees and Ea returned to more normal levels. Elevated LV stiffness was demonstrated at baseline and increased further following PTMC.

Conclusion: Our findings provide evidence of elevated LV contractility, increased arterial load and increased diastolic stiffness in severe MS. Following PTMC, both LV contractility and afterload tend to normalize.
AORTIC VALVE INTERVENTIONS

PS458 | BEDSIDE

The type of surgical indication determines patients’ prognosis in infective endocarditis

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Purpose: Current guidelines recommend surgery during the active phase of infective endocarditis (IE) in 3 situations, heart failure (HF), uncontrolled infection (UI), and prevention of embolic events (EE). Our aim was to assess patients’ prognosis according to the type of surgical indication.

Methods: From 1996 to 2014, 1053 patients with left-sided IE were prospectively and consecutively recruited at 3 referral hospitals, 614 of them underwent surgery. They were classified in 4 groups according to the type of surgical indication: HF-Group (n=232), patients with HF or severe valvar regurgitation; EE-Group (n=19), patients with embolisms or large vegetations; UI-Group (n=84), patients with perivalvular complications or persistent signs of infection; M-Group (n=279), patients with two or more indications.

Results: There were no differences in age, gender distribution and comorbidities between the 4 groups. S.aureus was more frequently isolated in UI-Group (p<0.001). Blood cultures were positive in a higher proportion of patients in EE and UI groups (p<0.001), and these remained positive after 48 hours more frequently in patients from UI-Group (p<0.001). Acute onset was more common in UI-Group (p<0.001). Post-surgical evolution revealed some differences according to the surgical indication. Patients from UI-Group developed more frequently septic shock despite surgery, and mortality was higher in this group (Table). In-hospital events after surgery

<table>
<thead>
<tr>
<th>Variables</th>
<th>HF-Group</th>
<th>EE-Group</th>
<th>UI-Group</th>
<th>M-Group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>35.8% (83)</td>
<td>42.1% (8)</td>
<td>41.7% (35)</td>
<td>37.7% (106)</td>
<td>0.781</td>
</tr>
<tr>
<td>Heart failure</td>
<td>32.3% (77)</td>
<td>5.3% (1)</td>
<td>32.1% (27)</td>
<td>25.3% (71)</td>
<td>0.033</td>
</tr>
<tr>
<td>Renal failure</td>
<td>32.3% (75)</td>
<td>31.6% (6)</td>
<td>32.1% (27)</td>
<td>25.3% (71)</td>
<td>0.307</td>
</tr>
<tr>
<td>Septic shock</td>
<td>10.8% (25)</td>
<td>0% (0)</td>
<td>19% (16)</td>
<td>7.1% (20)</td>
<td>0.006</td>
</tr>
<tr>
<td>Stroke</td>
<td>5.3% (12)</td>
<td>21% (4)</td>
<td>8.3% (7)</td>
<td>8.1% (21)</td>
<td>0.067</td>
</tr>
<tr>
<td>AV-block</td>
<td>8.6% (20)</td>
<td>0% (0)</td>
<td>14.3% (12)</td>
<td>10.7% (30)</td>
<td>0.219</td>
</tr>
<tr>
<td>Mortality</td>
<td>24.6% (57)</td>
<td>21.1% (4)</td>
<td>45.1% (37)</td>
<td>30.8% (86)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Statistically significant differences between HF-Group and EE-Group. **Statistically significant differences between HF-Group and UI-Group. ***Statistically significant differences between EE-Group and UI-Group.

Conclusions: Post-surgical evolution and prognosis are determined by surgical indication. The probability of success decreases in those patients with UI. Although more studies are necessary, patients with S.aureus infection and those with persistent positive blood cultures after 48h have the worst prognosis.

PS459 | BEDSIDE

Why do we need dedicated tools to quantify the tricuspid annulus by 3D transthoracic echocardiography?

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Background: Despite an accurate measurement of tricuspid valve (TV) annulus and TV regurgitant orifice area (EROA) = 1.35 cm² (Figure 3) There was a significant reduction in annular area (57%) and EROA (53%) measured, with 3D TEE respectively at 6.05 cm², 0.63 cm². Hemodynamic parameters also improved with a reduction in right atrial pressure from 22 mmHg at baseline, to 9 mmHg and an increase in LV stroke volume from 42 cc at baseline to 72 cc.

Conclusions: TTVR could become an effective treatment for high surgical risk patients that are non-responsive to optimal medical therapy.

PS458 | BENCH

In vivo tissue-engineered, autologous, valved conduit “Biovalve” with robust wall tissues

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Objective: Pediatric patients with congenital heart disease would benefit from replacement heart valves, particularly pulmonic valves. We developed an autologous valved conduit (Biovalve), formed by in-body tissue architecture technology (IBTA) using subcutaneously embedded plastic molds. Excellent hemodynamic performance and beneficial leaflet movement after implantation were observed in both goat and beagle experimental models. Moreover, Biovalves might potentially serve as pediatric replacement valves because they are composed of mainly autologous fibroblasts and collagen fibers. However, in the small-diameter molds required for pediatric patients, connective tissue formed based on active cell migration around the mold generally tends to be thin. Therefore, Biovalves with thin conduits have required careful surgical handling. Accordingly, we aimed to develop a mold with a paling structure to enhance IBTA for producing Biovalves with robust conduits.

Methods and results: The paling mold consisted of a two-layer structure. The inner part (outer diameter, 14 mm), which mainly formed the leaflets, was surrounded by the paling (width, 2 mm) that lined the conduit at equal intervals of 1.0 mm (total length, 20 mm). A 1-mm space was designed between the inner and outer parts as the conduit wall. After the embedding period, the space for the conduit wall was completely filled with connective tissue from outside the mold via palingings. After trimming the excess peripheral tissues and removing the mold, completely formed Biovalves with approximately 1-mm conduit walls (inner diameter, 14 mm) were obtained. There was a smooth and clear boundary between the conduit and leaflets, which consisted of mainly fibroblasts and collagen fibers. The paling mold allowed maintenance of the structure, including the lumen, and improved handling of the Biovalves.

Conclusion: The paling structure facilitated the formation of approximately 1-mm thick conduit wall and leaflets through a small aperture inside the inner portion. The paling mold with a two-layer structure enabled better handling of the Biovalves, and may eventually lead to clinical applications. We are planning an implant study of Biovalves to investigate their in-vivo durability. We hope that this type of Biovalve will be clinically used in heart valve replacement even in pediatric patients.
Aortic valve interventions

PS487 | BEDSIDE
Atrophicventricular disturbance after transcatheter aortic valve implantation: incidence and predictive factors
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Purpose: Atrophicventricular (AV) conduction disturbance leading to pacemaker (PM) implantation is frequent after transcatheter aortic valve implantation (TAVI). The aim of this study was to assess the incidence and the predictors of PM implantation after TAVI.

Methods: Between 2010 and 2014, 198 consecutive patients underwent TAVI in our center. 42 patients were excluded from the study because of a pre-existing PM before TAVI. 156 patients (62 Corevalve (CV), 94 Edwards Sapiens valve (ES)) were included and prospectively followed during 1 year.

Results: Complete AV block occurred after TAVI in 29 patients (19%), second degree AV block in 3 (0.5%), new left bundle branch block (LBBB) in 53 (34%). A PM was implanted in 40 patients (26%). CV patients were more frequently implanted than ES (35% vs 19%; p<0.03). Post-procedure PR, QRS duration were longer in the PM group (227 vs 196 ms; 159 vs 129 ms, respectively, p<0.001). LBBB was also more frequent (79% vs 53%; p<0.01). At hospital discharge, 83% of the PM group was stimulated. At 1 month, 10% were PM dependent and 4% at 6 months. At 1 month, 29% were stimulated less than 5% of the time and 25% at 6 months. Multivariate analysis showed that the predictors of PM implantation were a pre-existing RBBB (OR 4.7, CI 1.43–15.2, p=0.01), a pre-existing LBBB (OR 7.28, CI 2.34–22.6, p<0.001), a per-TAVI complete AV block (OR 4.21, CI 1.52–11.63, p=0.006), a high prosthesis/annulus diameter ratio (OR 1.1, CI 1.04–1.18, p=0.003) and post-procedure PR and QRS long duration (OR 1.03, CI 1.01–1.06, p=0.009; OR 1.04, CI 1.01–1.07, p=0.009 respectively). PM implantation had no impact on survival after TAVI (Logrank-p=0.92). The increase in LVEF post-TAVI was lower in PM group: 0.2 vs 8%, p=0.05 at 6 months and −5 vs 9.6%, p=0.004 at 1 year. The NYHA class was similar in both groups at follow up.

Conclusion: TAVI is associated in a great proportion of patients with AV disturbances which are mostly regressive over time. Patients with pre-existing RBBB, LBBB and high prosthesis/annulus diameter ratio are at increased risk of complete AV block. LVEF increase was lower in PM group even with a low percentage of stimulation time.

PS488 | BEDSIDE
Changes of implanted prosthetic valve stent morphology during transcatheter aortic valve implantation with a balloon-expandable valve
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Background: It has been reported that transcatheter aortic valve implantation (TAVI) with a balloon-expandable valve was associated with valve stent recoil after balloon deflation.

Methods: 3D transesophageal echocardiography (TEE) analysis of implanted prosthetic valve stent morphology in 57 consecutive patients who underwent TAVI with a balloon-expandable valve (SAPIEN XT) was performed. We measured cross-sectional area, minimum diameter and maximum diameter of implanted stent at the basal ring of aortic valve annulus 10 minutes after prosthetic valve implantation. We also measured those parameters at the time of valve implantation in 16 patients. Annulus ratio is defined as implanted valve stent area, divided by aortic valve annulus area which were evaluated before implantation.

Results: Implanted prosthetic valve stents were expanded as intended size at the time of valve implantation (412±6.1 mm², SAPIEN XT 23mm valve n=10, 522 mm², SAPIEN XT 26mm valve n=1, not nominal volume inflation were excluded). 10 minutes after implantation, stent areas got back to almost the same size of aortic valve annulus areas before implantation (annulus ratio 0.97±0.07). Annulus ratio was between 0.9 and 1.1 in 44 (77%) cases, between 0.8 and 0.9 in (16%) cases and less than 0.8 in 2 (4%) cases. These 2 cases had commissure fusions. Implanted stents were more circular than aortic valve annulus before implantation (Sphericity index; 1.10±0.05 vs 1.29±0.09, p<0.0001).

Conclusions: Implanted prosthetic valve cross-sectional area got back to almost the same size of intrinsic annulus areas soon after implantation.

PS489 | BEDSIDE
Comparison of feasibility and efficacy of transcatheter aortic valve implantation in patients aged 75 years and older versus patients less than 75 years of age

Background: Transcatheter aortic valve implantation (TAVI) is a treatment option for elderly patients with symptomatic severe aortic stenosis (AS) who seem to be at high risk for surgical aortic valve replacement due to significant co-morbidities. However, very few studies have investigated the feasibility and efficacy of TAVI for younger patients. Thus, the aim of this study was to evaluate the feasibility and efficacy of TAVI in younger and older patients.

Methods and results: Between October 2006 and October 2013, 790 consecutive patients undergoing TAVI were included in the current analysis. The cohort was divided into 2 groups: patients aged ≤75 years (n=79) and >75 years (n=711). There were significant differences with regard to major co-morbidities which were more frequent in patients aged ≤75 years compared to patients >75 years: history of cancer (22% vs 12%, p<0.001), previous coronary artery bypass grafting (30% vs 11%, p<0.001), and renal insufficiency requiring hemodialysis (11% vs 1%, p=0.007). With regard to echocardiography findings, ejection fractions were not significantly different between the 2 groups. However, regarding mid-term outcome, the survival rate of patients aged ≤75 years was significantly higher in comparison with patients aged >75 years (log-rank p=0.037). The COX regression model showed IDDM, life-threatening bleeding and creatinine clearance (<60 ml/min) as the independent predictors of mid-term cumulative mortality among younger patients.

Conclusions: Although patients aged ≤75 years have more co-morbidities compared to patients aged >75 years, TAVI can be feasible and safely performed. Furthermore, the mid-term outcome seems to be better among patients ≤75 years compared to patients aged >75 years.

PS490 | BEDSIDE
Feasibility and safety of early discharge after transfemoral transcatheter valve implantation with balloon-expandable prostheses: a prospective study
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Introduction: There is currently no consensus on the duration of hospitalization required after transfemoral transcatheter valve implantation (TF-TAVI). We recently reported, retrospectively, that early discharge (within 3 days) was feasible in 31% and safe without any death and a low rate of re-hospitalization at 30 days. We therefore aimed to confirm the feasibility and safety of early discharge after TF-TAVI in a prospective study.

Methods: After implementation of an early discharge pathway in our center in January 2014, we included prospectively, between January 2014 and January 2015, 130 consecutive patients scheduled for TF-TAVI with Edwards prostheses using exclusively local anesthesia. The primary end-point combined death and re-hospitalization from discharge to 30-day follow-up. The proportion of early discharge (within 3 days) and the cause of "non-early" discharge were also assessed.

Results: During the studied period, the mean length of stay was 4.0±2.7 days and 76 (58.6%) patients were discharged early within 3 days including 55 (42.3%) patients discharged within 2 days after the procedure. The main causes of non-early discharge were conduction abnormalities in 33 (25%) patients, major vascular complications in 18 (13.8%) patients, social issues in 11 (8.5%) patients, heart failure in 3 (2.3%) patients, and acute kidney injury in 2 (1.5%) patients. Finally, at 30 days, there was no death and only 5 (6.5%) patients required re-hospitalization.

Conclusions: Early discharge is feasible in slightly over 50% of cases in selected patients scheduled for TF-TAVI using a balloon-expandable and local anesthesia, and is associated with no death and a very low rate of readmission at 30 days. The two main causes of non-early discharge are occurrence of new conduction disturbances and major vascular complications.

PS491 | BEDSIDE
Prevalence and classification of mitral regurgitation in TAVI population
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Background: Mitral regurgitation (MR) is a frequent finding in patients with aortic stenosis (AS) and is associated with important clinical and prognostic implications. Aim of the study is to evaluate the prevalence and classify MR, and assess background differences between functional and organic MR in TAVI population.

Methods: Between 2007 and 2014, 642 patients underwent TAVI for native-
were AS. We classified MR etiology according to valve morphology: organic or functional (normal valve leaflets), unknown, mixed (functional plus organic). Among organic MR (OMR), pts were divided in to fibro-calcific changes group, prolapse, rheumatic and post-radiation group. Functional MR (FMR) was sub-classified in tethering, annular dysfunction/dilation and mixed (tethering + annular dysfunction) groups. MR severity was graded according to multiparametric approach. **Results: MR≥2+ was present in 43.4±5.4%. In this group, MR was organic in 72.7%, functional in 13.9%, mixed in 5.4%. OMR was found to be due to fibro-calcific degeneration, prolapse, rheumatic in 95%, 3.4%, 15% and 0.5% respectively. FMR was caused by tethering in 84.6%, annular dysfunction/dilation 12.8% and mixed functional mechanism in 2.6%. There were significant background differences between OMR and FMR groups in EF (31.6±12.4 vs 38±15.0; p=0.0001). Euroscore (22.2±15.4 vs 34.9±24.2; p<0.0001), left ventricle volumes (EDV 102.2±53.2 vs 150±61.3; ESV 49.9±28.3 vs 100.6±55.3; p=0.001) and mean trans-aortic gradient (53.9±16.9 vs 43±14.9 mmHg; p<0.004). Moreover, OMR was more frequent in females (60.8%) and FMR in males (63.2%) (p=0.04). In OMR group a significant negative correlation between MR severity and aortic valve area (p=0.03) was found, whereas no significant correlation was found in FMR group (p=0.07). **Conclusion: Our study shows that in TAVI population the most frequent cause of MR is fibro-calcific disease, especially in women. In these group of patients MR severity was negatively correlated to aortic valve area.
complete atrioventricular block. Secondary endpoints were the frequency of complete sinoatrial block, syncpe, atrial fibrillation, and cardiological resuscitation. Short-term mortality was determined 6 months after initial presentation. The primary endpoint was reached by 24 TTC patients (13.5%). The prevalence of ventricular tachycardia, ventricular fibrillation, asystole, and complete atrioventricular block was 7.3%, 3.5%, 5%, and 2.8%, respectively. 6-month mortality was significantly higher in patients experiencing life threatening arrhythmias compared to patients without arrhythmias (35% versus 8%; odds ratio = 5.96; 95% confidence interval 2.10 to 16.88; p<0.01). Cardiological resuscitation was performed in 16% of patients and 23% had a history of atrial fibrillation. This need for cardiological resuscitation and a history of atrial fibrillation were also associated with increased 6-month mortality.

Conclusion: Life threatening arrhythmias are a common finding in the acute and subacute phase of TTC and associated with increased short-term mortality.
P5499 | BEDSIDE
Diagnostic utility of whole exome sequencing for the elucidation of genetic architecture in familial dilated cardiomyopathy (DCM): examination of a representative Czech cohort with recent-onset DCM

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Introduction: Clinical heterogeneity of dilated cardiomyopathy (DCM) and its complex genetic architecture complicate disease risk stratification and genetic counseling. Genetic testing might be particularly useful in recent-onset DCM (RO-DCM) with highly variable outcomes.

Methods: Three generation family history was ascertained in 109 consecutive, unrelated patients with RO-DCM (i.e. history of symptoms <6 months, 72% males, mean age 44±10 years, median duration of symptoms 2 months, LV EF 23±7%). Familial DCM was defined as confirmed diagnosis of this disease in ≥2 family members. Cases with familial DCM underwent non-invasive cardiologic clinical workup followed by whole exome sequencing (WES; TruSight Exome; Illumina, USA). Detected variants were confirmed by Sanger DNA sequencing and the ACMG guidelines were followed.

Results: A total of 18/109 individuals (16%) with RO-DCM had familial disease. In 10 of 14 families (72%) indicated for WES we identified a pathogenic variant in the following genes: TTN in 3 cases (21%), followed by MYO1C, TNNI3, MYH7, FLMN, RSM20, SAG3 and DOK1 each in one family (7%, for each mutation), while WES was inconclusive in 4 families (28%).

Conclusion: Application of WES represents a promising strategy for the evaluation of genetic architecture of familial forms of DCM since we were able to identify a pathogenic variant in 72% of these families.

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P5500 | BEDSIDE
Assessment of systolic and diastolic function in systemic light chain amyloidosis: an echocardiographic and cardiac magnetic resonance study

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Background: Cardiac involvement in systemic light-chain amyloidosis (AL) is characterized by normal or slightly decreased left ventricular (LV) ejection fraction, using 2D-echocardiography (TTE) and typically a diastolic dysfunction with left atrial (LA) enlargement. To assess cardiac involvement, the Mayo Clinic staging (MC) using NTproBNP and troponin, allows risk stratification of patients into 3 groups with different outcomes. Cardiac magnetic resonance (CMR) assesses myocardial structure and function, and can complement TTE. The aim of this study was to assess cardiac involvement in patients with AL using both TTE and CMR.

Methods and results: Forty-two consecutive patients (66±10 years, 57% males) in sinus rhythm with confirmed AL, underwent simultaneously TTE and CMR within 24 hours. LAEF was calculated after assessing the maximal and minimal LA volume using 4 and 2 chambers views. Diastolic parameters of CMR were assessed in addition to the LAEF calculated by the area/length formula. LV GLS (−17.5±3.7, p=0.001) and DT TTE (158±45 ms, p=0.001) were significantly lower in patients with LAEF <17.5% (cutoff) vs. those with higher LAEF. LV GLS and DT TTE were correlated (rs=0.7, p<0.001). Mitral deceleration time, E/A ratio and lateral E/e’ ratio, were significantly altered in patients with LAEF <17.5% (cutoff) vs. those with higher LAEF, whereas, they were not significantly different according to maximal LAVi.

Conclusion: Multimodality imaging in patients with AL may allow complementary and functional parameters to be determined at entry and 6 months follow-up.

Results: LAEF ≤17.5% showed significantly lower cardiac viral titers compared to wild-type mice accompanied by a reduced inflammatory score and diminished expression of CD3+ T cells, CD14+ monocytes, as well as NKp46+ cells. Moreover, expression of proinflammatory cytokines was diminished in FOXO3a−/−mice at 7d p.i. Importantly, there was no difference in myocardial mRNA expression of Coxackievirus B3 receptor. Interestingly, FOXO3a gene transfer in vitro had no effect on viral adhesion and entry but significantly inhibited CVB3 replication in cardiac myocytes. On day 3 p.i. FOXO3a−/−mice showed cardiac accumulation of activated NK cells as well as enhanced cardiac IFNγ expression. Ex vivo, NKp46+ NK cells of FOXO3a−/−mice exhibited a higher activation status and enhanced cytotoxic activity with higher frequencies of activated CD69+ and CD27+CD11b+ effector NK cells as well as enhanced expression of IFN-γ accompanied by an upregulation of mIF-155. Moreover, healthy humans heterozygous or homozygous for the longevity-associated FOXO3a SNP rs12212067 exhibit a significantly reduced IFNg expression and cytoytic degranulation of NK cells. Carriers with this SNP suffering from virus(+)+DCMi showed a poorer outcome characterized by enhanced myocardial inflammation and attenuated viral clearance while susceptibility to viral infection was not regulated by FOXO activation.

Conclusion: Our results implicate FOXO3a in regulation of NK cell function and suggest that FOXO3a plays an important role in the innate immune response to viral infection. Thus, enhanced FOXO3a activity may be protective for diseases associated with chronic inflammation such as cancer and cardiovascular disease but disadvantageous to control acute viral infection.

P5502 | BEDSIDE
The impact of atrial fibrillation on a large population with hypertrophic cardiomyopathy

T. Zegkos, D. Parcharidou, G.K. Ethimmiadis, H. Karvounis. Ahepa University Hospital, 1st Cardiology Department, Thessaaloniki, Greece

Purpose: Conflicting evidence exists about the prognostic implication of atrial fibrillation (AF) in patients with Hypertrophic Cardiomyopathy (HCM). The aim of our study was to evaluate the prevalence and prognostic significance of AF in a large northern Greek population with HCM.

Methods: The echocardiographic and clinical correlates of AF were assessed in 509 patients with an established diagnosis of HCM (age first evaluation 52±15.8 years, mean LVEF 52±16.5% and mean LAVi 31±15.8 ml/m2).

Abstract P5500 – Table 1

<table>
<thead>
<tr>
<th>LA emptying fraction</th>
<th>CMR</th>
<th>LAVi (ml/m2)</th>
<th>LGE (ml/m2)</th>
<th>LGE (ml/m2)</th>
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<td>p</td>
<td>&lt;44</td>
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<td>p</td>
<td>p</td>
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<tr>
<td>≥−17.5%</td>
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<td>&lt;0.001</td>
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Results: AF was observed in 509 patients with an established diagnosis of HCM (age first evaluation 52±15.8 years, mean LVEF 52±16.5% and mean LAVi 31±15.8 ml/m2).
years: 67% male). Overall and HCM-related mortality were evaluated during a follow-up of 11±7 years.

**Results:** A total of 119 (23.37%) of 509 patients were diagnosed with AF at index evaluation visit. Paroxysmal AF was present in 79 (15.52%) and non-paroxysmal in 40 (7.85%) HCM patients. Functional impairment was more significant in patients with AF at first evaluation (NYHA class III-IV 29.4% vs 9.7%, p=0.001). Echocardiographically, left atrial (LA) size, E/E' of the intraventricular septum (IVS) and of the lateral (LAT) wall were significantly higher in patients with AF (LA size 4.6±0.6 vs 4.1±0.1 cm, E/E' IVS 16.8±8 vs 13.6±8 and E/E' LAT 11.7±7 vs 9.5±5, all p<0.01). The occurrence of stroke was highly associated with atrial fibrillation (13.4% vs 6.7%, p=0.019). AF conferred an increased risk for overall mortality in our cohort (HR=2.9, 95% CI 1.443–5.841) (figure). Also, AF displayed a high predictive value for HCM-related death (HR=3.238, 95% CI 1.462–7.172). Even in a multivariable model adjusted for established risk factors for HCM, AF remained an independent predictor for overall (HR 2.32, 95% CI 1.079–5.008) and HCM-related mortality (HR 2.49, 95% CI 1.047–5.945).

**Conclusion:** The prevalence of AF in northern Greek patients with HCM is 23.37%. AF was a strong predictor for overall and HCM-related mortality in this HCM population.

**PULMONARY CIRCULATION, IMAGING, OTHER I**

**P5504 | BENCH**

Underdeveloped bronchial arteries in patients with chronic thromboembolic pulmonary hypertension: a risk factor for hemothoptysis associated with balloon pulmonary angioplasty

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**Background:** In recent years, balloon pulmonary angioplasty (BPA) has been proposed as a new therapy for chronic thromboembolic pulmonary hypertension (CTEPH). However, concerns regarding complications such as hemothoptysis and perforation pulmonary edema require careful application to this new therapy. Although there have been a few reports assessing the risk factors for complication associated with BPA, definite risk factors for hemothoptysis have yet to be elucidated. Bronchial arteries (BAs) in patients with CTEPH are often markedly developed as source of collateral perfusion to lung. Since BAs supply up to 30% of cardiac output into lung in patients with CTEPH, and supply not only lung field, but also vasa vasorum of pulmonary artery, their dilatation may have some role in hemothoptysis associated with BPA.

**Purpose:** The purpose of this study was to investigate whether the development of BAs is protective or aggravating for hemothoptysis associated with BPA.

**Methods:** We analyzed the subjects who received BPA during Jan 2013 to Dec 2014. To assess the development of BAs, we analyzed enhanced computed tomography (CT) images of chest, obtained with 64-row multi detector CT scanner within 3 months prior to first BPA session. BAs were identified as round enhanced vessels running together with right and left bronchus. Cross sectional areas of BAs were measured at 1cm distant from their origin from aorta. 4 patients were excluded due to poor image quality, which left 50 patients underwent total of 231 BPA sessions. Patients were divided into two groups, developed BA group and underdeveloped BA group. BPA was performed in all cross-sectional areas of BAs. Hemothoptysis associated with BPA was defined as hemothoptysis observed during and within two days after each BPA session. Mann-Whitney’s U test, Student’s t test and Pearson’s chi square test were used as appropriate to compare patient’s characteristics between these two groups.

**Results:** Background patient’s characteristics such as age, sex, nor hemodynamic indices, such as mean pulmonary artery pressure, cardiac index, 6 minutes walk distance, and WHO functional class, were not significantly different between two groups. Of total of 231 BPA sessions, 18 hemothoptysis events were observed. The percent-age of hemothoptysis events in the developed and under-developed BA group were 3.8% (4 hemothoptysis in 105 sessions) and 11.1% (14 hemothoptysis in 126 sessions), respectively (p=0.039, Pearson’s chi square test).

**Conclusion:** Under-developed BAs was associated with increased risk for hemothoptysis associated with BPA in patients with CTEPH.

**P5505 | BENCH**

Non-invasive assessment of effect of exercise on Pulmonary artery systolic pressure in healthy subjects

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**Aims:** Exercise is increasingly being used to diagnose pulmonary hypertension in its early stages but there are no normal values for Pulmonary Artery Systolic Pressure (PASP) with peak exercise known for different age groups. The aim of current study was to explore the range of PASP with peak exercise in healthy individuals of various ages and look at the factors affecting them.

**Methods and results:** Our study involved patients free of pulmonary hypertension investigated in our centre with treadmill stress echo for atypical chest pain. 201 individuals with a good tricuspid regurgitation signal at rest and exercise were included in the study. Individuals with poor echocardiographic images, inadequate stress testing and evidence that might suggest other disease were excluded. PASP was estimated using four times tricuspid valve regurgitation velocity squared adding a right atrial pressure of 5mmHg. During exercise, PASP increased from rest (27±6±4) to peak (39±7±7). PASP at peak exercise was higher in individuals >50 years old compared with those ≤50 years (35±4±7 vs. 24±5±6, p=0.001). PASP at peak exercise ≥50mmHg was found in 14.8% of individuals >50 Years old compared with 3.7% of individuals ≤50 years old. Age and PASP at rest were independent predictors of PASP at peak exercise. There was no effect of gender.

**Conclusion:** PASP at peak exercise can reach values ≥50mmHg in healthy individuals older than 50 with good exercise capacity. However, high levels of PASP for low level of exercise should be considered abnormal.

**P5506 | BENCH**

Inhibitory effects of TIR/BB-loop mimetic AS-1 on proliferation of pulmonary artery smooth muscle cells from patients with pulmonary arterial hypertension

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**Background:** Pulmonary arterial hypertension (PAH) is characterized by pulmonary vascular remodeling with inappropriate increase of vascular cells and perivascular inflammation. Advanced glycation end-products receptor (RAGE) is implicated in PAH etiology. We have recently reported that Toll/IL-1 receptor (TIR) adaptor protein transduces RAGE signaling. In this study, we tested the hypothesis that TIR/BB-loop mimetic AS-1, an inhibitor of TIR domain-mediated signaling, has antiproliferative effects on pulmonary artery smooth muscle cells (PASMCs) from patients with PAH.

**Methods and results:** PASMCs were obtained from 12 patients with PAH (including 2 patients with BMPR2 mutation and one patient with SMO9 mutation) who underwent lung transplantation. PDGF-BB (10 ng/mL) stimulated proliferation of PASMCs as assessed by 3H-thymidine incorporation (P<0.001). Western blot analysis revealed that PDGF-BB increased the expression of RAGE in PASMCs. PDGF-BB also activated inflammatory signaling in PAH-PASMCs including translocation of NFκB from the cytoplasm to nucleus as assessed by immunofluorescence staining. AS-1 significantly inhibited PDGF-stimulated proliferation of PASMCs (P<0.0001).

**Conclusions:** TIR/BB-loop mimetic AS-1 had an antiproliferative effect on PAH-PASMCs. Inhibition of RAGE signaling may be therapeutically useful in patients with PAH.
Accuracy of echocardiography to evaluate pulmonary vascular and right ventricular function during exercise

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Background: Exercise echocardiography may enable early diagnosis of pulmonary vascular disease, but its accuracy is untested.

Objectives: We compared the accuracy of echocardiography and cardiac magnetic resonance imaging (CMR-MRI) for the assessment of pulmonary vascular and right ventricular function during exercise.

Methods: Exercise imaging was performed in 61 subjects (19 athletes, 9 healthy non-athletes, 8 asymptomatic subjects with familial pulmonary hypertension (CTEPH), 5 with dyspnea post pulmonary embolus and 20 patients with chronic thromboembolic pulmonary hypertension before (n=14) or after (n=6) pulmonary endarterectomy). Echocardiographic measurements included mean and systolic pulmonary artery pressure (mPAP and sPAP), cardiac output (CO), RV fractional area change (RVFAC), tricuspid annular systolic excursion (TAPSE) and RV end-systolic pressure-area ratio (RVESPR). ExCMRrip provided measurements of CO, RV ejection fraction (EF), mPAP and sPAP and RV end-systolic pressure-volume ratio (RVSP/ESV) at rest and during bicycle exercise. Abnormal pulmonary vascular reserve was defined as mPAP/CO slope > -3 mmHg/L/min by ExCMRrip.

Results: Determination of mPAP/CO was possible in 53 of 61 subjects (87%). One (4%) healthy subject, 1 (13%) BMPR2 carrier, 3 (60%) post-pulmonary embolus, 12 (86%) CTEPH and 6 (100%) post-pulmonary endarterectomy patients had abnormal pulmonary vascular reserve. mPAP/CO by echocardiography was higher than observed by ExCMRrip (+0.9 mmHg/L/min, 95% limits of agreement –3.6 to 5.4), but enabled accurate identification of patients with abnormal pulmonary vascular reserve [area under the receiver-operating-characteristic curve 0.88 (0.77 to 1.00; p < 0.0001)]. Simplified relationships between sPAP and exercise intensity had similar accuracy to identify subjects with pulmonary vascular disease [AUC 0.95 (0.88–1.01; p < 0.0001)]. RVFAC by echocardiography correlated strongly with sPAP by ExCMRrip, whereas a moderate correlation was found between TAPSE and RVEF.

Conclusion: Echocardiography is a feasible and accurate tool for the evaluation of pulmonary vascular and RV functional reserve during exercise in clinical practice. Simplified relationships between sPAP and exercise intensity in Watts can be used to identify pathology and may represent a simpler clinical tool by avoiding the need for CO quantification.

Effect of prostacyclin analogues on right ventricular function in patients with pulmonary hypertension

G. Claessen1, A. de Geriche1, F. Schnee2, T. Petit1, S. Dymarkowski3, J.U. Voigt1, R. Willems1, P. Claus1, M. Delcroix3, H. Heidbuchel1, 1KU Leuven, Department of Cardiovascular Sciences, Leuven, Belgium; 2KU Leuven, Department of Imaging & Pathology, Leuven, Belgium; 3KU Leuven, Department of Clinical and Experimental Medicine, Leuven, Belgium; 4Heart Centre Hasselt, Hasselt, Belgium

Background: Prostacyclin analogues are vasodilatory and antiproliferative agents used in the treatment of pulmonary arterial hypertension. The direct effects of prostacyclin analogues on right ventricular (RV) function are still poorly understood. The aim of this study was to investigate the direct effects of prostacyclin analogues on right ventricular (RV) function in patients with pulmonary hypertension.

Methods: Rats (n=31) were subjected to pulmonary trunk banding to induce right ventricular failure. Rats without banding served as healthy controls (n=30). Seven weeks after the operation RV failure was confirmed by echocardiography, showing hypertrophy and dilation of the RV and reduced tricuspid annular plane systolic excursion (TAPSE). The rat hearts were excised and connected to a pressure controlled Langendorff system and perfused with loprostil, treprostinil, epoprostenol or the selective IP receptor agonist, MRE-269 in increasing concentrations. The effect on RV function was evaluated using a balloon tipped catheter inserted into the RV, measuring the hemodynamics. The expression of prostacyclin receptors IP, FP, DP1, TP, EP1, EP2 and EP4 in the RV was examined using quantitative polymerase chain reaction.

Results: All four drugs increased coronary flow rate in healthy hearts as well as in hearts with RV failure. In healthy control hearts, loprostil, treprostinil and MRE-269 increased RV rate pressure product (p<0.015, p<0.0003 and p<0.035, respectively). Only treprostinil was effective in clinically relevant concentrations (0.5mg/mL and 1.5mg/mL). In the failing RV, MRE-269 decreased RV rate pressure product (p<0.0001), while loprostil and treprostinil showed no significant effect.

Conclusion: Echocardiography is a feasible and accurate tool for the evaluation of pulmonary vascular and RV functional reserve during exercise in clinical practice. Simplified relationships between sPAP and exercise intensity in Watts can be used to identify pathology and may represent a simpler clinical tool by avoiding the need for CO quantification.
P5511 | BEDSIDE
Right ventricular function assessed by 2D speckle-tracking echocardiography in pulmonary hypertension. Relation with cardio-pulmonary exercise testing
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Background: Right Ventricular (RV) function is an important prognostic marker in Pulmonary Hypertension (PH) that can be quantitatively assessed by 2D echocardiography speckle-tracking.

Objectives: To assess whether RV longitudinal strain (RVLS) acquired by 2D speckle-tracking predicts exercise performance measured by Cardio-Pulmonary Exercise Testing (CPET) in PH patients. We also related CPET and RVLS to prognostic markers recommended by the American Society of Echocardiography: Fractional Area Change (FAC), RV myocardial performance index (RVMPI), indexed Right Atroial (RA) area, Systolic and Diastolic left ventricular eccentricity index (Ea, Ei) and Tricuspid Annular Plane Systolic Excursion (TAPSE).

Methods: We prospectively recruited 93 consecutive patients with precapillary PH who were referred for CPET and transthoracic echocardiography within a month of each other. Global RVLS and free wall RVLS were analyzed from an apical four chamber view. CPET parameters included Peak oxygen consumption (PeakVO2), percentage of predicted VO2max, maximum workload, ventilatory equivalent of carbon dioxide (VE/VCO2) and O2pulse. Linear then multiple regression analysis was performed with RVLS and prognostic markers as predictors and the CPET parameters as dependent variables.

Results: RVLS predicted VE/VCO2. Global RVLS (R2=14%, p<0.001) was an independent predictor of VE/VCO2. Global RVLS was a stronger predictor of VE/VCO2 than FAC (R2=12%, p<0.001). Global and free wall RVLS were stronger predictors than RVMPI (R2=8%, p=0.003), Ea (R2=7%, p=0.006) and TAPSE. Global RVLS also predicted percentage of predicted VO2max (R2=5.2%, p=0.016) which was not an independent predictor of VE/VCO2. There was no relation between RVLS and peakVO2, maximum workload or O2pulse.

Conclusions: Global RVLS is closely related to function and is an independent predictor of VE/VCO2, a prognostic measure derived from exercise performance. It is a stronger predictor than TAPSE, RVMPI, Ea and FAC.

P5512 | BENCH
The cardioprotective effect of soluble guanosine monophosphate stimulation is abolished in the hypertrophic and failing right ventricle
Aarhus University Hospital, Skeby, Department of Cardiology, Aarhus, Denmark

Background and aim: Phosphodiesterase 5 inhibition protects the healthy right ventricle against ischemia and reperfusion injury. We aimed to investigate whether the cardioprotective effects of phosphodiesterase 5 inhibition and soluble guanylate stimulation is preserved in the hypertrophic and failing right ventricle.

Methods: De-compensated right ventricular failure was induced in male Wistar rats (n=47) by pulmonary trunk banding. The hearts were isolated and perfused in a pressure controlled modified Langendorff setup and randomised to control (CON), isometric preconditioning (IPc, 2 x 5 min of global ischemia) to investigate if cardioprotection by IPC was preserved. The cardioprotective effects of cGMP up-regulation were studied by adding the phosphodiesterase 5 inhibitor vardenafil (VAR, 66nM), the soluble guanylate cyclase stimulator BAY 41-2272 (3 uM, BAY) or their combination (VAR+BAY) to the buffer. To evaluate whether intrinsic cGMP up-regulation inherently induced cardioprotection, we added the cGMP-dependent protein kinase (PKG) blocker KT 5823 (1uM, KT) to the buffer in one group. Subsequently, we used 40 min of global ischemia and 120 min of reperfusion in all groups. The effects of IPC on the right ventricle were evaluated by measurement of the infarct size/area-at-risk ratio (IS/AA).

Results: Pulmonary trunk banding induced right ventricular hypertrophy and de-compensated heart failure. IPC did not induce protection against ischemia and reperfusion injury. Inhibiting cGMP breakdown, stimulating cGMP formation or a combination of both did not protect against ischemia and reperfusion injury. Blocking PKG did not increase infarct size (Fig. 1).

Conclusion: The cardioprotective effect of cGMP stimulation is abolished in the hypertrophic and failing right ventricle.

P5513 | BEDSIDE
Non-invasive multi-modality imaging to evaluate pulmonary arterial elastance in patients with pulmonary hypertension
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Introduction: Effective pulmonary arterial elastance (Ea: end-systolic pressure (ESP)/stroke volume (SV)) reflects a global measure of total afterload. In pulmonary hypertension (PH), ESP is best approximated by pulmonary artery mean pressure (mPAP). Along with SV, both are ideally assessed during right heart catheterization (RHC). Novel imaging modalities, mainly phase contrast (PC) MRI, may offer new insights in Ea estimation through non-invasive surrogates.

Purpose: To test if pulmonary arterial elastance can be assessed non-invasively as the ratio of mean pulmonary artery pressure issued from trans-thoracic echocardiography (TTE) to stroke volume estimated either by PC-MRI or TTE.

Methods: 121 patients were evaluated for group 1 and 4 PH with multimodal imaging and RHC within 48 hours. mPAP was estimated using 2 validated methods: the Chemla’s formula (mPAP = 0.61 x sPAP + 2 mmHg), mean tricuspid regurgitation (TR) gradient added with estimated right atrial pressure based on inferior vena cava. Right ventricle (RV) SV was either measured by PC MRI or extrapolated from Doppler left ventricle (LV) output track SV.

Results: There were good correlations and concordances between RHC and non-invasive derived Ea using TTE mPAP/MRI RV SV (TR: n=96, r2=0.805, Figure 1A; Chemla’s formula; n=100, r2=0.807, Figure 1B). Correlations were significant but weaker when using TTE derived LV SV (TR: n=98, r2=0.630, Chemla’s formula: n=102, r2=0.673).

Conclusion: Ea defined as the ratio of echocardiographic mPAP (mean TR gradient or Chemla’s formula) and PC-MRI SV correlated well with gold-standard RHC invasive values. Added to other parameters of RV morphology and performance, non-invasive Ea may help further estimation of right ventricle-arterial coupling in PH.

P5514 | BEDSIDE
Prevalence and prognostic significance of CT criteria for pulmonary veno-occlusive disease in systemic sclerosis-associated pulmonary hypertension
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Background: Radiological appearances of pulmonary veno-occlusive disease (PVOD) have been reported in more than sixty per cent of patients with systemic pulmonary circulation, imaging, other I / Chronic pulmonary hypertension
observer variabilities of OFDI measurements were almost perfect and better than measurements were highly significant (LA: r=0.77, VA: r=0.80). Inter and intra-

Balloon pulmonary angioplasty (BPA) to the patients with chronic Background:

Health and Medicine, Cardiology Division, Tokyo, Japan

The aim of this study is to evaluate the safety and feasibility of imaging vessel area (VA) were evaluated by two independent observers.

Methods: Eighteen consecutive attempts of OFDI and IVUS in BPA for the pa-

The OFDI imaging is safe and feasible in BPA for patients with chronic thromboembolic pulmonary hypertension

Comparison of intravascular optical frequency domain imaging with intravascular ultrasound in balloon pulmonary angioplasty for the patients with chronic thromboembolic pulmonary hypertension

N. Ikeda, S. Kubota, T. Okazaki, H. Hara, Y. Hiroi. National Center for Global Health and Medicine, Cardiology Division, Tokyo, Japan

Background: Balloon pulmonary angioplasty (BPA) to the patients with chronic thromboembolic pulmonary hypertension (CTEPH) is still an evolving procedure. To comprehend the complex structures of pulmonary arteries of CTEPH, high-resolution imaging system is useful.

Purpose: The aim of this study is to evaluate the safety and feasibility of imaging pulmonary arteries of patients with CTEPH by optical frequency domain imaging (OFDI) in comparison to intravascular ultrasound (IVUS).

Results: 73 patients had pulmonary hypertension secondary to SSc-PAH and 27 patients had pulmonary hypertension secondary to lung disease (PH-LD). In those with SSc-PAH, 62 (84.9%) had 0–1 features of PVOD and 11 (15.1%) had 2–3 features of PVOD. Of the PH-LD group, 20 patients (74.1%) had 0–1 features of PVOD and 7 (25.9%) had 2–3 features of PVOD. Therefore, a total of 18 out of 100 patients (18.0%) with SSc-associated pulmonary hypertension had 2–3 features of PVOD. Interestingly, only four of these 18 patients (22.2%) developed overt PVOD. In terms of survival, two or three radiological features of PVOD conferred worse survival than did 0–1 features of PVOD.

Conclusions: The majority of SSc patients with 2–3 radiological features of PVOD do not develop overt PVOD. However the presence of 2–3 radiological features of PVOD is associated with high mortality. Our results contrast sharply with those previously published in two respects. Firstly, we found that three times fewer SSc-PAH patients had 2–3 features of PVOD. Secondly, less than half as many of these patients developed pulmonary oedema following vasodilator therapy. Therefore, radiological features of PVOD may not be as common in SSc as previously thought. Moreover, the presence of these features does not confer the diagnosis of PVOD.

P5515 | BEDSIDE Comparison of intravascular optical frequency domain imaging with intravascular ultrasound in balloon pulmonary angioplasty for the patients with chronic thromboembolic pulmonary hypertension

N. Ikeda, S. Kubota, T. Okazaki, H. Hara, Y. Hiroi. National Center for Global Health and Medicine, Cardiology Division, Tokyo, Japan

Background: Balloon pulmonary angioplasty (BPA) to the patients with chronic thromboembolic pulmonary hypertension (CTEPH) is still an evolving procedure. To comprehend the complex structures of pulmonary arteries of CTEPH, high-resolution imaging system is useful.

Purpose: The aim of this study is to evaluate the safety and feasibility of imaging pulmonary arteries of patients with CTEPH by optical frequency domain imaging (OFDI) in comparison to intravascular ultrasound (IVUS).

Methods: Eighteen consecutive attempts of OFDI and IVUS in BPA for the patients with CTEPH were evaluated. All complications related to the procedure were recorded. For the OFDI and IVUS imaging comparison, 41 regions were identified by using side branch as landmark and analyzed. Lumen area (LA) and vessel area (VA) were evaluated by two independent observers.

Results: The OFDI catheter was positioned successfully to the target lesion without any angiographical adverse event at all attempts. High-resolution OFDI images were obtained without pre-dilation in 15 attempts. LA and VA measured by OFDI were smaller than those measured by IVUS (LA: 5.7±3.9 mm² vs. 9.1±6.0 mm², VA: 10.3±7.7 mm² vs. 15.1±9.7 mm²). The correlations between the two measurements were highly significant (LA: r=0.77, VA: r=0.80). Inter and intra-observer variabilities of OFDI measurements were almost perfect and better than IVUS measurements.

Conclusions: The OFDI imaging is safe and feasible in BPA for patients with CTEPH. The OFDI provided fair high-resolution images of pulmonary arteries. The correlations between OFDI and IVUS measurements were highly significant. OFDI images provided better inter and intra-observer variabilities than IVUS images, and may contribute to standardization of BPA.

P5517 | BEDSIDE Pulmonary hypertension connection formula provides a more realistic eight-year survival estimates than national institute of health and French registry equations

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National Institutes of Health (NIH) and Pulmonary Hypertension Connection (PHC) registry equations which are based on two different equations using same hemodynamic measures, and French Registry (FR) formula based on a different equation using survival estimates (SE) in patients (pts) with pulmonary arterial hypertension (PAH). Although, the differences among the SEs predicted by FR, PHC and NIH are reported, the clinical relevance of these equations for long-term SE remains to be determined.

In this single-center prospective study, we aimed to compare eight-year observed survival (OS) with baseline SEs predicted by NIH, PHC and FR equations (SE-NIH, SE-PHC and SE-FR) in 204 pts (F 127, M 77, age 43.6±17.4 yrs) with PAH. Sixty seven (82%) pts were under targeted PAH treatments. Subgroups were as follows; idiopathic PAH (n=55), PAH associated with congenital heart disease (APAH-CHD) (n=131), other subgroups of PAH (n=18). Functional class (FC) was 3.1±0.67 and six-minute walking distance was 274.5±132.2 m at diagno-

sis. Baseline pulmonary arterial systolic, diastolic and mean pressures and right atrial pressure (mm Hg) were 71.7±9.4, 47±17.9 and 62±21.3 and 10.5±5.5, respectively. Mean transpulmonary and diastolic pulmonary gradients (mm Hg), and cardiac index (l/min/m²) were 49.9±21.4, 28±18.3 and 2.5±0.83, respectively. Pulmonary vascular resistance was 112±7.9 WU. The eight-year curves of OS and SEs predicted by each equation showed that OS and SE-PHC were comparable at each time points (p=0.73), whereas OS was overestimated by SE - FR (p<0.05) and underestimated by SE - NIH along the survival curve (p<0.05) (Ta-

ble 1).

Table 1. Survival estimates and observed survival

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<td>PHC</td>
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<td>0.71</td>
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<td>0.67</td>
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<td>FR</td>
<td>0.96</td>
<td>0.92</td>
<td>0.90</td>
<td>0.87</td>
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<td>0.81</td>
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<tr>
<td>OS</td>
<td>0.83</td>
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<td>0.75</td>
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</table>

In conclusion, eight-year follow-up in our single-center registry confirmed that PHC equation provided a more realistic SE than NIH and FR models for long-
term survival in pts with PAH. However, NIH equation underestimates and FR equation overestimates the OS, significantly.

**Acknowledgement/Funding:** Evaluation of Pulmonary Hypertension Risk factors AssociatesTED with Survival.

**P5518 | BEDSIDE**

**Pulmonary arterial capacitance in heart failure with preserved and reduced ejection fraction complicated by pulmonary hypertension**

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**Aim:** Reactive pulmonary hypertension (PH) is a severe form of PH secondary to left-sided heart failure (HF). Given the structural and functional abnormalities in the pulmonary vasculature that occurs in reactive PH, we hypothesized that pulmonary artery capacitance (PAC) may be profoundly affected, with implications on clinical outcome.

**Methods and results:** The studied 393 HF patients with 124 (32%) classified as passive PH and 91 (36%) as reactive PH had pulmonary arterial hypertension (PAH). Mean PAC was highest in patients without PH (4.5±2.1 ml/mmHg), followed by passive PH group (2.8±1.4 ml/mmHg) and lowest in reactive PH (1.8±0.7 ml/mmHg) (P=0.0001). PAC and pulmonary vascular resistance (PVR) fitted well to a hyperbolic inverse relationship (PAC=0.25/PVR, R2 = 0.70), with reactive PH patients dispersed almost predominantly on the flat part of the curve where a reduction in PAC is associated with a small improvement in PAC. The hyperbolic curves for heart failure with preserved(PHPEF) and reduced (PHIEF) ejection fraction were similar when compared by slopes (P=0.32). Elevated pulmonary capillary wedge pressure was associated with a significant lowering of PAC for any PVR (P=0.036). During a median follow-up of 31 months, both reactive PH (hazard ratio [HR] 2.59, 95% confidence interval [CI], P=0.02) and reduced PAC (HR 0.72 per 1 ml/mmHg increase, 95% CI 0.59–0.88, P=0.001) were independent predictors of mortality.

**Conclusions:** The development of reactive PH is associated with a marked reduction in PAC. PAC is a strong independent hemodynamic marker of mortality in HF and may contribute to the increased mortality associated with reactive PH. Modifications of the pulmonary vessels characteristics were similar in both PHIEF and PHPEF.

**P5519 | BEDSIDE**

**The use of the diastolic pressure gradient in the diagnosis of group 2 pulmonary hypertension can identify patients at increased risk for adverse events**

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**Background:** The robustness of the transpulmonary gradient (TPG) in identifying a more active form of group 2 pulmonary hypertension (PH) has been criticized.

**Purpose:** To evaluate the prognostic risk associated with TPG and diastolic pressure gradient (DPG) in group 2 PH patients and to compare outcomes to those with pulmonary arterial hypertension (PAH).

**Methods:** A prospective cohort study of 261 patients with PH referred for right heart catheterization and followed for a median of 933 days. Elevated TPG and DPG were defined as > 12 mmHg and > 7 mmHg, respectively.

**Results:** Group 2 PH (n=103) patients experienced more dyspnea, fatigue, and angina compared to PAH patients (n=108), with no difference in death (9.8 vs. 9.3%; P=0.893) and a trend for greater hospitalization rates (55.9 vs. 48.2%; P=0.262). Amongst the group 2 PH patients, a high TPG (n=56) was associated with reduced 6-minute walk distance (266.8±98.7 vs. 377.8±90.1 m; P=0.001) but no difference in hospitalization (58.9 vs. 52.2%; P=0.494) or death (8.9 vs. 10.9%; P=0.751) when compared to the low TPG group. Among patients with high TPG, high DPG (n=13) was associated with worse outcomes compared to those with low DPG (n=43) on unadjusted Cox regression (hazard ratio [HR] 1.94, 95% confidence interval [CI] 0.92–4.10, P=0.001). When compared to patients with low DPG (n=89), those with high DPG (n=13) had greater risk of hospitalization or death on log-rank tests for equality of survival functions (P=0.047) and unadjusted Cox regression (HR 1.97, 95% CI 0.99–3.81, P=0.052).

**Conclusion:** Patients with group 2 PH have similar rates of adverse outcomes when compared to patients with PAH. DPG was more useful than TPG in identifying group 2 PH patients who are at increased risk of adverse events.

**Acknowledgement/Funding:** Mach-Gaensslen Foundation of Canada Studentship Award, University of Ottawa Heart Institute ORACLE Innovation Cluster

**P5520 | BEDSIDE**

**Reduction in NT-proBNP and its correlation with survival in patients with CTEPH treated with riociguat: 2-year results from the CHEST-2 long-term extension study**

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**Background:** In pts with pulmonary hypertension (PH), N-terminal prohormone of brain natriuretic peptide (NT-proBNP) is an established biomarker of disease severity. In the 16-week CHEST-1 study, riociguat significantly reduced NT-proBNP levels compared with placebo in pts with chronic thromboembolic pulmonary hypertension (CTEPH).

**Purpose:** We present the 2-yr NT-proBNP data from CHEST-2.

**Methods:** Pts with inoperable CTEPH, or persistent/recurrent PH after pulmonary endarterectomy entered CHEST-2 after completing CHEST-1 without ongoing drug-related SAEs. All pts received riociguat individually adjusted up to 2.5 mg tid. Primary endpoints were safety and tolerability; change in NT-proBNP was an exploratory endpoint.

**Results:** Of 243 pts completing CHEST-1, 237 (98%) entered CHEST-2. At 2 yrs, mean±SD NT-proBNP had improved by −31±1201 pg/ml (n=80) from CHEST-1 baseline in the overall population. In the inoperable and persistent/recurrent PH subgroups, NT-proBNP improved by −351±1308 pg/ml (n=60) and −194±816 pg/ml (n=20), respectively, from CHEST-1 baseline. A Cox proportional hazards regression analysis showed significant correlation between change from baseline in NT-proBNP levels and both survival (HR=0.85; 95% CI 0.79 to 0.92; p<0.0001) and clinical worsening-free survival (HR=0.87; 95% CI 0.83 to 0.92; p<0.0001), using −300 pg/ml as the unit of change for HR. Figure 1 shows the difference in survival for pts with NT-proBNP levels above and below the clinically relevant threshold of 1800 pg/ml at baseline and follow-up.

**Conclusion:** Reduction in NT-proBNP in pts with CTEPH treated with riociguat was sustained for up to 2 yrs in CHEST-2. Change from baseline in NT-proBNP correlated with survival and clinical worsening-free survival.

**Acknowledgement/Funding:** Editorial assistance was provided by Adelphi Communications Ltd (Bollington, UK), supported by Bayer Pharma AG.

**P5521 | BEDSIDE**

**Left main coronary artery extrinsic compression by enlarged pulmonary artery in patients with pulmonary arterial hypertension**

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**Background:** Extrinsic compression of the left main coronary artery (LMCA) by an enlarged main pulmonary artery (nPA) is a recognized cause of angina and sudden death in patients with pulmonary arterial hypertension (PAH).

**Purpose:** To evaluate prospectively the prevalence of LMCA compression in PAH patients and to identify the predictors of compression.

[Figure 1: Survival by NT-proBNP levels]
Results: The clinical evaluation of 765 patients with PAH revealed the presence of angina or angina-like symptoms in 121 patients (16%). All of them underwent CTA that showed C in 35 patients (29%), D in 49 (41%), P in 10 (8%) and N in 27 (22%). The 94 patients with C, D and P patterns underwent CA and LMCA stenosis ≥50% was found in 48 of them (48/121 = 40%); the prevalence of LMCA stenosis ≥50% at CA in C, D and P patterns was, respectively, 91%, 31% and 10%. Forty-five patients underwent PCI and stenting of LMCA and 3 underwent mPA surgical reduction without major complications. Symptomatic improvement was observed in all patients and after a mean follow-up of 23 months no deaths were observed. Logistic regression and ROC analysis identified a mPA diameter (mPAd) > 40 mm assessed at the CT scan as a predictor of LMCA stenosis ≥50%.

Conclusions: The prevalence of extrinsic compression of LMCA in our population is quite high ranging from 6% of all PAH patients to 40% those presenting with angina or angina-like symptoms. CTA is useful as a screening tool in symptomatic patients and CA is the gold standard for the final diagnosis. PCI with stenting is a safe and effective procedure. A mPAd > 40 mm at CT scan is the best predictor of LMCA compression.

P5524 | BEDSIDE
Hemodynamic effect of initial combination therapy as compared to initial monotherapy in pulmonary arterial hypertension: a single blinded evaluation of patients enrolled in the AMBITION study
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Background: Pulmonary arterial hypertension (PAH) is a severe disease with complex pathogenesis, for which upfront combination therapy is an attractive option.

Purpose: To compare functional and hemodynamic changes after 6 months of first line combination therapy (C) with Ambisentan (A) and Tadalafil (T) versus first line monotherapy (M) with A or T in subjects with PAH enrolled in a single centre in the AMBITION study.

Methods: Consecutive naive patients with World Health Organization (WHO) functional class III-IV PAH were included in the study. They were randomized to receive initial C (A and T) or M (A or T). At baseline and after 6 months of treatment, minute walk distance (6MWD) and right-heart catheterization were performed. Statistical analysis was performed using Student’s t-test for the analysis of baseline data versus 6 months within each group and for the comparison of the absolute changes between the C and M groups.

Results: Thirty patients were randomized: 19 in the C group [53% connective tissue disease PAH (CTD-PAH) and 47% idiopathic PAH (IPAH)] and 11 in the M group [64% IPAH, 36% CTD-PAH; 6 received A, 5 received T]. No statistically significant differences were found in baseline demographic, functional and hemodynamic characteristics between C and M groups. Hemodynamic and 6MWD changes after C or M treatment are shown in the Table.

Conclusions: Both initial C and initial M improved hemodynamics and exercise capacity; however initial C is associated with statistically significant larger improvements as compared with M in patients with PAH.

P5522 | BEDSIDE
RV free wall strain adds significantly to predicting functional capacity in PAH
L. Wright1, N. Dwyer2, T. Marwick1. L. Wright1, N. Dwyer2, T. Marwick1.
Background: Assessment of pulmonary arterial hypertension (PAH) is dependent on assessment of PA systolic pressure (PASP) and pulmonary vascular resistance (PVR), but often ignores RV function. We sought whether RV systolic strain adds to predicting functional capacity.

Methods: Echocardiography was performed on the same day as 6MWD on a PAH cohort (N=177, F:75%, 63±13.3 years; PASP 43±22 mmHg). Pts were on Rx for PAH therapy for mean 487 days (±470). Standard echo measurements were performed following ASE guidelines. RVGLS was performed using VVI. Linear regression was used to examine independent associations. Sequential models began with standard clinical variables and RV function parameters (RVGLS, FAC, TAPSE) were used to examine incremental benefit.

Results: Exercise capacity was associated with RV end-diastolic area (β=−0.73 p<0.001), fractional area change (β=0.27 p<0.001), PASP (β=−0.32 p<0.001), PVR (β=−0.29 p<0.001) and RV GLS (β=−0.48 p<0.001). The clinical model (Graph 1) consisting of age (β=−0.5 p<0.001), sex (β=0.38 p<0.001), BSA (β=−0.09, p=0.2), HR (β=−0.28 p<0.001), PASP (β=−0.23, p=0.008), PAH Rx (β=−0.16, p=0.012), 6MWD (β=−0.29, p=0.002) was improved by RV strain (β=0.21, p<0.01) (model R2=0.60, F change p=0.010). However, the clinical model was not improved by addition of TAPSE (β=0.08, p=0.27) (model R2=0.58, F change p=0.27) or FAC (β=0.03, p=0.67) (R2=0.57, F change p=0.67).

Conclusion: The functional status of patients with PAH is dependent on RV function (measured as RVGLS) as well as clinical factors and PASP.
PULMONARY CIRCULATION, IMAGING, OTHER II

P5525 | BEDSIDE
Resistance, compliance, and the time constant of the pulmonary circulation at exercise
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Background: The resistive (pulmonary vascular resistance, Rp) and pulsatile (pulmonary arterial compliance, Cp) components of right ventricular afterload are tightly coupled in an inverse hyperbolic relationship. Across different disease populations, the ratio of Rp and Cp is a consistent (RC-time), though apparently influenced by pulmonary arterial wedge pressure (PAWP). We examined whether RC-time was acutely modifiable during exercise.

Purpose: To describe the Rp and Cp of trained and untrained healthy adults at rest and during submaximal exercise, and the behavior of RC-time.

Methods: Sixteen sedentary subjects (10M/6F; age: 55±7 years) and sixteen athletes (16M; age: 54±6) were studied at rest and during Light (100bpm) and Moderate (sedentary, 120bpm; athletes, 130bpm) intensity cycle-ergometry exercise. Right heart catheterization was performed to measure pulmonary pressures, with simultaneous echocardiography. At each exercise intensity, pulmonary artery systolic, diastolic, mean, and wedge pressures were manually analyzed, offline, beat-by-beat. Stroke volume and cardiac output were derived from Doppler echocardiography.

Results: Data are presented in Table 1. Rp was unaffected by exercise, while Cp decreased at exercise (p≤0.05). Accordingly, RC-time decreased at exercise (p<0.01). PAWP increased at exercise (p<0.01).

Table 1. Exercise hemodynamic data

Control Sedentary Light Ex Moderate Ex Sedentary Athletes<br>HR (bpm) 63.8±6 63.1±11 56.4±4 62.1±10 63.2±11 63.6±11<br>PAWP (mmHg) 11±2 11±3 16±4 19±5 14±5 16±6<br>Rp (mmHg/ml/s) 0.08±0.03 0.09±0.03 0.08±0.04 0.07±0.03 0.07±0.03 0.07±0.03<br>Cp (ml/mmHg) 4.8±0.9 5.9±2.1 3.3±0.5 3.7±1.8 3.3±0.7 3.5±1.2<br>RC-time (s) 0.38±0.08 0.41±0.16 0.28±0.19 0.26±0.09 0.25±0.07 0.24±0.07**

Conclusions: In healthy adults, even submaximal exercise modifies the relationship between Rp and Cp, resulting in decreased RC-time. Right ventricular pulsatil afterload increases despite stable steady-flow resistance, possibly mediated by exercise-associated increases in PAWP.

Acknowledgement/Funding: Heart and Stroke Foundation of Ontario Grant-in-aid (#T7336), Canadian Institutes of Health Research Operating Grant (#130447)

P5527 | BENCH
Evaluation of right atrial function using speckle tracking strain in patients with pulmonary hypertension
Y. Fukuda, H. Tanaka, Y. Motoji, K. Ryo, H. Sano, T. Sawa, Y. Mochizuki, K. Matsumoto, N. Emoto, K. Hirata. Kobe University, Division of Cardiovascular Medicine, Department of Internal Medicine, Kobe, Japan

Background: Right atrial (RA) function could be a prognostic factors as well as right ventricular (RV) function in patients with pulmonary hypertension (PH), but its non-invasive evaluation is limited. Our objective was thus to evaluate RA function using two-dimensional speckle-tracking strain in PH patients.

Methods: Eighty-two PH patients with mean pulmonary artery pressure (mPAP) of 39±11mmHg (all: 25±mmHg) were recruited. RA function was assessed two-dimensional speckle-tracking strain from RV-focused apical 4-chamber view. RA strain was calculated as (trans-tricuspid gradient/cardiac output); Cp was calculated as (stroke volume/pulse pressure).

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Acknowledgement/Funding: Heart and Stroke Foundation of Ontario Grant-in-aid (#T7336), Canadian Institutes of Health Research Operating Grant (#130447)

P5528 | BENCH
The glucagon-like peptide-1 receptor agonist improves hypoxia induced pulmonary hypertension in mice model
T. Kimura, K. Tajiri, K. Kyo, N. Murakoshi, S. Sakai, K. Aonuma. Tskuba University, Cardiovascular Division, Faculty of Medicine, Tskuba, Japan

Background: Glucagon-like peptide-1 receptor (GLP-1R) agonist, liraglutide is an incretin hormone mimetics, a drug for diabetes mellitus. Recently, it is reported that GLP-1R agonist inhibits endothelial dysfunction, inflammation, and cell proliferation which are the major molecular findings for pathophysiology of pulmonary arterial hypertension (PAH). But the effect of GLP-1R agonist on PAH has been unclear.

Purpose: To investigate the effect of GLP-1R agonist on the development of PAH.

Methods: The study population included 282 subjects: 92 patients with PAH (age = 55±13 years; 62% female), 105 patients with systemic sclerosis (SSc) (age = 55±13 years; 82% female), and 85 comparable healthy control subjects. All the patients underwent a comprehensive clinical examination, standard Doppler echocardiography and 2DSE analysis by Vivid E9 ultrasound system (General Electrics – Horton - Norway). Analysis was performed for two-dimensional strain from the 4-chamber apical views for the basal and mid septal and lateral segments. RA reservoir function was calculated as (stroke volume/pulse pressure). Rp was calculated as (transpulmonary gradient/cardiac output); Cp was calculated as (stroke volume/pulse pressure). RC-time, right ventricular body weight ratio of liraglutide+hypoxia group were significantly smaller (32.3±13.2% in PAH vs. 40.2±8.9% in SSc and 57.2±8.1% in controls; PAH vs controls and SSc both p<0.0001) to predict the presence of PAH. In the overall population, by multivariable analysis, RA area index (OR: 3.1; 95% CI: 2.1–3.9; p<0.001) and PAH (OR: 2.3; 95% CI: 1.1–1.7; p<0.001) were powerful independent determinants of RA strain.

Conclusions: This study evaluated the first time RA reservoir function in patients with and without PAH. RA reservoir function is severely impaired in patients with PAH. This is probably an adaptive phenomenon of RA to increased RV afterload and decreased RV function induced by PAH as suggested by the correlation of RA strain with PAH and RA area. SSc patients, compared to healthy subjects, showed an impaired RA reservoir function despite still in the limits of normal.

Conclusion: RA strain may be of a valuable additive factor for the management of PH patients, thus have potential clinical applications.

P5529 | BENCH
The glucagon-like peptide-1 receptor agonist improves hypoxia induced pulmonary hypertension in mice model
T. Kimura, K. Tajiri, K. Kyo, N. Murakoshi, S. Sakai, K. Aonuma. Tskuba University, Cardiovascular Division, Faculty of Medicine, Tskuba, Japan

Background: Glucagon-like peptide-1 receptor (GLP-1R) agonist, liraglutide is an incretin hormone mimetics, a drug for diabetes mellitus. Recently, it is reported that GLP-1R agonist inhibits endothelial dysfunction, inflammation, and cell proliferation which are the major molecular findings for pathophysiology of pulmonary arterial hypertension (PAH). But the effect of GLP-1R agonist on PAH has been unclear.

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Conclusion: RA strain may be of a valuable additive factor for the management of PH patients, thus have potential clinical applications.
than that of saline-hyposia group (P < 0.01). And the RT-PCR analysis showed that the expression of ENOS mRNA in the lung tissue was significantly higher in liraglutide-hyposia group than saline+normoxia group.

Conclusion: GLP-1R agonist reduces right ventricular pressure in hyposxia induced PAH mice. This effect is suggested to be through the increased production of NO in pulmonary vessel.

P5559 | BEDSIDE
20 speckle tracking analysis of right atrium in patients with pulmonary hypertension
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Background: Right atrial (RA) strain analysis by two-dimensional speckle track (2DST) is a valid tool to assess RA function.

Aim: To analyze RA strain in a population of patients with pulmonary arterial hypertension (PAH) and to correlate its value with functional and haemodynamic parameters.

Methods: One hundred and three subjects (age = 57±15 years; 60% female) underwent a complete clinical examination, six minute walking distance (6MWD), standard Doppler echocardiography and 2DSE analysis by Vivid E9 ultrasound system (General Electrics - Norway) within one hour of right heart catheterization (RHC). Analysis was performed for two-dimensional strain from the 4-chamber apical views for the basal and middle segment of RA lateral wall. Right atrial systolic (RAa), right atrial early diastolic strain (RAe SR) and right atrial late diastolic (RAa) strain and strain rate (SR) were considered representative respectively of "reservoir", "conduit" and "contractile" function. All measurements were averaged on at least 3 consecutive cycles.

Results: At univariate analysis CI was related to 6MWD (p < 0.05; r 0.26), RAa strain and strain rate (SR) were considered representative respectively of pulmonary vascular resistance (PVR) (p < 0.05; r 0.26), right atrial pressure (RAP) did not correlate to 6MWD.

Conclusions: The 2DST derived strain and SR is a new tool for RA function assessment. Our findings suggest that RAe SR reflecting atrial stiffness has a significant role in PAH patients functional capacity. RA functional evaluation should be included in the non-invasive follow up of PAH patients.

P5560 | BEDSIDE
Right ventricular function in patients with systemic sclerosis without pulmonary arterial hypertension
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Background: Cardiac dysfunction in systemic sclerosis (SSc) is associated with poor clinical prognosis. Right ventricular involvement in these patients is typically associated with pulmonary arterial hypertension (PAH).

Aim: To evaluate right ventricular function and non-invasive hemodynamics by transthoracic echocardiography in SSc patients without overt cardiac dysfunction and no PAH show increased values of PASP and PVR, and borderline right ventricular involvement compared to controls.

Methods: We examined 75 women (mean age 53.13±10.1y) with confirmed SSc (mean disease duration-DD 7.19±1y) and 21 age-matched women volunteers (mean age 52.61±8.3y). Pulse wave velocity (PWV, Compitor SR) and transthoracic echocardiography (Philips I.E33) were performed. SSc patients were divided into 2 groups according to the median of DD: ≤3 years (39pts) and >3 years (36pts).

Results: There were no differences in PWV between SSc and controls. Patients with DD >3 years had higher PWV than DD ≤3 years (log PWV: 2.23±0.23 vs 2.13±0.16m/s, p=0.028). Patients with longer DD had higher PWV than controls (log PWV: 2.23±0.23 vs 2.11±0.16m/s, p=0.029). Moreover, echocardiographic indices showed impaired right ventricular function in the former (tab 1). In SSc pts with DD >3 years PWV correlated with clinical and echocardiographic parameters of pulmonary circulation: age (r=0.64; p<0.0001), AcT (r=−0.38; p=0.021), TRPG (r=0.34; p=0.04). Multiple linear regression analysis showed that PWV was independently associated with disease duration (r=0.22; p=0.02), AcT (r=−0.215; p=0.03) and age (r=−0.44; p<0.001).

Conclusions: Long lasting SSc simultaneously leads to the increased stiffness of large systemic arteries and to the progressive impairment of right ventricular function and its coupling to the pulmonary arterial bed.

P5561 | BEDSIDE
Follow-up of the pulmonary right-to-left shunt with transthoracic echocardiography in patients with hereditary haemorrhagic telangiectasia
V.M.M. Vorselaars 1, S. Velthuis 1, R.J. Snijder 2, C.J.J. Westerman 1, J.-A. Vos 3, J.J. Mager 2, M.C. Post 1, 2St Antonius Hospital, Department of Cardiology, Nieuwegein, Netherlands; 1St Antonius Hospital, Department of Pulmonology, Nieuwegein, Netherlands; 3St Antonius Hospital, Interventional radiology, Nieuwegein, February 2019

Introduction: Pulmonary arteriovenous malformations (PAVMs) are associated with severe neurological complications in patients with hereditary haemorrhagic telangiectasia (HHT). Transthoracic contrast echocardiography (TTCE) is the first-line screening technique for the detection of pulmonary right-to-left shunts (RLS) and only moderate and large shunts seem to have clinical implications.

Purpose: Five years after the initial TTCE we evaluated the evolution of the pulmonary RLS in a single centre cohort.

Methods: All HHT patients underwent a second TTCE five years after screening. Patients with a history of PAVM embolisation were excluded. Occlusion of the left ventricle was graded with a three grade scale. The TTCE after 5 years was compared to the TTCE performed at screening.

Results: In total 162 patients (55% female, 65.4% HHT type 2, age at follow up 50.6±14.0 years) were included (expected patient number at presentation 190). The median follow-up time was 5.4 years (interquartile range 5.1–5.9 years). A pulmonary RLS was present in 93 patients (57.4%) at screening and 104 patients (64.2%) at follow-up. Increase in shunt grade was seen in 27 patients (16.7%). A significant increase was seen in 15 of these patients (55.6%) and embolisation was indicated in 6 patients (22.2%). Embolisation was feasible in 3 patients (1.9%) in whom the shunt increased within one grade but with increase of the PAVM on computed tomography. There were no complications.
Conclusions: Even in patients with no treatable PAVMs at screening, after 5 years treatable PAVMs are present in 6%. In this population there is a number-needed-to-screen of 18.

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The availability of dual-energy computed tomography for the optimal diagnosis of chronic thromboembolic pulmonary hypertension
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Introduction: Balloon pulmonary angioplasty (BPA) improves clinical status and hemodynamics in patients with chronic thromboembolic pulmonary hypertension (CTEPH). Because the success of reperfusion of occluded vessels is considered to depend on the patency of the distal vessels, the assessment of regional perfusion and collateral circulation is critical for selecting the target lesions when performing BPA. Lung perfusion scintigraphy remains a widely used imaging modality for the diagnosis of CTEPH, this modality seems to lack sensitivity in spite of its high specificity and it cannot evaluate collateral circulation. Dual-energy CT (DECT) is a useful modality for evaluating lung perfusion and collateral circulation in CTEPH, but it has not been used in a single exam.

Purpose: The purpose of this study was to investigate the utility of DECT for the quantitative diagnosis of CTEPH.

Methods: A total of 59 patients (15 with CTEPH, 13 with acute pulmonary thromboembolism (APE), and 31 controls) who underwent DECT were enrolled. Diagnosis of CTEPH and APE was established by perfusion scintigraphy and pulmonary angiography. Patients with PH were defined as those showing a tricuspid regurgitation pressure gradient greater than 40 mmHg in echocardiography. All patients underwent DECT using the same protocols for both scanning and injection of contrast media. The iodine map on admission was analyzed, and the volume fraction in each range of CT values in the pulmonary arterial and the systemic arterial phase was investigated.

Results: The volume fraction with a CT value less than 20 Hounsfield Units (HU) was significantly higher in patients with CTEPH than in the other groups (CTPH: 56.5±6.0%, APE: 31.0±5.3%, PH: 27.6±4.6%, control: 27.9±4.2%, p<0.005). Receiver-operating characteristic curve analysis showed that a volume fraction with a CT value less than 20 HU had the highest cut-off value for the quantitative diagnosis of CTEPH, demonstrating 86.7% sensitivity and 79.5% specificity. Volume fraction with CT values greater than 20 HU in the other groups was significantly decreased between the pulmonary arterial phase and the systemic arterial phase, but these values in patients with CTEPH remained unchanged (CTEPH: 43.5±6.0% vs. 31.9±6.7%, p=0.21, APE: 69.0±5.3% vs. 21.5±4.3%, p<0.001, PH: 72.4±4.6% vs. 51.2±8.3%, p=0.04, control: 72.1±4.2± vs. 30.8±9.6%, p=0.001).

Conclusions: DECT would be useful not only for the quantitative diagnosis of CTEPH but also for the detection of optimal target lesions by evaluating collateral circulation when performing BPA.

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Clinical impact of treatment of atrial fibrillation in patients with pulmonary hypertension
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Purpose: Atrial fibrillation (AF) is frequently observed arrhythmia in patients with pulmonary hypertension (PH). Its prevalence and impact of treatment on prognosis of patients are not known.

Methods: We retrospectively studied the prevalence of AF and survival in 1021 patients with PH (aged 59±14 years, 454 males). Results: AF was observed in 156 (15%) patients (42% paroxysmal AF). Patients with paroxysmal AF were in lower NYHA functional class compared to the rest patients with PH (p=0.01). AF died during mean follow-up of 5.1±2.3 years. Treatment strategy and mortality rates are shown in Table. Amiodarone was the most frequently used drug in patients with PH. Forty-eight percent of patients with PH had more than one rhythm and treatment strategy was applied. Permanent AF was observed in 156 (15%) patients (42% paroxysmal AF). Patients with permanent AF had higher vWF activity than those without (133.5±69.3% vs. 95.3±36.8%, p<0.05) or atherosclerotic plaques (123±57% vs. 99±45%, p<0.05) than in those without.

Conclusions: Patients with PH had high prevalence of AF. Permanent AF is associated with worsening of functional class. Rhythm control strategy seems to have lower mortality rate in PH population.

P553 | BEDSIDE
Accelerated atherosclerosis in systemic lupus erythematosus patients with secondary antiphospholipid syndrome
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Introduction: Patients with antiphospholipid syndrome (APS) have been evaluated in the context of accelerated atherosclerosis in numerous studies, bringing this concept into the focus regarding proper treatment of this population of patients. Carotid intima-media thickness (cIMT) has been established as a distinct marker of cardiovascular risk. The aim of this study was to evaluate relationship between presence of more than one antiphospholipid antibody (aPL) and cIMT values in SEL patients with secondary APS.

Materials: We analyzed 80 patients with systemic lupus erythematosus (SLE) and secondary APS 74 female (92.5%) and 6 male (7.5%), average age 49.4±13.1 years. In all patients presence of lupus anticoagulans (LA), anticardiolipin (aCL IgG/IgM) and anti-j2 glycoprotein-I (anti-j2GPI IgG/IgM) antibodies has been established, and they were classified into group with only one or more than one aPL present in any combination. Measurement of cIMT has been performed on common carotid artery (CCA), its bifurcation (CCAbif) and internal carotid artery (ICA) on both sides. We defined cIMT values 1.1mm and higher as plaque presence.

Results: There were 63.8% patients with more than one aPL present. Prevalence of standard atherosclerotic risk factors was below 40%. Age, hypertension presence of diabetes mellitus and hyperlipidemia resulted in higher values of cIMT in studied group patients. Average values of cIMT were significantly higher in patients with more than one aPL present for almost all segments of carotid trunk (CCA bif, p=0.009, CCA bif right, p=0.034, CCA bif left, p=0.093, CCA bif right, p=0.632, ICA right, p=0.027, ICA left, p=0.544). After adjustment for age, current cigarette smoking, diabetes, hypertension and hyperlipidemia, the relative odds for atherosclerotic plaque presence on carotid arteries in SEL patients with more than one aPL present was 4.19 (95% confidence interval 0.09 to 0.95, p=0.041).

Conclusion: Presence of more than one aPL in SEL patients with APS is independent predictor of premature atherosclerosis. In this subgroup of APS patients more aggressive approach towards prevention and control of standard atherosclerotic risk factors is crucial.

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Advanced atherosclerosis in rheumatoid arthritis: the role of von willebrand factor activity
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Objective: To evaluate association between von Willebrand factor (VWF) activity, inflammation markers, disease activity, cardiovascular risk scores, and advanced subclinical atherosclerosis in patients with rheumatoid arthritis (RA) and low cardiovascular risk.

Methods: Abovementioned parameters were determined in blood samples of 74 nondiabetic, normotensive, nonlipemic, female subjects (42 patients and 32 matched healthy controls, age 45.3±10.0 vs. 45.2±9.8 years), Framingham, Reynolds, and QRISK2–2013 cardiovascular risk scores were calculated in all subjects. Intima-media thickness (IMT) was measured at common carotid, bifurcation, and internal carotid arteries. Subclinical atherosclerosis was defined as IMT above IMTmean+2SD in controls at each carotid level and atherosclerotic plaque as IMT>1.5 mm. Majority of RA patients were on methotrexate (83.3%), none on steroids >10 mg/day or biologics.

Results: Subclinical atherosclerosis was more frequent in RA patients than in controls (35.7% vs. 3.1%, p<0.001). RA patients with more advanced atherosclerosis had higher VWF activity than those without (133.5±69.3% vs. 95.3±36.8%, p<0.05). Predictive value of VWF was confirmed by logistic regression analysis. VWF activity correlated significantly with inflammation markers, disease activity, rheumatoid factor concentration, anti-CCP antibodies, Framingham, Reynolds, and QRISK2–2013 risk scores, Framingham, Reynolds, and QRISK2–2013 risk score, VWF activity was higher in participants with subclinical atherosclerosis (130±68% vs. 97±38%, p<0.05) or atherosclerotic plaques (123±57% vs. 99±45%, p<0.05) than in those without.

Conclusions: We demonstrated association of VWF activity and advanced subclinical atherosclerosis in low-risk RA patients as well as its correlation with inflammation markers, disease activity, and Framingham, Reynolds, and QRISK2–2013 cardiovascular risk scores. Therefore, VWF might be a valuable marker of early atherosclerosis in RA patients.
Background: Psoriatic arthritis (PA) is a cardiovascular risk factor but data regarding scope and time of cardiovascular involvement (including atherosclerosis) and inflammation role in the pathogenesis of atherosclerosis in patients with PA. In our study we assessed evaluation of early cardiovascular involvement in young patients with psoriatic arthritis.

Methods: Cross-sectional study involved 39 consecutive patients with psoriatic arthritis (PAGroup) diagnosis on the basis of ASAS criteria and modified CASP-PSA criteria. Both groups were comparable regarding date of diagnosis and duration ≤10 years. There were 90 patients in control group (CG) with performed CT coronary angiogram, who corresponded to PAG by age, gender, hypertension, hiperlipidemia, smoking, BMI. Cardiovascular assessment was performed using clinical and laboratory exams, echocardiographic examinations, carotid arteries ultrasound and CT coronary angiogram.

Results: Mean age of PAG was 45.1, 25–60 years, (53.9% women) and CG: 42.4, 23–59 years (46.7% women). The mean duration of disease was 18 months. Inflammation disease activity assessed with the scales: BASDAI and ASDAS were considered as high, PAG patients had significantly lower LDL cholesterol values: 51.2±14.5 vs. 59.2±15.9 mg/dL (p=0.0257) and significantly higher triglycerides (TG) concentrations: 117 vs 91.6 mg/dL (p=0.026). There was a strong correlation between elevated C-reactive protein, index of inflammation, and HDL cholesterol lowering. Ultrasound examination of carotid arteries in PAG compared with the CG showed marked thickening of intima-media complex (CIMT): 0.90±0.21 vs. 0.64±0.16mm, p<0.0001. Coronary atherosclerotic lesions were observed significantly more often in PAG than in the CG, p<0.0001. Strong correlation of atherosclerotic presence was observed with traditional cardiovascular risk factors. There was also a significant correlation between the presence of atherosclerotic lesions in both carotid and coronary artery and elevated concentrations of TG and lowered concentrations of HDL, which indirectly may indicate a role of inflammation in the pathogenesis of atherosclerosis in patients with PA. In echo exams thickened septum in PAG was observed, p=0.0025, despite a comparable incidence of hypertension in the study group and the control.

Conclusions: In patients with PA structural changes in the cardiovascular system, including atherosclerosis of coronary and carotid arteries are significantly increased in comparison with the control group. It confirms possible inflammatory etiology in the development of early changes in the circulatory system in these patients.

Background: Accelerated atherosclerosis in rheumatoid arthritis (RA) is well established during the last decade.

Purpose: To investigate the prevalence of insulin resistance in RA pts with normal glycoregulation and its association with carotid intima-media thickness (IMT) and therapy exposure.

Methods: Our study included 90 RA pts (age 52.4±9.9 yrs, 86.7% females, disease duration 9 yrs, range 4–13). We determined body mass index (BMI), waist circumference (WC), blood pressure, smoking habits, and disease activity score (mDAS28-SE). IMT was measured bilaterally, at common carotid (CCA), bifurcation (BF), and internal carotid arteries (CI). All pts were treated with disease modifying antirheumatic drugs, 65.6% were on steroids (-10 mg/day), and 27.8% were on biological therapy. IR was calculated using the updated-computer Homeostasis Model Assessment (HOMA2-IR), based on fasting plasma glucose and serum insulin concentrations (measured by ELISA). IR was defined as HOMA2-IR<2.

Results: IR was detected in 74.4% of pts with median value of 1.4 (range 1.0–2.3). Pts with IR compared with those without IR had increased IMT (mm) at all measured points: CCA max: 0.57±0.15 vs. 0.76±0.20, p<0.01; CCA mean: 0.740±0.129 vs. 0.653±0.097, p=0.004; BF max: 1.059±0.169 vs. 0.920±0.124, p=0.001; BF mean: 0.908±0.141 vs. 0.782±0.126, p=0.000; CI max: 0.678±0.085 vs. 0.620±0.121, p=0.014; CI mean: 0.599±0.077 vs. 0.553±0.091, p=0.020. Both groups were comparable regarding RA duration and duration of all anti-inflammatory therapy including glucocorticoids. In multivariate logistic regression adjusted for BMI, WC and triglycerides we found that statistical significance disappeared for CCA and CI but still persisted for BF (e.g. for age CI mean: β=0.031, p=0.001; CI max: β coefficient=0.178, p=0.006; CI max: β coefficient=0.097 p=0.026; while for other levels statistical significance was borderline (for CCI mean and CCA mean p=0.052, and for CCA max p=0.064). On the other hand we found significant association of logHOMA2-IR with disease activity: DAS28 ≥coef 0.034, p=0.037.

Conclusions: RA pts with IR had significantly increased carotid IMT at all evaluated levels. Significant difference persisted for carotid BF even after adjustment for well known risk factors for atherosclerosis. Significant association of IR and disease activity may indicate the important role of RA itself in the interplay of IR and atherosclerosis.

Testosterone deprivation accelerates cardiac dysfunction and cardiac mitochondrial impairments in obese-insulin resistant rats. W. Pongkan1, H. Pinta1, S. Sivisanprasarn1, N. Apaija1, S. Kumlu1, T. Jawongkan1, S. Chattipakorn2, N. Chattipakorn2 on behalf of Cardiac Electrophysiology Research and Training Center, Faculty of Medicine, Chiang Mai University. 1Chiang Mai University, Cardiac Electrophysiology Research and Training Center, Department of Physiology, Faculty of Medicine, Chiang Mai, Thailand; 2Chiang Mai University, Department of Oral Biology and Oral Diagnostic Sciences, Faculty of Dentistry, Chiang Mai, Thailand

Background: Low testosterone level is associated with increased risks of cardiovascular diseases (CVD). Since obese-insulin resistance subjects have been shown to have impaired cardiac function and that the incidence of obesity is increasing in aged men, a condition of testosterone deprivation may aggravate the cardiac dysfunction in obese-insulin resistant subjects. However, the mechanism underlying this hypothesis is unclear.

Purpose: We hypothesized that obese-insulin resistance accelerates and aggravates the impairment of metabolic parameters, heart rate variability (HRV), left ventricular (LV) function and cardiac mitochondrial function in testosterone-deprived rats.

Methods: Orchiectomized or sham operated male Wistar rats (n=36/group) were randomly divided to receive either normal diet (19.77% fat) or high-fat diet (57.60% fat) for 12 weeks. Metabolic parameters, HRV, LV function by echocardiography and cardiac mitochondrial function were determined at 4, 8 and 12 weeks.

Results: Insulin resistance was seen at 8 weeks in high-fat diet sham (HFS) and high-fat diet orchiectomized (HFO) rats, whereas insulin resistance was not observed in normal diet sham (NDS) and normal diet orchiectomized (NDO) rats. The development of HRV depression, LV contractile dysfunction and increased cardiac mitochondrial ROS production was observed earlier in orchiectomized (NDO and HFO) rats at week 4, whereas HFS rats exhibited these impairments later at week 8 (Figure). NDO rats did not have impaired insulin sensitivity. However, HFO rats had markedly higher cholesterol level and diastolic blood pressure than HFS rats.

Conclusion: Testosterone deprivation accelerates the impairments of cardiac autonomic function, LV function and cardiac mitochondrial function in obese-insulin resistant rats.

Testosterone level and Mitochondrial ROS

Testosterone deprivation accelerates cardiac dysfunction and cardiac mitochondrial impairments in obese-insulin resistant rats. N. Joakimidis, C. Vlachopoulos, A. Angelis, P. Pietri, D. Terentes-Prezintios, P. Xaplanteris, M. Abdelraouf, I. Gourrougli, C. Georgakopoulos, D. Tousoulis. Hippokration General Hospital, Athens, Greece

Purpose: It has been shown that decreased concentrations of testosterone and the white blood cell pressure (PP) are predictors of cardiovascular (CV) events in erectile dysfunction (ED) patients. We investigated, whether testosterone and PP have an independent or a complementary prognostic value in ED patients.

Methods: Serum total testosterone (TT) and PP were measured in a cohort of 425 ED patients followed six years for the occurrence of CV events (CV death, coronary artery disease, stroke). We prospectively stratified patients into groups, based on the value of the measured TT and PP and cardiac event-free survival curves were constructed by Kaplan–Meier analysis.

Results: Among 425 enrolled ED patients, 23 patients demonstrated a CV event. Baseline TT levels were significantly lower and PP was higher in CV-event group than the event-free survival group (all p<0.01). Kaplan–Meier analysis showed that patients with TT in the lower tertile (<4.0 ng/mL) had a worse prognosis than
patients with TT >4.0 ng/mL (log rank: 6.37, P=0.008), and that patients with PP in the upper tertile ≥60 mmHg had a greater risk of adverse events than patients with PP <60 mmHg (log rank: 5.32, P=0.021). Figure shows Kaplan–Meier survival curves for patients with combinations of low or high TT (≤ or >4.0 ng/mL) and high or low PP (≥ or <60 mmHg) values. The event-free rate in patients with combined low TT and high PP is significantly lower than that in patients with either low TT or high PP alone.

Conclusion: In patients with ED, the combination of low TT and high PP was associated with a shorter event-free period compared with either decreased TT or elevated PP levels alone. Measurement of testosterone concentration may be useful to further stratify the risk of ED patients who have high peripheral PP.

P5541 | BEDSIDE
Association between endogenous serum testosterone concentrations and aortic pressures and pulse wave amplification indices in erectile dysfunction patients
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Purpose: Erectile dysfunction (ED) is an independent predictor of future cardiovascular (CV) events. Aortic pressures (central) and low testosterone independently predict future CV events and mortality. The relationship between testosterone, central pressures and wave reflection indices in ED patients is unknown.
Methods: Total testosterone (TT) levels were measured in 407 consecutive ED patients (55±8 y/o) without CVD. Central (aortic) systolic and pulse pressure, augmentation index (AiX) and augmented pressure (AP) as indices of pulse wave amplification across the arterial tree were measured with Sphygmocor device (ACor Medical).
Results: TT levels were inversely correlated with systolic and pulse central pressures (r=-0.195 and r=-0.249, respectively) and wave reflection indices (Aix: r=-0.208 and AP: r=-0.168) (all P<0.001). In multivariate regression models adjusting for age and risk factors, TT was an independent predictor of central pressures and wave reflection indices (all P<0.01). The combination of low TT level (<4.0ng/ml) with central pulse pressure (<40 mmHg) and AiX (>27%) values showed greater effect on 10-year risk of a CV event (figure).

TT, wave reflections and CV risk

Conclusions: Our study was the first, to the best of our knowledge, to demonstrate in ED patients the independent association of low testosterone with central pressures and indices of pulse wave amplification across the arterial tree. This observation highlights the role of testosterone as a marker of arterial disease and predictor of CV events and imply a pathophysiological contribution of testosteronen deficiency to age and blood pressure-related processes associated with generalized arterial disease.

P5542 | BEDSIDE
Impact of ages on fibrinogen levels and its relationship with coronary artery disease (CAD). A single-centre study
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Background: Previous reports have suggested an association between elevated fibrinogen and CAD. Few studies so far have investigated the impact of age on fibrinogen levels and its association with coronary artery disease (CAD) as evaluated by coronary angiography in elderly patient, that are therefore the aims of the current study.
Methods: We measured fibrinogen in 3637 consecutive patients undergoing coronary angiography. Blood samples were collected at admission for fibrinogen levels assessment. CAD was defined for at least 1 vessel stenosis ≥50% as evaluated by QCA. Severe CAD was defined by the presence of at least a 50% stenosis involving the left main or a 3 vessel disease. Elderly were: 75 years old.
Results: A total of 1796 out of 3637 were elderly patients, which were more often females, with higher prevalence of hypertension, previous MI or CABG, renal failure, but less often smokers (p<0.001, respectively), with lower prevalence of hypercholesterolemia (p<0.035) and family history of CAD (p<0.001). Elderly patients were more frequently on ACE-inhibitors (p<0.001), ARBs (p<0.002), calcium-antagonists, diuretics, nitrates (p<0.001, respectively). Elderly patients displayed higher creatinine, HDL cholesterol (p<0.001, respectively), uric acid (p<0.03), C reactive protein (p<0.02), but lower total cholesterol, LDL cholesterol, triglycerides, PLT, haemoglobin (p<0.001, respectively) and WBC levels (p<0.002). Elderly patients displayed higher fibrinogen levels as compared to younger patients (464±153.4 mg/dl vs 422±122.1 mg/dl, p<0.0001). Among elderly patients higher fibrinogen levels were associated with the prevalence of CAD (adjusted OR [95% CI]=1.317 [1.118–1.460], p<0.0001). Similar results were found for severe CAD (adjusted OR [95% CI]=1.146 [1.052–1.248], p<0.0001).

Conclusions: This study shows that elderly patients display higher fibrinogen levels as compared to younger patients. Among elderly patients, elevated fibrinogen is associated with the prevalence and extent of CAD.

P5543 | BEDSIDE
The prognostic values of hypoalbuminemia in patients with ST-segment elevation myocardial infarction (STEMI).
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Background: Hypoalbuminemia is a marker of frailty and it is associated with a poor prognosis in patients (pt) with ST-segment elevation myocardial infarction (STEMI).
Purpose: The aim of this study was to examine the impact of hypoalbuminemia on prognosis of STEMI according to the age of the pt.
Methods: STEMI pt enrolled in the prospective “Cardio-STEMI Sanremo” registry (February 2011 - June 2014) were divided on the base of the values of albumin at admission: albumin ≥ 3 g/dl (normA group) and albumin <3 g/dl (hypoA group). Age was considered for a sub-analysis at a cut off of 75 years old. The endpoints were hospital MACE (cardiovascular death, MI, stroke) and long term survival.
Results: Out of 519 pt, 21.2% (110) had albumin values <3 g/dl. HypoA pt were older (71 vs 65 years old; p<0.01), mainly female (39.1% vs 24.0%; p<0.01) and with a lower body mass index (BMI 25 vs 27; p<0.01). There were no significant differences for cardiac risk factors or previous cardiac disease between the two groups. The incidence of initial TIMI grade 0 flow was higher in HypoA (57.7% vs 45.4%; p=0.03) whereas final TIMI grade 2–3 flow was achieved in the same proportion of the pt. The incidence of BARC bleeding ≥2 was not different in the two groups, but HypoA experienced a higher rate of blood transfusion (5.5% vs 1.7%; p=0.04) and had a longer median in-hospital stay (6 vs 4 days, p<0.01). Hospital MACE were nominal more frequent in HypoA (7.4% vs 3.7%, p<0.01). At long term follow-up median 741 days, [IR 443–1079] all-cause mortality and cardiovascular mortality were higher in HypoA (respectively 21.8% and 16.4% vs 8.6% and 5.4%). In the Cox proportional hazard model [considering sex, ejection fraction, BMI, diabetes, glomerular filtration rate and hemoglobin values], pt younger than 75 years old showed no differences in mortality according to albumin values (Hazard Ratio 1.43, 95% confidence interval 0.77–2.65, p=0.26). Conversely analyzing pt over 75 years old, hypoalbuminemia resulted as an independent predictor of mortality (Hazard Ratio 2.80, 95% confidence interval 1.32–5.94, p<0.01). In older patients all-cause mortality and cardiovascular mortality were respectively 50.3% vs 23.5% (Log Rank p<0.01) and 39.6% vs 22.9% (Log Rank p<0.03) in HypoA group vs normA group.

Conclusions: Low albumin values (<3 g/dl) at admission are associated with a worse in-hospital outcome in STEMI pt. Focusing on pt over 75 years old, hypoalbuminemia is a strong independent predictor of long-term mortality.

P5544 | BEDSIDE
3-year health related quality-of-life outcomes after percutaneous coronary intervention in elderly patients
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Background: Health-related quality-of-life (HRQoL) is an important but often neglected outcome measure for elderly undergoing percutaneous coronary intervention (PCI).
Purpose: We aim to evaluate long-term impact of PCI on health status in elderly patients.

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Methods: We analyzed 998 consecutive patients undergoing PCI at our institution from September 2009 to January 2011. EuroQoL-5D (EQ-5D) health survey was used to assess HRQoL. Baseline, 6-12, 24 and 36 months after PCI were compared among ≥3 age groups (<60, 60–79, and ≥80 years). Utility score improvement of 0.11 was considered a clinically important difference (MCID).

Results: Patients aged ≥60, 60–79, and ≥80 years accounted for 32.5%, 59.5% and 8.0% of all patients undergoing PCI, respectively. Patients aged ≥80 years had highest 3-year all-cause mortality rates compared to patients 60–79 and <60 years of age (20% vs. 9.4% vs. 5.9%, respectively, p = 0.01) Mean EQ-5D scores improved from 0.55 at baseline to 0.87 at 36-month follow-up in patients aged 60 years, 0.56 to 0.84 in patients aged 60–79 years and 0.56 to 0.83 in patients aged ≥80 years (All p < 0.01). EQ-5D VAS scores at baseline (48.3 ± 20.0 vs. 65.3 ± 19.0 vs. 67.5 ± 20.4, p = 0.56) and 36 month (72.9 ± 13.6 vs. 71.6 ± 15.4 vs. 75.0 ± 19.3, p = 0.311) were similar among three age groups. Quality-adjusted life-years gained after 3 years were comparable between age groups (0.86 vs. 0.83, p = 0.24). Proportion of patients who experienced MCID improvement in HRQoL at 36-months were similar among age groups (82.6% vs. 81.5% vs. 82.5%, p = 0.84).

Conclusion: Elderly patients who underwent PCI experienced similar improvement in quality-of-life compared to younger patients up to 3 years follow-up. Our findings suggest that age per se should not deter from revascularization because of potential benefits in quality-of-life.

Aim: To investigate the prevalence of myocardial amyloid in patients with severe AS.

Methods: 130 patients with severe AS awaiting valve replacement (AVR) underwent cardiovascular magnetic resonance (CMR) and intra-operative myocardial biopsies (screened for amyloid with Congo red). If positive, tissue was sub-typed by immunohistochemistry, and patients were referred for DPD scintigraphy (Fig. 1).

Results: 97 patients had calcific AS (cAS) [73±8 years; 57% male]; the remainder had bicuspid (n=31), rheumatic or unicuspid AS (1 each). Myocardial amyloid (all ATTR) was found in 5 cAS patients (5.2% of ≥65 years; Table 1); none in the other cohorts. CMR detected 3 of 5, but missed 2, 1-year post-op, of 5 affected patients had died compared to 5% in the whole cohort.

Patients with AS and ATTR amyloid

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<tr>
<th>Age/gender</th>
<th>73F</th>
<th>69M</th>
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<td>AVAi (cm²/m²)</td>
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<td>CMR (± amyloid)</td>
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Background: Elderly patients with chronic heart failure (CHF) are well known to have poor instrumental activities of daily living (IADL) after hospital discharge. Decreased six-minute walk distance (6MWD) was reported to be a strong predictor of rehospitalization and mortality in them. This study aimed to investigate whether decreased 6MWD measured at hospital discharge reflected poor IADL after discharge in elderly CHF patients.

Methods: We recruited 333 elderly patients, 203 males and 130 females, who were ≥65 years and admitted to our hospital because of heart failure. We assessed patients’ characteristics, plasma brain natriuretic peptide, left ventricular ejection fraction and 6MWD at hospital discharge. IADL was evaluated using the Frenchay activities index (FAI) 3 months after discharge, while FAI score of <21 in males and <27 in females indicated poor IADL. We used multivariate logistic regression analysis and the area under the receiver operating characteristics (ROC) curve to determine significant predictors affecting poor IADL and their cut-off values.

Results: Of all patients, 129 male and 93 female patients had poor IADL. The multivariate logistic regression analysis identified 6MWD as a significant independent predictor for poor IADL in male and female patients (p < 0.001, respectively). The odds ratio of poor IADL with each 10-meter decrease of 6MWD and its cut-off value were 1.10 (95% confidence interval: 1.05–1.17, p = 0.001) and 350 meters in males, and 1.22 (95% confidence interval: 1.14–1.44, P = 0.001) and 300 meters in females (figure).

Conclusion: Decreased 6MWD at hospital discharge was identified as an independent strong predictor for poor IADL after discharge, and its cut-off value was 350 meters and 300 meters in male and female elderly patients with CHF, respectively.

P5547 | BENCH

Vitamin K supplementation inhibits cardiovascular calcification in a murine model of chronic kidney disease

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Background: Biological aging and diseases like diabetes mellitus or chronic kidney disease are characterized by cardiovascular calcification associated with enhanced morbidity and mortality. Matrix Gla protein (MGP) is a key calcification inhibitor within the arterial tunica media. Its activity is critically dependent on activation by vitamin K (VK)-dependent carboxylation.

Hypothesis: Vitamin K supplementation may prevent cardiovascular calcification in a murine model of extrarenal osteoporosis.

Methods: Experimental extrarenal calcification was induced by a 5/6-nephrectomy in combination with a high-phosphate diet in Wistar rats (n=28). Animals received high VK (CKD-K) or low VK diet (CKD). 20 sham-operated rats served as controls receiving both diets (Co-Co-K). Up to 12 weeks, we assessed longitudinal vital parameters, serum chemistry, creatinine clearance and cardiac function (echocardiography). After 12 weeks we investigated cardiovascular calcification (atomic absorption spectrometry) as well as structural alterations (elastic fibre breaking points, alkaline phosphatase staining) and mRNA expression of calcification regulating proteins.

Results: As expected, nephrectomy with high phosphate diet induced aortic (1.3 foldp <0.05) and myocardial (2.4foldp <0.05) calcification. In parallel, these animals exhibited increased vascular deposits of alkaline phosphatase (ALP) (2.2 foldp <0.01) indicative of osteblastic transdifferentiation. VK supplementation prevented extrarenal calcium deposits in aorta and myocardium as well as increased aortic ALP tissue concentrations in the CKD-K group. Tissue mRNA expression was affected by VK supplementation with increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induction (1.4 foldp <0.01) and increased MGP induc.

Conclusion: VK supplementation rescues cardiovascular calcification in a murine model of extrarenal osteoporosis.
murine model of extrasseous calcification. The protective influence of VK on tissue calcium content may be related to inhibition of secondary mineralisation of damaged vascular structures and mediated via activation of MGP and alteration of MGP gen regulation.

**P5548 | BEDSIDE**
The association between antihypertensive drug use, mortality, and hospital admissions related to medication in community dwelling elderly of 80 year and older: a retrospective cohort study

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**Introduction:** Blood pressure (BP) treatment in the elderly is much debated. Although ESH/ESC hypertension (HT) guideline advises to leave treatment decisions for frail elderly at the discretion of the treating physician, it still remains a challenge to select those patients who will benefit from antihypertensive drugs (AHD) and those in whom AHD may be harmful.

**Purpose:** We performed a real life survey on the association between AHD, mortality and potential Hospital Admissions Related to Medication (HARMs) in the light of polypharmacy and multimorbidity in the very old.

**Methods:** All 336 community dwelling elderly from our Academic General Practice who were >80 years on 1 January 2011 were included. Retrospective chart review was performed on baseline characteristics, incidence of acute hospital admissions, and death in the following years. Polypharmacy was defined as ≥5 separate drugs, multimorbidity as ≥1 chronic disease.

**Results:** Baseline characteristics were: age 85 (62–88) years, 28% male, 67% HT, 42% CVD, 30% CHF, 55% polypharmacy, 86% multimorbidity. A recent BP was documented in only 62% (146±24/77±14 mmHg). AHD were used in 73% (33% ≥3 AHD). Mortality was 10% per year. In 2 year follow-up, 34% were admitted to a hospital least once (8% CVD, 2% CHF, 20% potential HARM, 4% other). AHD use was associated with lower mortality: HR (95% CI) 0.51 (0.33–0.79) after adjustment for CVD, multimorbidity, polypharmacy, and CHF. None of these were associated with hospital admissions or HARMs.

**Conclusion:** In this retrospective study, AHD use was highly prevalent in community dwelling elderly and associated with lower mortality. Surprisingly, AHD were not associated with HARMs. One explanation may be that AHD are already withheld or discontinued in the most sick and vulnerable.

**P5549 | BEDSIDE**
Antplatelet therapy in the very elderly: should tolerability of therapy after percutaneous coronary intervention guide patient and device selection?

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**Introduction:** Compliance and tolerability of dual antplatelet therapy (DAPT) after percutaneous coronary intervention (PCI) have been poorly studied in the very elderly greater than 85 years old. The elderly have high rates of bleeding, need for operative bridging therapy. 352 pts (41%) received perioperative bridging therapy of which 124 pts (35%) had a vitamin K antagonist and 549 pts (65%) had a new oral anticoagulant, (apixaban N=82, dabigatran N=95, rivaroxaban N=372). In 2 pts the medication was missing. 499 pts (59%) did not receive perioperative bridging therapy. 352 pts (41%) received perioperative bridging therapy (13 pts received new oral anticoagulants, 6 pts unfractionated heparin and 333 low molecular weight heparin).

**Methods:** This study investigates outcomes and duration of DAPT in patients greater than 80 years on 1 January 2011 were included. Retrospective chart review was performed on baseline characteristics, incidence of acute hospital admissions, and death in the following years. Polypharmacy was defined as ≥5 separate drugs, multimorbidity as ≥1 chronic disease.

**Results:** Baseline characteristics were: age 85 (62–88) years, 28% male, 67% HT, 42% CVD, 30% CHF, 55% polypharmacy, 86% multimorbidity. A recent BP was documented in only 62% (146±24/77±14 mmHg). AHD were used in 73% (33% ≥3 AHD). Mortality was 10% per year. In 2 year follow-up, 34% were admitted to a hospital least once (8% CVD, 2% CHF, 20% potential HARM, 4% other). AHD use was associated with lower mortality: HR (95% CI) 0.51 (0.33–0.79) after adjustment for CVD, multimorbidity, polypharmacy, and CHF. None of these were associated with hospital admissions or HARMs.

**Conclusion:** In this retrospective study, AHD use was highly prevalent in community dwelling elderly and associated with lower mortality. Surprisingly, AHD were not associated with HARMs. One explanation may be that AHD are already withheld or discontinued in the most sick and vulnerable.

**P5550 | BEDSIDE**
New oral anticoagulants: perioperative bridging therapy versus no bridging therapy

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**Background:** Perioperative management of anticoagulation is not well established in patients with new oral anticoagulants. The purpose of this study was to evaluate the current strategies of perioperative anticoagulation in a large cohort of patients and to assess the risk of bleeding.

**Methods:** 851 consecutive bridging episodes were collected in the German BNK online bridging registry (BORDER 2). The incidence of bleeding and ischemic events was assessed and risk factors for bleeding events determined.

**Results:** 300 patients (pts) (35%) had a vitamin K antagonist and 549 pts (65%) had a new oral anticoagulant, (apixaban N=82, dabigatran N=95, rivaroxaban N=372). In 2 pts the medication was missing. 499 pts (59%) did not receive perioperative bridging therapy. 352 pts (41%) received perioperative bridging therapy (13 pts received new oral anticoagulants, 6 pts unfractionated heparin and 333 low molecular weight heparin).

**Conclusion:** Perioperative bridging therapy is uncommon in patients with new oral anticoagulants. Independent risk factors for clinical relevant perioperative bleeding are major surgery, an increased clinical risk score for bleeding (HAS-BLED >2) and bridging therapy.

**Acknowledgement/Funding:** Supported by Sanofi Germany

**P5551 | BEDSIDE**
Long-term effect of antihypertensive drugs on the risk of new onset osteoporotic fractures in the elderly - A population-based longitudinal cohort study

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**Background:** Antihypertensive drugs have been linked to new-onset osteoporotic fractures (NOF); however, data on the effect of these drugs on the development of NOF in hypertensive patients has not been well determined.

**Purpose:** To investigate the association between antihypertensive drugs and NOF.

**Methods:** Our data were taken from claim forms provided to our National Health Insurance from January 2002 to December 2012. Prescriptions for antihypertensive drugs before the index date were retrieved from a prescription database. We estimated the hazard ratio (HR) of NOF associated with antihypertensive drug use; non-NOF subjects served as the reference group.

**Results:** A total of 128 NOF cases were identified among 1144 elderly hypertensive patients during the study period. The mean age of NOF group was 78.9 years and that of non-NOF was 75.6 years. There was a significant difference in age between the two groups of patients (P<0.0001). The risk of NOF after adjusting for sex, age, comorbidities, and concurrent medication was higher among users of NOF. The concomitant use of beta-blockers and diuretics increased the risk of NOF.

**Conclusions:** The results of this study suggest that hypertensive patients who take calcium channel blockers (HR 0.70; 95% CI 0.49 – 1.00) are at a lower risk of developing NOF than non-users. Diuretics, beta-blockers, angiotensin receptor blockers, and alpha-blockers were not associated with risk of NAF.

**References:**

1. Iakos G, et al. Blood pressure (BP) treatment in the elderly is much debated. Although ESH/ESC hypertension (HT) guideline advises to leave treatment decisions for frail elderly at the discretion of the treating physician, it still remains a challenge to select those patients who will benefit from antihypertensive drugs (AHD) and those in whom AHD may be harmful.

2. Beldom A, et al. In this retrospective study, AHD use was highly prevalent in community dwelling elderly and associated with lower mortality. Surprisingly, AHD were not associated with HARMs. One explanation may be that AHD are already withheld or discontinued in the most sick and vulnerable.

3. Omran P, et al. Perioperative bridging therapy is uncommon in patients with new oral anticoagulants. Independent risk factors for clinical relevant perioperative bleeding are major surgery, an increased clinical risk score for bleeding (HAS-BLED >2) and bridging therapy.


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OBJECTIVE: To investigate the dynamics of velocity parameters of heart electrical activity in healthy males aged 1 to 64 years.

METHODS: Healthy males of different age groups were randomly sampled; children were in aged 1 to 16 years (n=324), divided into age groups 1–3 (n=47), 4–6 (n=95), 7–10 (n=94), 11–16 (n=88), and adult population aged 18 to 64 years (n=99), divided into age groups 18–24, 25–34, 35–44, 45–54, 55–64 years old. Velocity parameters of cardiac electrical activity were measured by the vectorcardiographic method (VAR), detected by using ECG and first ECG derivative methods. Statistical analysis was performed using t-test for independent samples, Pearson's correlation, nonparametric Spearman rank correlation. Results are performed as M±SD.

RESULTS: In healthy boys the dynamics of VAR was age-related, it had a form of undulating curve with the nadirs in the age of 7–8 years and 14–16 years. Data did not reveal statistical differences in VAR between age groups 1–3 years old and 4–6 years old (53.4±0.4 sec–1 vs. 52.4±0.28 sec–1, P>0.001), their VAR didn’t differ from adults aged 25 to 34 years. Data revealed negative correlation between age and VAR in pediatric population (r=−0.57, P<0.001), between age and heart rate (r=0.6, P<0.001). Data revealed positive correlation between VAR and heart rate (r=0.33, P<0.001). In adult population VAR was significantly lower than in pediatric population, VAR gradually lowers with ageing, in boys with arterial hypertension velocity parameters demonstrate significantly lower than in healthy boys of same age (VAR 45.8±0.9 sec–1 vs. 48.8±0.23 sec–1, P>0.001 respectively).

Conclusions: Data establish the pattern of lowering cardiac velocity parameters with ageing, in boys with arterial hypertension velocity parameters demonstrate premature cardiovascular ageing. In childhood there was found a tendency to heart rate variability during the heterogeneous heart development. Absence of a strong correlation between velocity parameters of cardiac electrical activity and the heart rate confirms that ventricular activation rate is an independent significant marker of the electrical activity of the heart.

P5554 | BEDSIDE
Prevalence and prognosis of Brugada electrocardiogram patterns in an elderly Han Chinese population: a nation-wide community-based study (HALST cohort)

Background: The exact world-wide prevalence of Brugada electrocardiogram (ECG) pattern is still unclear, especially in adults aged 55 years and older.

Methods: The study was conducted as part of the Healthy Aging Longitudinal Study (HALST) in Taiwan. Using a stratified random sampled method, a sample of community-dwelling subjects was recruited from seven community-based regions across Taiwan. All enrolled subjects were follow-up annually and cause of death was documented by citizen death records.

Results: A total of 5214 subjects were enrolled (male/female: 2530/2684) with a mean age of 69 years. The overall prevalence of Brugada ECG patterns was 3.32%. Four subjects carried spontaneous type 1 Brugada ECG pattern, 68 carried type 2, and 101 carried type 3. Compared to the world-wide average prevalence of Brugada ECG patterns, the prevalence of spontaneous type 1 Brugada ECG pattern 18.0% and from the HALST cohort was similar (0.22% vs. 0.07%) and the combined prevalence of type 2 and type 3 Brugada ECG pattern was 10 times higher (3.24% vs. 0.28%) even the mean age of study subjects was significantly higher (69±8 vs 35±8, P<0.001). However, all-cause and cardiovascular mortality rates were not significantly different between subjects with or without Brugada ECG patterns during the 4-year follow-up (log-rank test, P=0.21, 0.24, respectively).

Conclusion: The prevalence of Brugada ECG pattern in adults aged 55 years and older in Taiwan was higher than the average world-wide prevalence but was not associated with increased mortality.

P5555 | BEDSIDE
The natural history of multifocal atrial rhythms in elderly outpatients.
Prospective data from the ‘Ikaria study’

Purpose: Multifocal atrial tachycardias confer an adverse prognosis in hospitalized patients. We assessed the prognostic impact of multifocal atrial rhythms (MARs) on the outcome of patients with paroxysmal atrial fibrillation during follow-up of patients with atrial fibrillation (AF).

Methods: 953 patients, 62% males, aged from 5 to 85 years, mean 53±17, were referred for PS. Clinical, electrophysiological and exercise testing data were collected. Patients were followed from 3 months up to 10 years (5.4±5 years).

Results: 71 patients were aged from 60 to 85 years (mean age 68.4±6). 882 were <60 (mean 50.3±14). Heart disease (HD) was more frequent in patients ≥60 (20% vs 6.7%) (P<0.0001). Gender did not differ. Accessory pathway (AP) location did not differ except for right lateral, anterosetal, nodoventricular AP only noted in patients <60. Patients ≥60 were more frequently symptomatic than patients <60 (60 vs 63%) (P=0.007). No arrhythmias were induced in patients ≥60 at exercise testing but PS pattern disappeared in 20 patients. At EPS, maximal rate conducted over AP was similar in patients ≥60 and <60 in CS (181±58.5 vs 190±65 bpm) (0.35) or after isoproterenol (230±57 vs 232±61 bpm) (0.35). The number of inducers confirming tachycardia was lower in patients ≥60 (39% vs 54.6%) (0.014), but induced AF (28% vs 23.6%) and malignant forms (14% vs 15%) did not differ significantly in patients ≥60 and <60. During follow-up AP ablation was indicated as frequently in patients ≥60 (42%) and in patients <60 (48%) (0.05). Failure or recurrences in age groups ≥60 and <60 (P=0.209) and in patients ≥60 (0.16). Late occurrence of AF predicted by AF induction was more frequent in patients ≥60 than in patients <60 (respectively 13%,5% (P<0.001). No differences in the rates of AF between age groups (P=0.209). Mortality rate was 6% in patients with MARs and 1% in patients ≥60 (P=0.01). Effects of age at multivariable analysis on AF occurrence and spontaneous poorly-tolerated arrhythmias adjusted on previous HD, gender and induction of AF at EPS indicated that only age ≥60 was associated with the risk of adverse events (0.000) and that age ≥60 (0.01) and AF induction (0.000) were predictors of the risk of AF.

Conclusions: Despite the low prevalence of preexcitation syndrome in patients ≥60 years (7.5%), elderly patients have a higher risk of AF and of poorly-tolerated tachycardia than younger patients. Exercise testing was not useful but the risk of AF risk was predicted by electrophysiological study. Therefore elderly patients with a preexcitation syndrome require the same management as younger patients.
P5556 | BEDSIDE
Prognosis of the elderly patients after implantation of bradycardia pacemaker
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Purpose: The aim of the present study was to assess the prognosis of the elderly patients (aged ≥85 years) needed for the implantation of bradycardia pacemaker (PM).

Methods: A total of 869 patients (men 49.0%, 76.6±10.6 years) receiving a first bradycardia PM between January 2006 and June 2013 were enrolled, and the clinical outcome was compared between the elderly group (201 patients, 86±3.2 years) and the younger group (667 patients, 73.0±9.3 years).

Results: At the end of a mean follow-up of 430±556 days, 128 patients (14.7%) died, mostly of non-cardiac cause (73%). The mortality rate was similar between the elderly group and the younger group (15.4% vs. 14.5%, P=0.09). The mortality rate was similar regardless of the indication for implantation (atrioventricular conduction disturbance or sick sinus syndrome, P=0.59), initial rhythm (sinus bradycardia or atrial fibrillation with slow ventricular response, P=0.62), pacing mode (dual chamber or single chamber, P=0.70), and the position of the leads (septum or apex, P=0.38). Predictors for all-cause mortality were history of myocardial infarction, stroke, and heart failure.

Conclusions: The mortality rate of the elderly patients receiving PM was not inferior to the younger patients. The prognosis was determined not by age, indication for implantation, initial rhythm, pacing leads and mode but by the comorbid diseases.

P5557 | BENCH
Osteopontin-deficient mice are protected against age-related myocardial dysfunction, structural remodelling and senescence

Background: Aging induces osteopontin (OPN) expression in skeletal muscle and vasculature that compromises function and ability for renewal. Whether OPN has an impact on myocardial aging, contractility and structure is currently unknown.

Purpose: To explore whether OPN deficiency is able to prevent age-related cardiomyopathies.

Methods: OPN KO (n=10) and wild-type C57BL6 WT (n=10) mice were followed up until the age of 14 months. To explore if OPN deficiency impacts on age-related cardiac dysfunction, myocardial function was monitored by echocardiography in non-sedated mice and explored by left ventricular ejection fraction (LVEF, %) and deformation parameters such as myocardial strain rate (SR, s⁻¹) within the anterior and posterior walls. Cardiac structural remodelling was evaluated by heart weight to tibia length (HW/TL), wheat-germ agglutinin (cardiomyocyte size) and Sirius red staining (fibrosis). Myocardial senescence was estimated by p21 and p16 expression. Oxidative stress was measured by malondialdehyde levels, whilst apoptosis rate by TUNEL-assay. All data were collected at a young (2–3 months) and old age (13–14 months).

Results: As shown in the table, young WT and OPN KO did not differ in terms of myocardial function. With age, LVEF and SR values remained in the range of young values in OPN KO hearts, but significantly declined in WT (p<0.05 vs. young WT and aged OPN KO). Whilst HW/TL, cardiomyocyte size and fibrosis increased with aging in WT hearts, they were preserved around young levels by OPN deficiency. Induction of p16 and p16 in WT hearts with aging was rescued in OPN KO hearts. Myocardial malondialdehyde levels as well as TUNEL positivity were elevated by aging but without any difference between WT and OPN KO hearts.

Conclusions: OPN deficiency protects against age-dependent cardiac remodelling and dysfunction, independent of age-related oxidative stress or apoptosis. These results raise the possibility of OPN inhibition as cardioprotective strategy against myocardial aging.

P5558 | BENCH
Increased expression of the aging related splice variant progerin in patients with cardiomyopathy
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Objective: Defined mutations in the human lamin A gene or in enzymes processing the important nuclear membrane protein LMNA (e.g. Zmpste24) are causally involved in premature aging syndroms like progeria. The most prevalent and recurrent point mutation is depicted by a single C to T (1824) nucleotide substitution in exon 11 of the lamin A gene. This results in the activation of a cryptic splice donor site and production of a truncated prelamin A protein (LMNA Δ50 aa), also called progerin. Besides, low levels of progerin also play a prominent role in the process of aging in healthy individuals. Since LMNA mutations are associated with dilated cardiomyopathy, we aimed to address whether progerin and Zmpste24 play a role in patients with cardiomyopathy.

Methods: To quantitatively analyze the expression of progerin and Zmpste24, blood and endomyocardial biopsies (n=6) were obtained from non-ischemic cardiomyopathy patients. For controls, blood samples from age matched healthy individuals as well as biopsies from healthy transplanted hearts (n=6) were analyzed. Total mRNA was extracted and quantitative RT-PCR analyses were performed. Total LMNA expression was determined utilizing primers spanning exon 8 to 9. To specifically quantify progerin expression, we designed optimized primers spanning the splice junction site between exon-11 and 12. Progerin expression was related to total LMNA expression. Zmpste24 expression was related to housekeeping genes rpl32 and polr2a.

Results: Progerin mRNA levels were not significantly different in blood samples from controls and DCM patients (0.84±0.14 vs. 0.81±0.33; p=0.67). In contrast, progerin levels were significantly upregulated in failing hearts compared to heart biopsies derived from healthy controls after heart transplantation (1.66±0.56 vs. 1.06±0.07; p<0.01). Zmpste24 mRNA level were not significantly different between patient and control blood samples (1.31±0.23 vs. 1.11±0.15, p=0.12) and hearts (1.05±0.13 vs. 1.00±0.20, p=0.62).

Summary and conclusion: In conclusion, our preliminary data suggest that elevated levels of the aging related splice variant progerin are involved in human heart failure.

CARDIOVASCULAR MORTALITY IN ELDERLY
P5559 | BEDSIDE
Heart failure mortality in the elderly in Brazil: time trend analysis from 1996 to 2012
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Background: Heart failure (HF) presents epidemic characteristics with considerable impact on morbidity and mortality, especially among the elderly. In Brazil, HF is responsible for high mortality rates.

Objective: To evaluate the HF mortality rate trend variation in the elderly in Brazil, comparing with the variability of population growth by age group in the last decades.

Methods: Information was obtained from data published by the Informatics Department of Brazilian Health System (Datusus) regarding mortality rates. We
left ventricular hypertrophy (1.947, 95% CI 1.3, 3.922), thyroid stimulating hormone (1.06, 95% CI 1.006, 1.11), and depression (1.076, 95% CI 0.99, 1.17) were positively associated with mortality. Coffee consumption (0.99, 95% CI 0.99, 1.00), tea (0.992, 95% CI 0.985, 0.998), fruit intake (0.995, 95% CI 0.991, 0.999), olive oil (0.97, 95% CI 0.951, 0.989) and left ventricular ejection fraction (0.932, 95% CI 0.885, 0.976) were inversely associated with CVD.

Conclusion: Common CVD factors were not associated with CVD incidence in older individuals; whereas other biological and nutritional factors were placed in this anti-athero-pathologic puzzle.

P5560 | BEDSIDE
Identifying the last year of life in patients presenting with acute coronary syndrome: a multicentre prospective study (FATE-ACS study)

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Introduction: Acute Coronary Syndromes (ACS) are common in elderly and frail populations. An accurate and reliable tool to identify ACS patients approaching end-of-life remains to be determined.

Methods: This is a multicentre study of consecutive unselected patients admitted between May 2012 and July 2013 with a diagnosis of ACS. Patients were assessed during admission using the Gold Standards Framework prognostic indicator guide (GSF) and clinical risk scores including GRACE, ACEF and New York PCI risk score. Pre-specified primary outcome was all-cause mortality at one-year; secondary outcomes were cardiovascular death, non-cardiovascular mortality, re-hospitalization for ACS and re-hospitalization for non-ACS causes.

Results: Six hundred and thirty-six (636) ACS patients were enrolled and one-year follow-up data were available for 626 patients. Fifty-two (8.3%) met GSF criteria (GSF(+) for end-of-life care). GSF(+) patients were more likely to be older, female and with lower BMI compared to GSF negative (-) patients. GSF(+) patients underwent angiography and coronary intervention less frequently (95% vs 75%, p < 0.001; 77% vs 56%, p < 0.001). Compared with GSF(-) patients, GSF(+) patients had higher 12 month all-cause mortality (42.3% vs. 4.5%; p < 0.001), cardiovascular mortality (15.4% vs. 2.8%; p < 0.001) and non-cardiovascular mortality (38.9% vs. 3.7%; p < 0.001). Multivariate analysis confirmed the independent correlation of GSF with all-cause and non-cardiovascular death.

Conclusion: The GSF used in a hospital setting identifies those ACS patients who are at high risk of death within 12 months. The GSF or a similar tool should be used to screen ACS patients for end of life care.

P5561 | BEDSIDE
Factors, associated with in-hospital mortality of acute myocardial infarction: results from the single-center registry in Ukraine


Purpose: To evaluate in-hospital mortality of acute myocardial infarction (MI) patients (pts) and examine its predictors in the single-center registry in Ukraine.

Methods: Retrospective analysis of 548 pts prospectively enrolled in the Center’s MI registry between 2010 and 2014 (mean age 72±10.9 ys; 306 males (67%), 345 STEMI pts (63%), 175 recurrent MI pts (31.9%), Group 1 (G1) included 449 (81.9%) survived pts, group 2 (G2) – 99 (18.1%) pts who died in hospital. Some registers were selected as comparators: Ukrainians (UR, n=262), RECORD (Russia, n=796), Polish Registries (PR) STEMI (n=31298) and NSTEMI (n=2663), ACS-I registries STEMIs (n=4431) and NSTEMI (n=5367).

Results: In-hospital mortality rate for the Center’s MI pts (18.1% [95% confidence interval (CI) 14.9–21.6]) was higher than that in the UR (6.2% [95% CI 3.5–10.0]) and ACS-I (4.9%: 518 of 10484 pts). The same was observed for the Center’s STEMI pts (26.1% [95% CI 21.5–31.1]), compared with the UR (7.4% [95% CI 4.1–11.0]) and PR (9.3%).

In-hospital mortality rate for NSTEMI pts was comparable among studied registries. In-hospital mortality for the Center’s MI pts was associated with more advanced age (72 (63–87) and 80 (74–85) ys in G1 and G2, respectively; p < 0.001), higher BMI (58%, 90% and 90%, respectively; p < 0.001) and recurrent MI frequencies (26.5% and 56.6%, respectively; p < 0.001), with significant differences. According to a generalized linear model, age was the most significant independent in-hospital mortality predictor. The Center’s MI pts were older (72 [95% CI 71–73] ys) than those in the UR (64 [95% CI 62–66] ys), RECORD (65±12.4 ys), PR STEMI (64±12.4 ys), PR NSTEMI (68±11.8 ys), ACS-I STEMIs (63±13 ys) and ACS-I NSTEMI (66±12 ys). The frequencies of the Center’s MI pts with age ≥ 85 ys (44.3% [95% CI 40.1–48.5]) > 85 ys (13.7% [95% CI 10.8–16.6]) were higher than those in PR STEMIs (22.8% and 3.8%, respectively) and PR NSTEMI (33.3% and 5.4%, respectively).

Conclusions: In the single-center registry, older were those than in the national and some European MI registries. In-hospital mortality rate for the Center’s STEMI pts was higher than those for STEMI pts in the studied registries. In-hospital mortality was associated with age, STEMI.
and recurrent MI, with the age as the most significant independent predictor. The higher the Center’s MI cases in-hospital mortality rate could be partially related to the higher prevalence of comorbidities in the elderly pts.

P5564 | BEDSIDE
Residual lesion in left anterior descending artery is associated with 3-year mortality in super-elderly patients with acute coronary syndrome
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Background: Super-elderly patients, defined as those aged >85 years, often present with multiple lesions in clinical setting of acute coronary syndrome (ACS). Non-culprit lesions sometimes seem not to be treated with percutaneous coronary intervention (PCI) only because of their advanced age.

Purpose: The purpose of this study is to reveal whether PCI for non-culprit lesions is beneficial for super-elderly patients.

Methods: This study included consecutive 91 patients with ACS. We calculated SYNTAX score to evaluate the complexity. The associations of residual lesions and complexity with 3-year mortality were investigated using Cox regression.

Results: In 91 patients (mean age, 88.2±3.0, 52% male), culprit lesions were as below: left anterior descending artery (LAD): 50, Left circumflex artery (LCx): 29, right coronary artery (RCA): 31. The median of SYNTAX score was 14 (interquartile range, 8–22). Complete vascularization was not performed in 43 patients during hospitalization. Residual lesions were as below. LAD: 20, LCx: 22, RCA: 21. Residual lesion in the LAD was associated with higher 3-year mortality (p=0.04), but residual lesion in the LCx or RCA was not (p=0.27 and 0.77, respectively). The Cox regression model demonstrated that those with residual lesion in the LAD had increased risk of 3-year mortality in relation to those without the one (HR: 2.43, 95% CI 1.21–4.87, p=0.01). A 1-unit increase in SYNTAX score was associated with 1.07-fold increased risk for 3-year mortality (95% CI 1.03–1.10, p<0.001).

Conclusion: Even though the most of the super-elderly patients with ACS presented with less complicated lesions, no treatment with PCI for residual lesion in the LAD might be associated with higher 3-year mortality.

P5565 | BEDSIDE
Predicting clinical outcomes in elderly patients with acute myocardial infarction undergoing primary percutaneous coronary intervention
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Background: Consistent with the aging population in the Western world, there is a growing number of elderly patients with ST-elevation myocardial infarction (STEMI). Validated risk models to determine which of these patients are prone to poor clinical outcomes are essential.

Purpose: The purpose of this study is to identify risk factors for both serious adverse events (SAE) and minor adverse events (AE) in elderly STEMI patients undergoing primary percutaneous coronary intervention (pPCI).

Methods: All STEMI patients (aged ≥70 years) treated with pPCI in 2013–2014 were assessed. The safety management system (SMS) score to identify frail elderly patients was used in the risk model in addition to established risk factors. The primary endpoint was a combination of 30-days mortality, re-infarction, revascularisation, major bleeding, cerebrovascular accidents and major peri-procedural events. The secondary endpoint combined minor adverse events with the primary endpoint. Logistic regression analysis was used to identify predictors.

Results: A total of 151 patients were included with a mean age of 78.2±5.9 years and 91 (60.3%) were male. Median SMS score was 0 [IQR 0–1]. Primary and secondary endpoint rates were 24.8% and 43.9% respectively. SMS score was an independent predictor of serious adverse events [OR 1.3, p=0.029]. A trend was observed that the SMS score was associated with increased occurrence of the secondary endpoint [OR 1.4, p=0.056].

Conclusion: The rate of SAE 30 days after admission in STEMI patients ≥70 year is 24.8%. The SMS score for frail elderly patients is an independent predictor of the combined endpoint of mortality and other major events.

P5566 | BEDSIDE
Performance of Euroscore II compared to additive and logistic Euroscore in predicting hospital and midterm mortality, ICU and hospital length of stay in octogenarians undergoing cardiac operation
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Background: Euroscore II is a very useful tool in predicting mortality in cardiac surgery procedures. However, its use is suggested for patients below the age of eighty years old.

Purpose: Our intention is to assess the performance of Euroscore II in comparison to additive and logistic Euroscore in predicting hospital and midterm mortality, as well as ICU and hospital length of stay (LOS) in octogenarians undergoing cardiac operation.

Methods: We evaluated prospectively collected data for 508 octogenarians (mean age 83±2.6 years, n=231 females), who underwent isolated CABG (n=146), isolated non-CABG (n=97), 2 procedures (n=219) and 3 procedures (n=46) from March 2008 to April 2013. Midterm follow-up was 34±19.9 months. Logistic and Cox regression analyses were used to calculate odds ratios and hazards ratios, while C statistic (ROC curve), Hosmer-Lemeshow test and Extreme Quartile Odds Ratio (EQuOR) were used to assess the discriminative ability and calibration of the algorithms.

Results: There were 33 (6.5%) hospital deaths and 159 (31.3%) midterm deaths. The mean ICU LOS was 4.3±10 days and the mean hospital LOS 15.7±25.1 days. Mean Euroscore II was 8.6±8.7, additive Euroscore 9.4±2.5 and logistic Euroscore 16.9±13.5. Euroscore II had the best discriminatory ability, as measured by area under the ROC curve statistic in predicting hospital (0.87 vs. 0.74 and 0.75), ICU (0.70 vs. 0.67 and 0.67) and hospital LOS (0.69 vs. 0.64 and 0.64), while it showed good calibration in these outcomes (P=0.140, P=0.587 and P=0.140 respectively). Euroscore II was an independent predictor of midterm mortality (HR=1.042, 95% CI:1.030–1.055, P<0.001) and had the best discriminatory ability as measured by EQuOR (2.67 vs. 2.50 and 2.50).

Conclusions: Euroscore II showed the best performance in predicting hospital and midterm outcomes in octogenarians undergoing cardiac operation as compared to the previous versions.

P5567 | BEDSIDE
Laboratory tests combined into a frailty index predict mortality and cardiovascular events in hypertensive older adults
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Background and introduction: Older adults suffering from hypertension are at increased risk of cardiovascular events/mortality and risk increases with increasing frailty. Few longitudinal data are available in such older adults despite high prevalence of hypertension and an ageing population. Methods to identify those at highest risk, the frailest, vary from scales to indices. One such is the Frailty Index (FI). The FI counts the “deficits” (symptoms/signs/disease eg diagnosis of diabetes or uric acid >900 or <100) dividing by the total number to give a value between 0–1, higher values mean greater frailty. The FI robustly predicts mortality but can be challenging to use in clinical practice. Recent research suggests that an FI based solely on routine laboratory (lab) data may allow the identification of older adults at risk of death and be more practical in clinical settings (1). The FIpension in the Very Elderly Trial (HYVET) was a double blind placebo controlled trial of antihypertensives which showed benefit of treatment and collected data on cardiovascular events/mortality. The HYVET data present an opportunity to investigate the utility of a lab-FI in this population.

Purpose: To investigate the utility of a lab-FI in the HYVET population.

Methods: To enter the HYVET trial participants had to be ≥80 years with a systolic blood pressure of ≥160mmHg. Blood pressure and lab values for creatinine, glucose, haemoglobin, potassium, sodium, urea, haematocrit, uric acid, total and HDL cholesterol were collected at baseline and combined into a lab-FI. Incident cardiovascular events and mortality were collected and validated by an independent blinded committee. Cox proportional hazard regression was used to examine the relationship between the baseline lab-FI and subsequent events.

Results: The HYVET trial randomised 3845 participants and had a mean follow-up of 7.9 years. The SMS score was associated with increased occurrence of the secondary endpoint [OR 1.4, p=0.056].

Conclusion: Even though the most of the super-elderly patients with ACS presented with less complicated lesions, no treatment with PCI for residual lesion in the LAD might be associated with higher 3-year mortality.
up of 2 years. There were 431 deaths, of which 220 were cardiovascular, and 329 cardiovascular events (fatal + non-fatal). The lab-FI ranged from 0.03 to 0.19 with a median value of 0.19. Baseline lab-FI was associated with increased risk of death (HR 1.024 95% Confidence Interval: CI 1.012:1.036), increased risk of cardiovascular death (HR 1.021 95% CI 1.004:1.039) and increased risk of cardiovascular events (HR 1.021 95% CI 1.015:1.027) during hospitalization.

Conclusion: Initial analysis of a lab-FI calculated using the HYVET data suggests that it may be useful for assessing risk of mortality and cardiovascular events in an elderly hypertensive population.

Reference:
Howlット, S. et al. Standard laboratory tests to identify older adults at increased risk of death.

Acknowledgement/Funding: This work did not receive funding. The HYVET trial was funded by the British Heart Foundation and Servier International.

**Table 1**

<table>
<thead>
<tr>
<th>Age &lt;80 (n=1646)</th>
<th>Age ≥80 (n=250)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any PCI during hospitalization</td>
<td>27 (1.3%)</td>
<td>127 (5.0%)</td>
</tr>
<tr>
<td>IIb/IIIa antagonist use during PCI</td>
<td>118 (7.2%)</td>
<td>77 (3.0%)</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>21 (1.3%)</td>
<td>21 (8.4%)</td>
</tr>
<tr>
<td>In-hospital major bleeding</td>
<td>12 (0.7%)</td>
<td>25 (10%)</td>
</tr>
<tr>
<td>30-day MACE</td>
<td>179 (12%)</td>
<td>66 (27%)</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>35 (2.2%)</td>
<td>17 (7.1%)</td>
</tr>
</tbody>
</table>

Conclusion: Octogenarians ACS patients have significantly worse in-hospital and 30-day outcome compared to those <80 years.

**AGEING: COGNITIVE, VASCULAR AND AUTONOMIC IMPAIRMENT**

P556 | BESIDE

Outcome of acute coronary syndrome octogenarian patients in Israel

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Background: While patients ≥80 years old constitute the fastest growing segment of the population and have a high prevalence of coronary artery disease (CAD), few data are available regarding the outcome of octogenarians with acute coronary syndrome (ACS).

Methods: We evaluated in-hospital and 30-day clinical outcome of 1,896 patients (250 [13%] ≥ 80 years old) from the ACS Israel Survey (ACSIS), by analyzing data from ACS patients hospitalized in all coronary care units in Israel during a two-month period in 2013.

Results: ACS patients ≥80 years (mean age 85±4) had higher incidence of CAD risk factors, prior cardio-cerebrovascular events, chronic renal failure and cardiac medication use compared to patients <80 years (mean age 61±11). Time from chest pain onset to hospitalization and myocardial infarction (MI) location were similar in both groups. Killip class on admission was higher, while left ventricular ejection fraction was lower in ACS ≥ 80 years. ST elevation MI (STEMI) on admission was more common in ACS patients < than ≥80 years (41% vs 21%).

The in-hospital and 30-day mortality rates were significantly lower in ACS patients ≥80 years who underwent any percutaneous coronary intervention (PCI) during hospitalization compared with those who did not (4.8% vs 13% and 7.2% vs 22.8%, p<0.01) and the use of IIb/IIIa antagonist did not increase major bleeding and/or mortality. Seventy-seven patients >80 years had STEMI: 48 (62%) underwent primary PCI (18 patients with and 30 without IIb/IIIa), while 29 (38%) patients did not. No significant major bleeding was observed between the groups (Table 1).

Conclusion: In-hospital and 30-day outcome compared to those <80 years.

P557 | BESIDE

Predicators of aortic pulse wave velocity in the very elderly with severe aortic stenosis

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Background: Aortic stiffness increases with age and is associated with increased mortality in patients with severe aortic stenosis (AS). Aortic pulse wave velocity (ApPW) is a robust method to detect increased aortic stiffness in the elderly, with previously determined normal reference values in Europeans. It is unknown if severe AS in the very elderly (>70 years) is associated with increased ApPW. Predictors of ApPW in this population were not studied.

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 Aim of study: Compare the AoPWV in the very elderly with severe AS with age, gender, and coronary artery disease (CAD) matched controls and to study the predictors of AoPWV in this population.

Methods: We measured the AoPWV invasively during cardiac catheterization in 40 patients with severe AS and 20 matched control subjects referred for cardiac catheterization. In every case, we used femoral arterial access and through 6 French sheath and we placed a 4 French pigtail catheter in ascending aorta above the aortic valve. We recorded pulse pressure waves simultaneously from the pigtail catheter and side arm of the femoral artery sheath on a calibrated pressure and multifrequency pulse wave transit time in 1022 consecutive waves using foot to foot method. Pulse travel length was the length of pigtail catheter Segment inside the Patient. AoPWV was determined by dividing travel length/transit time.

Results: AoPWV in AS group (13.3 (10.9, 15.9) m/s) was not significantly different compared to non-AS group (12.4 (12.1, 17.5) m/s), p = 0.198. Central SBP at 78 years was associated with AoPWV (β = 0.45, p = 0.001) and glomerular filtration rate (GFR) (adjusted β = -0.29, p = 0.023) were independent predictors of AoPWV in AS group. AoPWV was not related to aortic valve area. Central SBP ≤141 mmHg predicted abnormal AoPWV (≥14.6 m/s) with 100% sensitivity and 70% specificity, area under the curve = 0.87, p = 0.015, and GFR <48 ml/min/1.73 m2 predicted abnormal AoPWV with 69% sensitivity and 82% specificity, area under the curve is 0.77, p = 0.006 in AS group.

Conclusion: AoPWV is not increased in the very elderly with severe AS compared to controls and is best predicted from the central SBP.

P5572 | SPOTLIGHT
Cardiovascular risk factors over the adult life course: associations with carotid intima-media thickness and carotid-femoral pulse wave velocity in older British men

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Background: It is increasingly recognized that cardiovascular disease (CVD) and cardiovascular ageing are processes which may begin well before later life. However, few prospective epidemiological studies have distinguished the influence of key cardiovascular risk factors exposures at different stages of the life course to relevant markers of cardiovascular disease and ageing in later life.

Purpose: We aimed to examine the time course of established cardiovascular risk factors at three points during adult life (median age 45, 65 and 78 years) on carotid intima media thickness (cIMT) and carotid-femoral pulse wave velocity (CFPWV) at 78 years.

Methods: The British Regional Heart Study is a prospective study of cardiovascular disease originally based on 7735 men aged 40–59 years from 24 British towns. Men took part in cardiovascular risk assessments providing information on cigarette smoking, body mass index (BMI), SBP, DBP, total, HDL-cholesterol, non-HDL-cholesterol, plasma glucose) at median ages 45, 65 and 78 years and had carotid intima-media thickness (cIMT) measured by B-mode ultrasonography at 78 years. Life course modelling approaches were used to define models of accumulation, sensitive period and mobility for the development of risk.

Results: Among 3137 surviving men, 1696 men (54%) had cIMT measurements and 1328 participants had pulse wave velocity measurements at 78 years. Ankle-brachial pressure index (ABI) at 78 years. Life course models suggested a sensitive period at 78 years for both SBP and DBP but were inconclusive for the other risk factors. CFPWV was positively associated with BMI at 45, 65 and 78 years (stronger at 45 and 65), with SBP at 45, 65 and 78 years (stronger at 45 and 65), with plasma glucose and HDL-cholesterol (inversely) at 78 years and with cigarette smoking at 45 years. Life course models suggested risk accumulation over all three age points for BMI and SBP but were inconclusive for the other risk factors. These results were not materially affected by adjustment for blood pressure and lipid lowering medications.

Conclusion: Established CVD risk factors (particularly blood pressure) are strong influences on these markers of cardiovascular disease and ageing. The influence of BP on cIMT appeared to be cumulative, while the influence of BP on CFPWV mainly reflected recent BP. Cardiovascular ageing is likely to be influenced by both longer term risk accumulation and by recent risk factor exposures.

P5573 | SPOTLIGHT
Incidence of carotid plaque components: a 4-year follow-up study using serial magnetic resonance imaging

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Background: Carotid atherosclerotic plaque components such as intraplaque hemorrhage (IPH), calcification and lipid-cores are important markers of plaque vulnerability. How these components change over time and which factors lead to the development of each component remain unknown.

Methods: 198 participants (mean age 67.5±10.6yrs) from a population-based study, all with carotid wall thickening on ultrasound, underwent two magnetic resonance imaging scans for carotid plaque characterization (mean interscan interval of 4.1±0.2yrs). Presence of IPH, calcification and lipid-core was assessed in both sides on baseline and follow-up scans. The association between cardiovascular risk factors and incidence of each carotid plaque component was assessed.

Results: In the 396 arteries, incidence of IPH, calcification and lipid-core was, respectively, 17.3%, 51.4% and 38.7%. The factor most strongly associated with incidence of IPH was use of antihypertensive drugs (multivariate adjusted OR 2.5 [1.2–5.2]). Incidence of calcification was associated with total cholesterol levels (multivariate adjusted OR per SD increase in cholesterol 1.5 [1.1–2.2]) and diastolic blood pressure (multivariate adjusted OR 2.1 [1.5–3.4]). Higher cholesterol levels were also associated with incidence of lipid-cores (multivariate adjusted OR per SD increase in cholesterol 1.3 [1.1–1.7]).

Conclusions: In community-dwelling subjects, hypertension and its treatment, and serum cholesterol levels were the main risk factors for the incidence of atherosclerotic plaque components over time.

Acknowledgement/Funding: This study was supported by The Netherlands Heart Foundation, (grant no. 2009BO044) and the Netherlands Organization for Scientific Research.
Cognitive aging and the incidence of cardiovascular events and diabetes: a meta-analysis of the HPS, SEARCH and HPS2-THRIVE studies


Purpose: Cognitive aging has been linked to stroke and vascular risk factors, such as diabetes, but small study sizes have limited inference. The relationship of cognitive aging to the incidence of cardiovascular events and diabetes was investigated among >45,000 individuals at high vascular risk who participated in the HPS, SEARCH and HPS2-THRIVE studies.

Methods: Participants in the studies were followed-up for the incidence of events during a mean of 5 years (>11,000 major vascular or diabetic events). Cognitive function at the end of follow-up was assessed via a modified Telephone Interview for Cognitive Status (TICS-m) test. In each study the associations of standardized cognitive Z-scores with incident events were assessed by a linear regression adjusting for years of follow-up and baseline predictors of cognitive function. Results were then combined in a meta-analysis. The relationship between Z-scores and age was used to convert Z-score differences to years of cognitive aging.

Results: The strongest baseline predictors of cognitive function were age, shorter height, prior stroke and diabetes. The incidence of stroke was associated with 7 years greater cognitive aging and incidence of transient ischemic attack (TIA) was associated with 3 years greater cognitive aging.

Conclusions: Clinical events were associated with 2–7 years of cognitive aging whereas undergoing a revascularisation procedure was not associated with cognitive aging, highlighting the value for cognition of vascular disease prevention.

P5575 | BEDSIDE

A combined cognitive-exercise training improves endothelial function in patients with mild cognitive impairment: the train the brain study


Background: Vascular factors are possibly involved in development of cognitive decline, presumably on a vascular basis, in apparently asymptomatic patients without previous cerebrovascular events.

Purpose: IMPLAC (imaging della placca carotidea) is a prospective study designed to investigate the clinical value of carotid computed tomography (CT) and contrast enhanced ultrasound (CEUS) for the prediction of ischemic cerebral burden and cerebral atrophy measured by longitudinal magnetic resonance imaging (MRI). Here we present the baseline data of this study concerning the relationship between carotid plaque characteristics and brain atrophy.

Methods: Between 4/2012 and 6/2014 we screened 218 patients. Of these 161 was excluded due to potential causes of cerebral damage such as overt neurological disorder and atrial fibrillation. Carotid CEUS, CT and brain MRI were performed in 60 asymptomatic patients with carotid stenosis >70% based on Doppler flow velocity. Common carotid artery [CCA], carotid bulb, external and internal carotid artery [ICA] were examined bilaterally. Brain volumes (total brain, grey matter [GM] and white matter [WM] volumes) were measured.

Results: Mean age of the study population was 69.9±8 years (56% males) and had an average Framingham risk score at 10 years of 9%. Based on ultrasound duplex examination, median carotid artery stenosis in the most affected district was 54% and on CT scan was 50% as estimated by ECST criteria, and 4 carotid segments were involved on average in each patient. Measure of GM atrophy correlated with some carotid characteristics. Since, as expected, GM volumes inversely correlated with age, all correlations were age-adjusted. Degree of plaque stenosis was not associated with GM volumes whereas markers of extent of carotid atherosclerotic disease, such as mean intimal-media thickness and total plaque area, were associated with decreased GM volumes. GM atrophy also correlated with increased grey-scale scoring (r=−0.50, p=0.001) and increased levels of Hounsfield unit (r=−0.32, p=0.02), suggesting a higher calcium content in the plaque. No association was found with total brain and WM volumes.

Conclusions: A larger total plaque area and higher calcification of the carotid plaques were specifically associated with the decrease of the brain GM volume in asymptomatic patients with non-obstructive carotid lesions. This findings underline the need to consider the carotid atherosclerotic disease not only as a potential risk factor for ischemic stroke but also as a significant marker of GM atrophy and possibly vascular cognitive decline.

Acknowledgement/Funding: Grants from Merck, the Medical Research Council and the British Heart Foundation for studies conducted and reported independently of funding sources

P5576 | BEDSIDE

Cognitive impairment predicts future cardiac events in elderly patients with heart failure

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Background: Cognitive impairment is a common condition among elderly patients with heart failure, data have been published on the relation of cognitive impairment to increased risk of mortality in elderly patients with heart failure (HF). However, little is known about the association between cognitive dysfunction and long-term cardiac prognosis.

Purpose: We hypothesized that the risk of mortality or future cardiac events is associated with cognitive impairment in HF patients.

Methods: We enrolled consecutive 180 patients (38 males) with hospitalized HF over the age of 65 in this study. The Mini-Mental State Examination (MMSE) was administered to assess global cognitive function. All patients were divided into 3 groups based on MMSE; the High-group (27–30 pts), the Middle-group (22–26 pts), and the Low-group (0–21 pts). All patients were followed up at the average period of 567 days.

Results: Blood pressure (BP) was significantly reduced after 7 months both in the training and in the non-training group (see Table), whereas in the non-training group more patients increased the number of BP-lowering drugs (16% vs 2%, p=0.007). There was a significant interaction between time and treatment arm for BA diameter. FMD was increased only in the training group. No significant changes in PWV, shear rate and response to GTN were observed over time.

Conclusions: A combined 7-month cognitive and exercise training is able to improve endothelial function as well as cognitive function in individuals with MCI or mild AD.

Acknowledgement/Funding: Fondazione Pisa
Results: The mean age, left ventricular ejection fraction, and plasma brain natriuretic peptide level at discharge were 78.4 years old, 48.8%, and 312pg/mL. As for cardiac events, Kaplan-Meier survival analysis revealed that composite end-points (cardiac related death and hospitalization due to worsening HF) were significantly higher in the Low-group (Figure; left panel). In addition, composite cardiac events were higher in the sub-group without social and/or family support availability in Low-group. On the other hand, there was no difference between 3 groups in all-cause deaths (Figure; right panel).

Conclusions: Global cognitive function assessed by the MMSE predicts future cardiac events and mortality in HF patients. Individual social and/or family support is required especially for the HF patients with severe cognitive impairment.

P5579 | BEDSIDE
Skeletal muscle atrophy is associated with presymptomatic hippocampal atrophy in elderly patients with heart failure

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Background: Cognitive impairment is increasingly prevalent in elderly patients with heart failure (HF), and is associated with frequent hospitalization and increased mortality because of reduced adherence to optimal medications and self-care regimens. On the other hand, age-related atrophy of skeletal muscle, known as a sarcopenia, is also common in elderly HF patients and is closely related to poor prognosis in these disease states. Additionally, exercise training has been shown to increase cognitive function as well as improve exercise capacity in elderly adults. These findings suggest that cognitive impairment and skeletal muscle atrophy seen in HF could be closely associated with each other. However, structural alterations between skeletal muscle and hippocampus in elderly HF patients has never been well characterized. The purpose of this study is to investigate the association between cross-sectional area (CSA) of thigh muscle and that of hippocampus by using magnetic resonance (MR) imaging. Furthermore, we also performed quantitative evaluation of presymptomatic atrophic change in hippocampus by using voxel-based specific regional analysis system (VSRAD) in these patients.

Methods and results: Ten stable elderly HF patients without dementia (5 females, 76±11 years old, NYHA functional class I-III) were studied. CSA of thigh muscle was 86±23 cm², and that of hippocampus was 1.7±0.4 cm². Z score of VSRAD was 1.1±0.7, indicating the mild degree of hippocampal atrophy compared to normal limit (<1.0). Six minutes walking test (6MWT) distance was 306±103 m. By univariate analysis, there was a significant positive correlation between thigh muscle area and hippocampus area (r=0.748, p=0.013). Muscle CSA and 6MWT distance were also negatively correlated with Z score (r=-0.644 and -0.638, respectively, p<0.05). By multivariable analysis, CSA of thigh muscle was identified as an independent determinant of hippocampal atrophy after adjusting for age and gender (β-coefficient 0.017, 95% CI 0.003–0.032, p=0.027).

Conclusions: Skeletal muscle atrophy and exercise intolerance are associated with the presymptomatic hippocampal atrophy in elderly HF patients. These results suggest that early intervention of cardiac rehabilitation program is required to preserve cognitive function as well as exercise capacity in elderly HF patients.

P5580 | SPOTLIGHT
Impaired orthostatic blood pressure stabilization is highly prevalent and a novel risk factor for unexplained falls in older adults: Findings from a prospective national cohort study

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Background and introduction: Impaired orthostatic blood pressure stabilization is highly prevalent in older adults, but it is unknown if it is an independent risk factor for incident all-cause or unexplained falls in older adults.

Purpose: To determine if impaired orthostatic blood pressure stabilization is an independent risk factor for incident all-cause and/or unexplained falls in older adults.

Methods: Data were analysed from the first two waves of a prospective, randomly sampled, national cohort study of older community dwelling adults. Continuous beat-to-beat blood pressure recordings measured during active standing were analysed. Impaired blood pressure stabilization (OH(40)) was defined as a systolic blood pressure drop of >20mmHg and/or diastolic blood pressure drops >10mmHg below resting values at 40 seconds after standing. Relationships with the number of all-cause and unexplained falls were assessed using negative binomial regression and modified Poisson regression respectively after covariate adjustment.

Results: 4128 participants were included in analyses (mean age 61.5 years, 54.2% female, mean (SD) time between waves 743 (83.9) days). At baseline, OH(40) was present in 15% of the population and symptomatic in 42%. When accompanied by hypertension and dizziness, those with OH(40) were at increased risk of an unexplained fall (Relative risk: 3.04, 95% CI: 1.5–6; 0–0.01), but not of more all-cause falls (Incidence rate ratio: 1.25, 95% CI: 0.78–2.01; P=0.356).

Conclusion: Impaired orthostatic BP stabilization 40 seconds after standing is common and is a novel risk factor for future unexplained in older adults, especially in the presence of hypertension and symptoms. Impaired BP stabilization is an easily measurable, early physical sign of cardiovascular ageing in older adults and should be considered in the future assessment of falls risk in older adults.

P5581 | BEDSIDE
Age and outcome of head-up tilt table testing in syncope patients

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Background: The head-up tilt test (HUTT) is a useful diagnostic tool for syncope. We described the outcome of HUTT in syncope patients and identified the relationship between age and different hemodynamic outcomes.

Methods: In this cross sectional study, we prospectively enrolled consecutive patients who presented with syncope and underwent HUTT with clinical suspicion of neurocardiogenic syncope after excluding orthostatic hypotension cases. HUTT consisted of consecutive passive and active phases. In the passive phase, patients were tilted at 70° for 20 minutes; and if negative, the test was repeated with 400 micrograms sublingual TNG for another 20 minutes. Positive responses were classified according to the Vasovagal Syncope International Study (VASIS) classification and compared for age and gender.

Results: A total of 498 patients were enrolled [age= 44.9±18.77 years; male=271 (54.4%); Overall, 291 (58.4%) patients had a positive HUTT while 256 (88.5%) patients had a positive result during the active phase. The test results were as follows: 107 (36.7%) mixed type (VASIS I), 103 (35.3%) cardioinhibitory (VASIS III). There was no relationship between gender and the type of syncope. The trend of HUTT result significantly changed by age and the rate of cardioinhibitory syncope decreased after middle-ages (p-value for trend<0.02).

Figure 1. Age & HUTT

Conclusion: Hemodynamic response to tilt test depended on age. Cardioinhibitory response became less frequent with aging due to exaggerated vagal activity in the younger patients as compared with the older subjects.
Assessing cardiovascular risk and incidence across the lifespan

P5582 | BENCH
Avoidable deaths from cardiovascular diseases: 40-year follow-up of 19,000 London Civil Servants
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Purpose: Death rates from cardiovascular diseases (CVD) have declined substantially in the UK over the last half-century. We examined trends in proportional mortality from CVD and the major causes of CVD (ischaemic heart disease [IHD], stroke and other vascular causes) in a 40 year follow-up of a prospective study of 19,019 male London Civil Servants.

Methods: The participants in the Whitehall study were men aged 40–69 years who worked in central London when first examined between 1967 and 1970. All participants were flagged with the Office for National Statistics who provided the date and cause of death. Deaths were classified by cause into CVD and non-CVD and CVD deaths were further classified into IHD, stroke and other vascular causes. Death rates were also classified by decade of follow-up (1970's, 1980's, 1990's, 2000's) and logistic regression was used to adjust for age at death.

Results: Among the 15,006 deaths with a known cause of death, 7020 died from CVD (47% of all deaths) of which, 4285 were from IHD (29%), 1400 from stroke (9%) and 1335 from other vascular causes (9%). The mean age at death was 75 years for IHD, 80 years for stroke and 78 years for other vascular causes. Hence, IHD accounted for a higher proportion of premature deaths before 70 years compared with deaths from stroke or other vascular causes (39% IHD, 5% stroke and 7% other vascular causes). The proportion of all deaths due to CVD declined progressively by increasing decades of follow-up (54%, 51%, 45% and 41%). Most of the decline in CVD deaths was due to a decline in IHD deaths (42%, 34%, 27% and 20%), respectively. In contrast, the proportion of all deaths due to stroke increased (6%, 9%, 10% and 12%), as did the proportion due to other vascular causes (7%, 9%, 9% and 10%). After adjusting for age at death, the odds of IHD declined by 19% per calendar decade, whereas there were no significant trends over calendar time in stroke (–1%, p=0.75) or other vascular causes (p=0.3).

Conclusions: Consistent with UK national mortality statistics, CVD death rates declined progressively over the last four decades. However, CVD remained the single most important cause of death. Most of the decline in CVD deaths reflected reductions in IHD deaths, which still account for a substantial burden of premature death.

Acknowledgement/Funding: British Heart Foundation

P5583 | BEDSIDE
Correlation of ankle brachial index measurement: all the techniques
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Objective: The ankle-brachial index (ABI) is a tool for the diagnosis and management of peripheral arterial disease, and a marker of atherosclerosis. The objective of this study was to determine the correlation of ABI measured by a pocket Doppler device compared to ABI determination at the echo Doppler vascular laboratory.

Methods: We evaluated the ABI in patients referred to the echo Doppler vascular laboratory for an arterial and/or venous lower limb study between March 2014 to December 2014. Resting ABI was determined with a pocket Doppler (continuous Doppler) and then by Doppler at the echo vascular laboratory (pulsed Doppler).

Results: A Bland-Altman plot is shown (Figure 1).

Conclusions: A high correlation between values of ABI measured by a pocket Doppler and the ABI measured at the vascular laboratory were consistent and can be replaced with each other. When used properly, the ABI remains an invaluable tool for assessment not only of peripheral arterial disease, but also a good prognostic marker for cardiovascular disease.

P5584 | BEDSIDE
Phytate (IP6) and age-related cardiovascular calcification
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Purpose: Cardiovascular calcification is not just a degenerative process linked to traditional cardiovascular risk factors; it seems to be strongly linked to processes intrinsic to aging itself. There is growing evidence of the molecular aspects of both processes. Myo-inositol hexaphosphate (phytate, IP6), a natural component of the Mediterranean diet has been shown to prevent cardiovascular calcification in experimental animals. We aim to identify whether a difference in IP6 levels may be involved in cardiovascular calcification in elderly humans.

Methods: An elderly patient population of 178 consecutive patients (mean 68 years, 81 female) were selected for echocardiography were studied. These were grouped according to IP6 urinary levels in low (LIP6) –0.61 μM, moderate (MIP6) 0.61–1.21 μM and high (HIP6) > 1.21 μM. Valve calcification was estimated by echocardiography (Rosenhek score) post acquisition and data on concomitant diseases, pharmacological treatment and diet were collected.

Results: Mitral annulus calcification was present in 24% HIP6 group, 36% MIP6 group and 49% LIP6 group (p=0.015). Patients with mitral calcium had significantly higher IP6 urinary levels (1.30±1.21 μM urinary IP6, n=117) than patients with mitral annulus calcification (0.89±0.68 μM IP6, n=61). A trend to present moderate to severe aortic calcification with less urinary phytates (35% LIP6, 34% MIP6 and 28% HIP6 respectively) was observed. Furthermore patients with lower IP6 showed a higher prevalence of diabetes, hypercholesterolemia, chronic kidney disease and peripheral vascular disease (p<0.05).

Conclusions: An inverse correlation between the level of IP6 urinary levels and calcium estimation by echocardiography was found and the presence of traditional cardiovascular risk factor also kept this relation. Further studies are needed to determine the role of phytates enhancing cardiovascular aging and its potential in the treatment and preventing disease.

P5585 | BEDSIDE
Temporal trends in the prevalence of ischaemic heart disease in Catalonia
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Background: An increase in the incidence and attack rates of definite and possible acute myocardial infarction (AMI) was observed in a well delineated geographical area of 1,000,000 plus inhabitants through a population AMI death registry during a ten year period. The objective of the present study was to analyze the trends in the prevalence of ischaemic heart disease during the same period from population surveys.

Methods: Data from the initial and third MONICA population surveys, separated by a period of ten years carried out in independent random samples of the general population (n=2571 and n=3484 men and women aged 25 to 64 years (response rates 74% and 72% respectively) were used. Survey methods followed the WHO-MONICA protocol. Effort angina and possible acute myocardial infarction were assessed by the Rose questionnaire and a resting 12-lead electrocardiogram which was coded manually with the Minnesota code by two independent observers. Data was analyzed with SPSS-13.

Results: Prevalence of effort angina as assessed by the Rose questionnaire remained stable: 2.6% and 2.2% in men and 3.1% and 2.1% in women (p NS). However, prevalence of definite Q waves (Minnesota codes 1.1 and 1.2) or ischemic changes (ST-T alterations in the electrocardiogram (Minnesota codes 4.1–3 or 5.0–3) increased from 5% (95% CI 1–7) to 7% (6–8) in men and from 7% (6–9) to 13% (11–15) in women. Prevalence of ischemic signs alone (ST-T) were more prevalent in women 12% (10–14) versus 6% (4–7) in men. Prevalence of ischemic changes (ST-T) significantly doubled in women aged 45–54, 6.8% (4.2–9.5) to 12.1% (10.3–16.8) while remained non-significant in younger women and were nearly significant in men 4% (3–5) to 6% (4–7).

Conclusions: Prevalence of ischemic signs in the electrocardiogram were more prevalent in women. Chronic objective forms of ischemic heart disease increased...
in women and tended to increase also in men. These findings corroborate the existence of an increasing epidemic of coronary heart disease during the studied period, as it was previously shown with the increase in the AMI.

Acknowledgement/Funding: Funded by the Department of Health of Catalonia

P5586 | BEDSIDE
Is the extent of coronary arterial plaque associated with non-coronary vascular outcomes in asymptomatic type 2 diabetics? A prospective CT angiography based 7 year outcomes study
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Background: Extent of coronary arterial plaque predicts coronary heart related events in asymptomatic type 2 diabetics (DM) but its relation to non-coronary vascular events (NCVE) is unclear. We examined this relationship in a prospective 7 year outcomes study.

Methods: A population based cohort of DM (N=630) underwent baseline risk assessment by United Kingdom Prospective Diabetes Study coronary heart disease risk score (UKPDS). Maximal treadmill exercise tolerance (METs) (N=526), coronary artery calcium (CAC) scoring (Agatston method) and total coronary plaque length (CPL) on coronary CT angiography (CTA) were assessed. NCVE (stroke/transient ischemic attack, carotid or peripheral vascular intervention/amputation, diabetic ulcer, retinopathy or renal failure) were measured over 6.5±1.0 yr.

Results: Coronary plaque was found in 500 (79.4%) of pt and NCVE occurred in 96 (15.2%). CAC and CPL were univariate but not independent predictors of outcome. UKPDS score, maximal exercise tolerance and baseline retinopathy were independent outcome predictors and their combination improved discrimination of NCVE on ROC analysis (C-statistic) (Table). Addition of METs to combined baseline risk from prior retinopathy and UKPDS resulted in continuous event net reclassification improvement (NRI) of 34.2%, non-event NRI 17.7%.

Outcome predictors

Baseline variable | Univariate Hazard ratio | p-value | Multivariate Hazard ratio | p-value | C-statistic
---|---|---|---|---|---
UKPDS* | 1.3 (1.2–1.4) | 0.001 | 1.3 (1.2–1.5) | 0.001 | 0.628
Retinopathy | 4.0 (2.7–6.1) | >0.001 | 3.6 (2.1–5.9) | <0.001 | (0.640)
Insulin treated | 2.1 (1.4–3.3) | 0.001 | 1.2 (0.70–1.9) | 0.56
Exercise tolerance (METs) | 0.86 (0.79–0.94) | 0.001 | 0.89 (0.81–0.97) | 0.009 | 0.639
Log (CAC+1)* | 1.4 (1.1–1.6) | 0.001 | 1.2 (0.82–1.6) | 0.41
Total plaque length* | 1.2 (1.1–1.5) | 0.001 | 0.99 (0.68–1.4) | 0.94
UKPDS + retinopathy + METS 0.762

*Per 10% 10 yr risk; *per quartile: $p=0.018 vs UKPDS + retinopathy combined.

Conclusion: In DM with no history of CAD independent predictors of NCVE were: 1. UKPDS risk score, baseline retinopathy and maximal effort tolerance. 2. Coronary calcium and plaque extent were univariate but not independent predictors of NCVE. 3. Maximal exercise tolerance improved discrimination and reclassification when added to other baseline risk predictors.

Acknowledgement/Funding: European Foundation for the Study of Diabetes

P5587 | BEDSIDE
The prevalence of cardiovascular events and short-term mortality increase in the elderly with stable coronary artery disease and hospitalization for acute lower respiratory tract infection
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Background: Earlier studies for the relationship between respiratory infection and the risk of CVD did not address cardiac comorbidities in the patients suffered from infection at the baseline.

Purpose: We try to investigate the prevalence of CVEs and mortality in the elderly with sCAD after hospitalization 90 days for acute lower respiratory tract infection (ALRTI).

Methods: This is a prospective, controlled cohort study. Participates were collected from the elderly patients with sCAD and hospitalized for ALRTI and sCAD without ALRTI as the controls. The CVEs and all-cause mortality after admission were followed up and recorded during 90 days.

Results: The researchers compared 257 cases (infection group) with 169 age-matched controls (No infection group), mean age 88±5 years. In the subsequent 90 days, of 257 subjects in infection group, 82 CVEs (31.9%) and 34 all-cause death (13.2%) were occurred; of 169 controls in no infection group, 23 CVEs (13.6%) and all cause mortality (1.8%) were recorded. Within 90 days, sCAD patients with ALRTI had a 2.3 fold increased risk for CVEs (31.9% vs. 13.6%, p<0.001), and 7.6 fold increased risk for all cause mortality (13.2% vs 1.7%, p<0.001) compared with controls. The risk of CVEs was highest during the first 2 weeks in infection group, but not in no infection group. The association between ALRTI and an increased risk for CVEs and all cause mortality was adjusted for multiple potential confounders, ALRTI (OR 2.162, 95% CI 1.023–4.569) is an independent risk factor for the increment of CVEs and all-cause mortality.

Discussion: We found that elderly patients hospitalized for ALRTI had a higher risk of CVEs and all cause mortality within the 90 days. Our results also suggested that the infection could have consequences on CVE outcome and death for several months after ALRTI, and hinted that patients who got over the acute event still had an increased risk for CVE events and all cause mortality during 90 days after infection; persistent inflammation might explain risk increase.

Conclusion: Hospitalization for ALRTI was associated with an increased risk for CVEs and all cause mortality in elderly patients with sCAD during 90 days. ALRTI should be considered an independent risk factor for adverse outcome after respiratory infection. So, monitoring and stratifying for future risk of CVEs and all cause mortality in elderly patients with sCAD during 90 days after hospitalization should help to increase the medication rates but it was also intended to reduce the readmission rate. In addition, our data might help to prevent CVEs and decrease death rate as well as acute infection.

P5588 | BEDSIDE
Association between dynamic penile peak systolic velocity and major adverse cardiovascular events in men with arterial hypertension
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Purpose: Hypertension is associated with an approximately two-fold increase in the likelihood of having an abnormal penile blood flow. Reduced penile peak systolic velocity (PSV) correlates with adverse cardiovascular outcomes. Aim of this study is to investigate whether low PSV predicts major adverse cardiovascular events (MACE) in hypertensive males.

Methods: Penile PSV was measured in 298 hypertensive males (55±19 y/o) without known cardiovascular disease by Doppler ultrasound after intracorporal injection of prostaglandin E1.

Results: During the mean follow-up period of 4.9 years, a total of 22 MACE occurred. Compared to patients who did not experience MACE, subjects who developed MACE had lower PSV (28±10 vs 32±8 cm/s, p<0.001). The whole population was divided into tertiles according to PSV (low tertile <25 cm/s; middle tertile 25–35 cm/s; high tertile >35 cm/s). PSV was associated with MACE and the differences between the tertiles were significant (log-rank test: 6.54; p<0.01, figure). A Cox model showed that subjects with arterial insufficiency (low tertile) had an approximately 3-fold higher MACE risk compared to those with arterial sufficiency (high tertile) and mild arterial insufficiency (middle tertile) after adjustment for age, systolic pressure, metabolic parameters, smoking, C-reactive protein and testosterone (HR 2.9, 95% CI 1.35 to 7.12, p=0.02). A PSV value of 38.6 cm/sec was associated with a negative predictive value (ability to rule out MACE) of 97.5%.

Penile PSV and MACE in hypertensive men

Conclusions: Our study is the first to investigate the prognostic role of penile blood flow in hypertensive patients. The principal finding is that low PSV predicts MACE in long-term follow-up independent of hypertension severity and decreased testosterone that is often present in such patients.

P5589 | BEDSIDE
Decreasing incidence of cardio-vascular events or deaths in CAD patient cohorts 2004-2011. Results from the disease management program (DMP) for coronary artery disease (CAD)
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Background and purpose: In 2004 the DMP CAD was initiated primarily to improve secondary prevention among patients with CAD. Principally the DMP CAD should help to increase the medication rates but it was also intended to reduce mortality and mortality. The purpose of this study was to analyse differences in the incidence of myocardial infarction, acute coronary syndrome, apoplexy or death in cohorts of CAD patients inscribed 2004–2011.

Methods: Data from all patients inscribed 2004–2011 were analysed retrospectively (n=30239, 63.3% male 68.5±10.7 y/o, ). Composite endpoint was documented until 2013 in 50442 (16.7%) patients. Total incidence and incidence of the composite endpoint within the first two years after inscriptions in the DMP were calculated for the patient cohorts of 2004/05, 2006/07, 2008/09, and 2010/11. Risks were calculated using separate regression models (odds ratios, 95% confidence intervals) for 1, total incidence, and 2, incidence within first two years.

Results: Between 2004/05 and 2010/11 incidence of composite endpoint within the first two years in the DMP decreased from 911 to 505 cases per 10000 pa.
Table 1

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Model 1</th>
<th>Model 2</th>
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<tr>
<td></td>
<td>OR %</td>
<td>CI %</td>
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<tr>
<td>Sex (male vs. female)</td>
<td>0.78</td>
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</tr>
<tr>
<td>Age (≥76 vs. &lt;65 years)</td>
<td>1.30</td>
<td>1.26–1.34</td>
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<td>Heart failure</td>
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<tr>
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<td>Cohort 2006/07 vs. 2004/05</td>
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<td>Cohort 2010/11 vs. 2004/05</td>
<td>0.22</td>
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Number of patients in model 1: 170,024; model 2: 145,363.

Table 2

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Number of patients in model 1: 170,024; model 2: 145,363.

P5590 | BEDSIDE
Association of polymorphisms of FURIN and ZPR1 with metabolic syndrome in Japanese individuals
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Purpose: Although genome-wide association studies (GWAS) have identified various genes and loci in predisposition to metabolic syndrome or each component of this condition, the genetic basis of metabolic syndrome in Japanese individuals remains to be identified definitively. Various genes and loci that confer susceptibility to coronary artery disease (CAD) or myocardial infarction (MI) have also been identified for Caucasian populations by meta-analyses of GWASs. Given that metabolic syndrome is an important risk factor for CAD, we hypothesized that certain polymorphisms may contribute to the genetic susceptibility to CAD through affecting the susceptibility to metabolic syndrome. The purpose of the present study was to examine the possible association of metabolic syndrome in Japanese individuals with 29 polymorphisms previously identified as susceptibility loci for CAD or MI by the meta-analyses of GWASs in Caucasian populations.

Methods: The study population comprised 1822 subjects with metabolic syndrome and 1996 controls. Subjects with metabolic syndrome had three or more of the five components of the diagnostic criteria for metabolic syndrome, whereas control individuals had none or one of the five components. The genotypes for 29 polymorphisms were determined by the multiplex bead-based Luminex assay.

Results: Comparisons of allele frequencies by the chi-square test revealed that 10 of the 29 polymorphisms were in Hardy-Weinberg equilibrium, having a tendency of decreasing death rates of patients suffering from CAD or heart failure which has been demonstrated for the last 10 to 15 years in Germany and worldwide.

Conclusions:

P5592 | BEDSIDE
Prevalence of abnormal glucose regulation 7 years after a ST-elevation myocardial infarction in patients without known diabetes at baseline: results of repeated oral glucose tolerance testing
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Background: Screening for undetected type-2 diabetes (DM) in patients with myocardial infarction, including an oral glucose tolerance test (OGTT), has been recommended in current guidelines.

Purpose: The aims of the present study were to: 1) study the long-term progression of glucometabolic abnormalities in ST-elevation myocardial infarction (STEMI) patients without known DM and 2) to evaluate the use of OGTT in STEMI patients in order to identify patients at risk of developing DM.

Methods: All eligible patients without DM with known DM, age ≥85 years or s-creatinine ≥200 μmol/l, were included. A standardised OGTT was performed in 140 STEMI patients during the acute phase (baseline, 17 h after PCI) and repeated after 3 months and 7 years follow-up and patients were classified according to the OGTT results.

Results: OGTT 7 years after STEMI: 16 (11.5%), 25 (18%) and 11 (8%) of the patients had criteria for DM, impaired glucose tolerance (IGT) and impaired fasting glucose (IFG), respectively. The prevalence of abnormal glucose regulation (DM + IGT + IFG) was 37, 22 and 37% at baseline, 3 months and 7 years, respectively, however, about 50% of the patients were reclassified during follow-up. Four patients fulfilled the DM criteria at all time-points, additionally, 12 patients were classified with DM at 7 years.

Conclusions: Results of a very early OGTT during the acute STEMI do not provide reliable information about long-term glucometabolic abnormalities and should not be recommended. A DM diagnosis 3 months after index STEMI, was confirmed in all patients 7 years later. On the contrary, only 2 of 17 patients diagnosed with DM at 3 months only 2 patients fulfilled criteria for DM 7 years later and 5 of these patients were reclassified as having normal glucose tolerance. Five of the 109 patients with normal glucose tolerance at 3 months were classified with DM at 7 years.

P5591 | BEDSIDE
Design and recruitment of the ROBINSCA trial: screening for cardiovascular disease
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Background: ROBINSCA (Risk Or Benefit IN Screening for Cardiovascular dis-
P5593 | BEDSIDE
Association of genetic variants of the alpha-kinase 1 gene with type 2 diabetes mellitus in a longitudinal population-based genetic epidemiological study
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Purpose: We previously identified nine genes and chromosomal region 3q28 as susceptibility loci for myocardial infarction, ischemic stroke, or chronic kidney disease in Japanese by genome-wide and candidate gene association studies. Given that diabetes mellitus (DM) is an important risk factor for these diseases, we hypothesized that certain polymorphisms in the 10 loci may contribute to genetic susceptibility to them by affecting the susceptibility to type 2 DM. The purpose of the present study was to examine the possible association of 13 polymorphisms in the 10 loci with the prevalence of type 2 DM in community-dwelling Japanese.

Methods: Study subjects comprised 6027 individuals (797 subjects with type 2 DM, 5230 controls) who were recruited to the Inabe Health and Longevity Study, a longitudinal genetic epidemiological study of atherosclerotic, cardiovascular, and metabolic diseases. The subjects were recruited from individuals who visited the health care center at Inabe General Hospital for an annual health checkup, and they are followed up each year (mean follow-up period, 5 years). Subjects with type 2 DM had a fasting plasma glucose level of >6.93 mmol/L or a blood hemoglobin A1c content of >6.5%, or were taking antidiabetes medication. The control individuals had a fasting plasma glucose level of <6.05 mmol/L and a blood hemoglobin A1c content of <6.2%, and had no history of DM.

Results: Longitudinal analysis with a generalized estimating equation and with adjustment for age, sex, and body mass index revealed that rs2116519 (C→T) of the family with sequence similarity 78, member B gene (FAM78B, P=0.0188) as well as rs2074379 (G→A, P=0.0121) and rs2074388 (A→G, P=0.0053) of the alpha-kinase 1 gene (ALPK1) were significantly (P<0.05) associated with the prevalence of type 2 DM. Longitudinal analysis with a generalized linear mixed-effect model and with adjustment for age, sex, and body mass index among all individuals revealed that rs2116519, rs2074379, and rs2074388 were significantly related to fasting plasma glucose level (P=0.0352, 0.0017, and 0.0010, respectively) and to blood hemoglobin A1c content (P=0.0065, 0.0090, and 0.0079, respectively). Similar analysis among individuals not taking antidiabetes medication revealed that rs2074379 and rs2074388 were related to fasting plasma glucose level (P=0.0073 and 0.0042, respectively) and blood hemoglobin A1c content (P=0.0142 and 0.0126, respectively), whereas rs2116519 was related to blood hemoglobin A1c (P=0.0470).

Conclusion: ALPK1 may thus be a susceptibility locus for type 2 DM in Japanese.

P5594 | BEDSIDE
Endovascular Treatment in Ischemic Stroke: A Meta-analysis of 11 Randomized Trials with Trial Sequential Analysis
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Aim: Endovascular treatment (ET) has been increasingly used in patients with ischemic stroke. However, there is controversial data about its efficacy and safety. Therefore we performed meta-analysis (MA) to compare efficacy and safety of ET plus intravenous thrombolysis (IVT) and IVT alone. Also, we performed trial sequential analysis (TSA) to differentiate conclusive vs inconclusive results and to demonstrate presence or absence of futility.

Methods: We searched PubMed, Embase and Scopus and international congress until February 2015. Eleven randomized controlled trials (RCTs) included to MA. The primary endpoint was independent outcome assessed by modified Rankin scale ≥2 at 90 days. Secondary endpoints were symptomatic intracerebral hemorrhage (ICH) and death. Our assumptions for TSA included two-sided testing, type 1 error=5%, power=80% and 20% relative risk reduction (RRR).

Results: Eleven RCTs with 2592 patients comparing ET+IVT (n=1426) and IVT (n=1166) were included in the meta-analysis. In ET plus IVT arm, significantly more patients achieved independent outcome than IVT alone (42.6% vs 31.5%; RR=1.441; 95% CI, 1.67 to 1.780; p<0.001). However, there were no significant differences between ET plus IVT and IVT alone arms in terms of death (15.6% vs 16.4%; RR=0.981; 95% CI, 0.758 to 1.025; p=0.161) and ICH (8.6% vs 6.0%; RR=1.300; 95% CI, 0.968 to 1.748; p=0.081). TSA analysis results showed that to draw firm conclusion, the optimal information size would be 3780 and the cumulative effect size measure did not enter the futility area.

Conclusions: This meta-analysis indicates that ET plus IVT seems to be associated with improved independent outcome. However, there are similar safety outcomes between groups. To draw any conclusion, we need new RCTs.

STROKE
P5595 | BEDSIDE
Early recurrence and cerebral bleeding in patients with acute ischemic stroke and atrial fibrillation: effect of anticoagulation and its timing.

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Background: Anticoagulation timing in acute cardioembolic stroke remains controversial. In a prospective cohort of patients with acute stroke and atrial fibrillation (AF), we evaluated: 1) the risk of recurrent ischemic event and severe bleeding; 2) the risk factors for recurrence and bleeding; 3) the risk of recurrence and bleeding associated with anticoagulant therapy and its starting time after the acute stroke.

Methods: This was a prospective cohort study. The primary outcome was the risk of a secondary ischemic event within 90 days of acute stroke. In the present study was to examine the possible association of 13 polymorphisms as susceptibility loci for myocardial infarction, ischemic stroke, or chronic kidney disease in Japanese by genome-wide and candidate gene association studies. Given that diabetes mellitus (DM) is an important risk factor for these diseases, we hypothesized that certain polymorphisms in the 10 loci may contribute to genetic susceptibility to them by affecting the susceptibility to type 2 DM. The purpose of the present study was to examine the possible association of 13 polymorphisms in the 10 loci with the prevalence of type 2 DM in community-dwelling Japanese.

Results: Longitudinal analysis with a generalized estimating equation and with adjustment for age, sex, and body mass index revealed that rs2116519 (C→T) of the family with sequence similarity 78, member B gene (FAM78B, P=0.0188) as well as rs2074379 (G→A, P=0.0121) and rs2074388 (A→G, P=0.0053) of the alpha-kinase 1 gene (ALPK1) were significantly (P<0.05) associated with the prevalence of type 2 DM. Longitudinal analysis with a generalized linear mixed-effect model and with adjustment for age, sex, and body mass index among all individuals revealed that rs2116519, rs2074379, and rs2074388 were significantly related to fasting plasma glucose level (P=0.0352, 0.0017, and 0.0010, respectively) and to blood hemoglobin A1c content (P=0.0065, 0.0090, and 0.0079, respectively). Similar analysis among individuals not taking antidiabetes medication revealed that rs2074379 and rs2074388 were related to fasting plasma glucose level (P=0.0073 and 0.0042, respectively) and blood hemoglobin A1c content (P=0.0142 and 0.0126, respectively), whereas rs2116519 was related to blood hemoglobin A1c (P=0.0470).

Conclusion: ALPK1 may thus be a susceptibility locus for type 2 DM in Japanese.

P5596 | BEDSIDE
Comparison of antplatelet regimens in secondary stroke prevention: a nationwide cohort study
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Purpose: The purpose was to determine whether acetylsalicylic acid, clopidogrel or combination of acetylsalicylic acid and dipyridamole was superior in preventing recurrent stroke and bleeding.

Methods: From Danish nationwide registries, patients discharged with first-time ischemic stroke in the period 2007–2010, and no history of atrial fibrillation were identified. Hazard ratios and 1-year risk of recurrent ischemic stroke and bleeding were calculated according to antiplatelet regimen.

Results: A total of 3043 patients were treated with acetylsalicylic acid, 12.295 with acetylsalicylic acid and dipyridamole combined, and 3885 with clopidogrel. Adjusted hazard ratios (HR) for clopidogrel versus combination of acetylsalicylic acid and dipyridamole were 1.02 (95% confidence interval [CI], 0.89–1.17) for ischemic stroke and 1.06 (95% CI, 0.83–1.35) for bleeding. Adjusted HRs (see Figure) comparing acetylsalicylic acid versus combination of acetylsalicylic acid and dipyridamole was 1.48 (95% CI; 1.31–1.67) for stroke and 1.47 (95% CI;
1.18–1.82) for bleeding. Clopidoless versus acetylsalicylic acid yielded a HR of 0.69 (95% CI: 0.59–0.81) and 0.72 (95% CI: 0.55–0.96) for stroke and bleeding, respectively. For acetylsalicylic acid, acetylsalicylic acid and dipirodione, and clopidogrel one-year predicted risk of ischemic stroke was 11.1 (95% CI: 10.2–12.2), 7.7 (95% CI: 7.3–8.3) and 8.0 (95% CI: 6.9–8.7), respectively, and 3.4 (95% CI: 2.8–3.9), 2.4 (95% CI: 2.1–2.7) and 2.4 (95% CI: 1.9–2.9) for bleeding, respectively. 

Conclusion: The combination of acetylsalicylic acid and dipirodione, and clopidogrel were associated with similar risk of recurrent ischemic stroke and bleeding, whereas acetylsalicylic acid was associated with higher risk of stroke and bleeding.

**P5597 | BEDSIDE**

**Thrombectomy for acute ischemic stroke: retrieval of larger thrombi is associated with improved neurological recovery**

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**Background and introduction:** In the Multicenter Randomized clinical trial of endovascular treatment for acute ischemic stroke in The Netherlands (MR CLEAN), thrombectomy restored flow and led to improved functional outcome. We hypothesize that the characteristics of the retrieved thromb reflect disease etiology and therefore may predict clinical outcome.

**Purpose:** To study macroscopy of thrombi retrieved during thrombectomy and correlate this with AIS baseline characteristics and changes in AIS severity between presentation and discharge.

**Methods:** 35 thrombi were collected from AIS patients undergoing thrombectomy. Thrombi were fixed in 4% buffered formaldehyde and calibrated images were taken. Length, width, area and numbers of particles were measured. An linear regression analysis was used to associate thrombus characteristics with patient characteristics and clinical outcome. Clinical parameters used in our analysis were, National Institutes of Health Stroke severity Scale (NIHSS), stroke etiology (modified TOAST-score), location of occlusion on CT-angiography, cardiovascular risk factors and the use of rPA. Results were considered statistically significant if p < 0.05.

**Results:** Most patients included in this study had a severe stroke, with median NIHSS of 17 (IQR 11–19). 17 (49%) patients had a stroke of cardiac origin and 7 (20%) due to large vessel atherosclerosis. CTA revealed that 32 (91%) of the occlusions were present in the middle cerebral artery, 28 (80%) of our patients received intravenous treatment with rPA. We saw no association between macroscopy and gender, cardiovascular risk factors (except a history of symptomatic atherosclerosis and TOAST criteria after adjustment for baseline NIHSS). Patients with atherothrombotic disease had larger and longer thrombi (p < 0.0035 and p = 0.045 respectively). With increasing thrombus length (β = −1.42; p = 0.03) and width (β = −2.28; p = 0.04) a significantly improved NIHSS outcome was observed after IAT at discharge. Interestingly, an increased number of particles retrieved during thrombectomy showed a trend (p = 0.07); β = 0.71 towards a worse NIHSS at discharge.

**Conclusions:** Retrieval of a large thrombus during thrombectomy is associated with improved neurological recovery: size matters!

**P5599 | BENCH**

**A preclinical study of honeycomb microporous covered stents for the treatment of large wide-necked cerebral aneurysms**

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**Background:** The treatment of large wide-necked cerebral aneurysms is extremely difficult, and carries a high risk of rupture, when even surgical or endovascular methods are available. The covered stent is one of the most promising advances in the treatment of complicated intracranial aneurysms (e.g., giant or very large wide-necked aneurysms), which have a high tendency to rupture. This treatment strategy is very simple, as the aneurysm neck is shielded with a cover film to stop the flow of blood into the aneurysm cavity. In this study, the in vivo performances of the newly developed microporous covered stents with a fine-tuned pore design (which provided a honeycomb pattern mesh-like cover film) were evaluated in 3 animal models.

**Methods and results:** The microporous covered stents were prepared using specially designed balloon-expandable stents (diameter 3.5–5.0 mm; length 15–20 mm), which were prepared by dip-coating to completely cover their strut with polyurethane (thickness 20 μm) and microprocessing to form the honeycomb pattern after expansion. 1) In an internal carotid artery canine model (diameter 5 mm, n=12), all stents that were mounted on the delivery catheter passed smoothly through the tortuous vessel with minimal arterial damage. 2) In a outer-sidewall aneurysm canine model (n=15), almost all parts of the aneurysms had embolized immediately after stenting, and histological examination at 1 month revealed neointimal formation with complete endothelialization at all stented segments and entirely organized aneurysms. 3) In a perforating artery rabbit model (diameter 3 mm, n=15), the lumbar arteries remained patent, with minimal change in the vascular flow pattern for over 1 year, even after placement of a second, overlapping stent. At 2 months after stenting, the luminal surface was covered with complete thin neointimal formation.

**Conclusion:** Based on the results obtained from these experimental models, the following successful outcomes were observed: 1) easy navigation of the covered stent delivery system into the 3-D tortuous arteries, 2) instant occlusion of large aneurysms, even those that were located at the outer-sidewall of the curved arteries, 3) preserved patency of the perforating arteries after stenting. Based on these successful preclinical results (additional details will be published shortly), an investigator-initiated first-in-human clinical trial of the honeycomb microporous covered stents will be conducted in 2015.
tient with AF. The estimated number of patients with lone AF is in line with previous reports.

Conclusions: This study demonstrates a high prevalence of stroke among veteran endurance athletes with AF. Our National Neurosurgical Centre has an estimated referral population of 4 million in Japan. Patients with AF progression were more frequently prescribed oral anticoagulants (OAC) (95% confidence interval, 1.02 to 4.11; p=0.04). Stroke or systemic embolism occurred in 11 patients (6.7%) with AF progression, and in 47 (3.2%) without AF progression with a much higher odds ratio adjusted by age and OAC prescription. Atrial fibrillation is associated with stroke in veteran endurance athletes in line with general guidelines.

Acknowledgement/Funding: Boehringer Ingelheim, Bayer Healthcare, Pfizer, Bristol-Myers Squibb, Astellas Pharma, AstraZeneca, Daiichi-Sankyo, Novartis Pharma and MSD

P5603 | BEDSIDE
Insertible cardiac monitors for detection of atrial fibrillation in patients with embolic stroke of undetermined source (ESUS) selected by risk factors

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Background: Clinically silent paroxysmal atrial fibrillation (AF) was recently detected in 12.4% of patients with embolic stroke or transitory ischemic attack (TIA) of undetermined source (ESUS) who have undergone insertion of an implantable cardiac monitor (ICM), after 12 months of monitoring. However, the large majority of these patients still undergo implantation of the ICM without clinical benefit. Our aim was to assess (1) if a risk factor-based pre-selection of ICM candidates would enhance the rate of AF detection within 12 months and (2) to determine which risk factors have significant predictive value for AF detection.

Methods: A cohort of 75 patients with ESUS were prospectively enrolled at the Stroke Unit of a university in Germany, if at least one risk factor was present: a CHADS2-VASc score ≥4, atrial runs in Holter monitoring, left atrial (LA)-size >45 mm, left atrial appendage (LAA)-flow <0.2 m/s, or spontaneous echo contrast in the LAA as assessed by transesophageal echocardiography. Study end-point was the detection of ≥1 episodes of AF (lasting ≥2 minutes according to the software algorithm of the ICM).

Results: A total of 75 male patients were enrolled from July 2013 to January 2014. During the median follow-up of 777 days, progression from paroxysmal to sustained AF occurred in 11 patients (6.7%) with AF progression, and in 47 (3.2%) without AF progression with a much higher odds ratio adjusted by age and OAC prescription. Atrial fibrillation is associated with stroke in veteran endurance athletes in line with general guidelines.

Acknowledgement/Funding: AKF research grant (intramural research-funding program of University of Tuebingen, Germany)

P5604 | BEDSIDE
Underreporting of intracranial haemorrhage associated with antipatelet and anticoagulant use to the health products regulatory authority versus referrals to a national neurosurgery centre

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Intracranial Haemorrhage (ICH) is a much feared side effect of antipatelet and anticoagulant agents. It is of particular prominence with the advent of the novel antipatelet and anticoagulant agents. Postmarket reports of bleeding highlighted the fact that newly marketed products, by virtue of their novelty alone, may elicit adverse-event reports at high rates; reporting rates decreasing over time (the ‘Weber effect’). Hence established medications, such as Warfarin and Aspirin, would be far less likely to elicit adverse-event reports than would newer medications with similar risks.

The hypothesis of this study was to compare the number of referrals of ICH associated with antipatelet and anticoagulant use to our National Neurosurgical Centre with the number of reports received by the Health Products Regulatory Authority (HPRA) as an adverse event of these medications.

Our National Neurosurgical Centre has an estimated referral population of 4 million. All consecutive referrals from July 2013 to January 2014 were reviewed. Data
collected included baseline demographics, antiplatelet/anticoagulation usage and indication for same, and CT brain findings of the ICH. The HPRA were contacted and supplied their adverse event reports for the same period. There were 977 consecutive patients with an ICH referred in this period. Of these 328 (33.6%), with a mean age of 77yrs, female 42.6%, were on an antiplatelet and/or an anticoagulant agent: ASA alone (n=168, 50.6%), Warfarin alone (n=106, 32.3%), Clopidogrel alone (n=11, 3.3%), Rivaroxaban alone (4, 1.2%), Dabigatran alone (4, 1.2%), ASA/dipryridamole alone (3, 0.9%). Thirty one (9.4%) patients were on two agents. 19 on ASA & Clopidogrel, 7 on ASA & Warfarin, 2 on Clopig- drorel of AF Burden and optimization of oral anticoagulation agents (OACs) to maintain normal sinus rhythm (NSR) may allow safe-withdrawal of OACs (p<0.0001: I2<8%). There was no evidence of publication bias by funnel-plot method. To control for heterogeneity, we did subgroup and sensitivity analysis, and this revealed that intracardiac SEC, particularly left atrial or left ventricular SEC, was primarily responsible for this association (22.8% vs 5.8%) (RR 4.69, 95% CI 3.42, 6.43; P<0.0001; I2=0%).

Estimation of sensitivity and specificity was done using receiver operator characteristic (ROC) curves. Area under the ROC curve (AUC) was determined for each model. Results: Discontinuation of OAC (p<0.00003). 6 (7%) pts died from unrelated causes including respiratory failure, cancer and sepsis.

P5605 | BEDSIDE
Spontaneous echo contrast is associated with increased risk for cardioembolic events a metaanalysis
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Method: We aimed to determine the association of spontaneous echo contrast (SEC) with cardio-embolic (CE) events (stroke and peripheral embolism). Its association with cardio-embolic (CE) events, however, is not yet established.

Inclusion criteria: Studies were (i) observational studies; (ii) whose populations were of adults >19 years old with documented SEC either in the cardiac chambers and/or the aorta; (iii) reported data on CE events, especially stroke; (iv) and controlled for confounding variables by doing logistic regression and/or multivariate analysis.

Methods: We conducted a systematic search of studies using MEDLINE, EMBASE, ScienceDirect, and Cochrane Central Register of Controlled Trials databases in all languages and examined reference lists of studies. We identified 14 studies that met inclusion criteria, and obtained full articles of all of them. Each study was assessed for quality using the Newcastle-Ottawa Quality Assessment Scale. The outcome of interest was assessed using Mantel-Haenzel analysis of random effects to compute for risk ratios, carried out using Review Manager (RevMan) 5.0.10 (The Nordic Cochrane Centre, The Cochrane Collaboration).

Results: Pooled analysis from the 14 studies enrolling 4,659 patients showed that the presence of SEC was associated with increased CE events (27.9% vs 5.8%) (RR 4.69, 95% CI 3.42, 6.43; P<0.0001; I2=8%). There was no evidence of publication bias by funnel-plot method. To control for heterogeneity, we did subgroup and sensitivity analysis, and this revealed that intracardiac SEC, particularly left atrial or left ventricular SEC, was primarily responsible for this association (22.8% vs 5.8%) (RR 4.69, 95% CI 3.42, 6.43; P<0.0001; I2=0%).

Conclusion: The presence of SEC is associated with significantly increased risk for cardio-embolic events among adult patients. This supports the need to be aggressive in the management of patients with SEC particularly in reducing CE event risk. Clinical trials are warranted.

P5606 | BEDSIDE
Discontinuation of oral anticoagulation agents in patients with atrial fibrillation and concomitant risks of stroke and bleeding using therapy approach guided by insertable cardiac monitors
B.K. Kantharia1, M.U. Farooq2, D.A.N. Mascarenhas2.

Introduction: In patients (pts) with atrial fibrillation (AF) who are at high risk for bleeding, long-term usage of oral anticoagulants (OACs) used for stroke prevention may not be safe.

Purpose: To investigate whether insertable cardiac monitor (ICM)-guided assessment of AF burden and optimization of oral antithrombotic agents (OACs) to maintain normal sinus rhythm (NSR) may allow safe-withdrawal of OACs.

Methods: In pts at dual risk of stroke and bleeding, we inserted ICM (Medtronic Reveal), after cardioversion, treatment with OAC (Ic, III) and OAC (warfarin, NOACs). Upon discontinuation of OACs we categorized the pts into 3 groups/11 Group A (NSR/low AF burden, <1%), (2) Group B (intermediate AF burden, 1–2%), and (3) Group C (high AF burden >2%) (Figure 1). We allowed discontinuation of OACs only if NSR/low AF burden for 3 months was maintained.

Results: 83 pts (median age 74 years; 53% male) were followed over 15.3 months (mean, range 6–48); Group A, B, and C had 45 (54%), 29 (35%) and 9 (11%) pts with similar demographics and CHADS2 scores: 2.09±0.63, 2.03±0.8 and 2.10±3.33, CHA2DS2-VASc scores:3.09±0.97, 2.76±1.1, and 2.92±0.73, and HAS-BLED scores: 3.13±1.03, 3.24±0.80 and 3.10±0.71 (p=0.05) respectively.

With OAs 25 (86%) pts in Group B maintained NSR/low AF burden. Overall, 68 (82%) pts (43 in A Group, 25 in Group B) had NSR/low AF burden. 60 (88%) pts (40 in Group A, 20 in Group B) discontinued OACs without any untoward outcomes. 5 (6%) pts, all on OAC, suffered severe bleeding compared to none who discontinued OAC (p<0.0003). 6 (7%) pts died from unrelated causes including respiratory failure, cancer and sepsis.

Conclusions: In pts with AF who are at high risk of bleeding, a strategy of ICM-guided rhythm control with OAA and assessment of AF burden may allow safe discontinuation of OAC.
According to the CHA2DS2-VASc score. Whether carotid atherosclerosis is a risk factor for stroke/TIA recurrence in these patients is unknown. Methods: Ambulatory patients with AF on oral anticoagulant treatment were included in a multicenter, prospective study. All patients underwent carotid ultrasonography for the assessment of internal carotid stenosis defined according to the carotid stenosis criteria by the risk of risk of stroke. Observation increased the value of the assessment of CHA2DS2-VASc score when considering the use of anticoagulant treatment. Acknowledgement/Funding: No financial support.

P5609 | BEDSIDE
Carotid atherosclerosis and the risk for ischemic stroke in patients with atrial fibrillation on oral anticoagulant treatment.

A. Becattini1, A. Sembolini1, G. Manina1, F. Dentali2, G. Camporese3, C. Tonello4, G. Agnelli5 on behalf of the studied was performed without external support. 1 University of Perugia, Perugia, Italy; 2 University of Insubria, Varese, Italy; 3 University Hospital of Padova, Padua, Italy

Background: Ischemic heart disease, peripheral artery disease and aortic plaque are risk factors for ischemic stroke in patients with atrial fibrillation (AF) according to the CHA2DS2-VASc score. Whether carotid atherosclerosis is a risk factor for ischemic stroke in these patients is undefined.

Methods: Ambulatory patients with AF on oral anticoagulant treatment were included in a multicenter, prospective study. All patients underwent carotid ultrasonography for the assessment of internal carotid stenosis defined according to the carotid stenosis criteria by the risk of risk of stroke. Observation increased the value of the assessment of CHA2DS2-VASc score when considering the use of anticoagulant treatment. Acknowledgement/Funding: No financial support.
P5612 | BEDSIDE
Does the left atrial appendage morphology correlate with stroke risk in patients with sinus rhythm?
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Objectives: Ischemic strokes without a well-defined etiology are labeled as cryptogenic, and account for 30–40% of strokes in the registries. The left atrial appendage (LAA) is the most typical origin for intracardiac thrombus formation when associated with atrial fibrillation. We examined whether LAA morphology detected with transesophageal echocardiography (TEE) constitutes a risk factor of thrombotic events associated with atrial fibrillation. We examined whether LAA morphology detected by TEE with the incidence of stroke/transient ischemic attack (TIA) in patients without atrial fibrillation.

Methods: 110 consecutive pts (65 F, 45 M) with a mean age of 31.2±17.2 (16–52) years with the history of cryptogenic cerebrovascular event (TIA/stroke) and normal sinus rhythm, who underwent TEEs, were analyzed. The patients with PFO were excluded.

The diagnosis of stroke was based on the occurrence of a new and abrupt focal neurological deficit, with neurological signs and symptoms persisting for >24 hours, subsequently confirmed by computed tomography and/or MRI.

A group of 1 coronary artery bypass grafting

Patients with Cauliflower LAA morphology are more likely to have an embolic event even in case of sinus rhythm. If confirmed, these results could have a relevant impact on the anticoagulation management of patients with cryptogenic stroke/TIA.

P5613 | BEDSIDE
Predictors of stroke after aortic valve replacement with or without concurrent coronary artery bypass grafting

Background: Stroke is arguably the most important and devastating non-mortality complication after cardiac surgery, and also an important outcome to compare between aortic valve replacement (AVR) and transcatheter aortic valve implantation.

Purpose: We analysed for the predictors of stroke after AVR with or without concurrent coronary artery bypass grafting (CABG).

Methods: All patients undergoing AVR +/- CABG at our City Hospital during 2005–2012 were included, and univariate multivariate analyses were conducted to identify predictors for post-operative stroke, defined as in-hospital new neurological deficits lasting more than 24 hours after surgery.

Results: There were 620 isolated AVR and 450 AVR+CABG patients studied. Rates of stroke was significantly higher for AVR+CABG 3.3% (15 compared to AVR alone 1.3% (8), P=0.031. Independent predictors of stroke (odds ratio and 95% confidence interval) for isolated AVR included age (1.02, 1.00–1.04), syncope (6.07, 1.03–35.8), critical pre-operative state (6.07, 2.08–25.6) and history of stroke (7.23, 1.20–43.6), while the only independent predictor identified for AVR+CABG was diabetes on insulin (6.19, 1.63–23.5). Receiver-operator characteristic analysis found the original EuroSCORE having the highest C-statistic for detecting stroke after isolated AVR 0.845 (0.783–0.907), while the Society of Thoracic Surgeon’s Score had the highest though moderate C-statistic after AVR+CABG 0.642 (0.500–0.778).

Conclusion: Although rates of stroke are low at our centre, performing CABG concurrent on top of AVR was associated with significantly higher risk. We have identified a number of conventional cardiovascular risk factors that independently predict stroke in aortic valve surgery which should be taken into consideration when deciding for modality of aortic valve intervention.

P5614 | BEDSIDE
Neuroprotective effect of sitagliptin after ischemic stroke in type 2 diabetic patients: a nationwide cohort study
T.H. Chen, D.Y. Chen, S.H. Wang. Chang Gung Memorial Hospital, Taiwan, ROC

Objectives: The aim of this study was to assess the efficacy and safety of sitagliptin in type 2 diabetic patients with ischemic stroke.

Background: The cardiovascular safety and efficacy of sitagliptin, a dipeptidyl peptidase 4 inhibitor, in type 2 diabetic patients with ischemic stroke remains uncertain.

Methods: We analyzed data from the Taiwan National Health Insurance Research Database (NHIRD) between March 1st, 2009 and December 31st, 2011. Ischemic stroke patients were identified from individuals with type 2 diabetes. Subjects using sitagliptin were compared with those not using sitagliptin for cardiovascular safety and efficacy evaluation. The primary outcomes were a composite of ischemic stroke, myocardial infarction (MI) or cardiovascular death.

Results: A total of 5,145 type 2 diabetic patients with ischemic stroke met our inclusion criteria and were followed for up to 2.83 years (mean, 1.17 years). Overall, 1,715 patients (33.3%) were exposed to sitagliptin therapy and 3,430 patients (66.7%) who did not use sitagliptin were in the comparison group. The events of primary composite outcomes occurred in 190 patients in the sitagliptin group (11.1%) and in 270 patients in the comparison group (10.8%) (HR, 1.02, 95% CI, 0.85–1.21). Patients treated with sitagliptin had similar risk of ischemic stroke, hemorrhagic stroke or all-cause mortality with HR of 0.95 (95% CI, 0.78–1.16, P=0.612), 1.07 (95% CI, 0.95–2.21, P=0.834), and 1.00 (95% CI, 0.82–1.22, P=0.988) respectively, compared with non-sitagliptin group.

Conclusions: The use of sitagliptin in type 2 diabetic patients with recent ischemic stroke was not associated with increased or decreased risks of adverse cardiovascular outcomes.

P5615 | BEDSIDE
Silent neuronal ischemias after elective percutaneous coronary intervention
H. Gokslamuk, S. Gulec, O.U. Ozcan, M. Gerede, V.K. Vurgun, N. Ozyuncu, C. Erol. Ankara University, Cardiology Department, Ankara, Turkey

Introduction: Increased plasma levels of neuron specific enolase (NSE) is related to damage of neurons and neuroendocrine cells. We aimed to investigate elevation of NSE after elective percutaneous coronary intervention (PCI) on the prediction of silent neuronal ischemias (SNIs).

Methods and results: Patients scheduled for elective PCI (n=80) and age and sex-matched controls (n=80) with normal coronary arteries were assessed. NSE levels were studied before and 12 hour after the procedure. Patients with high baseline levels of NSE (16 patients in normal coronary artery group and 11 patients in elective PCI group) (n=27) were excluded. Elevation of NSE was significantly more prevalent among patients with PCI than that of controls.

Thirty-five of the 133 study patients had NSE after the procedure. NSE elevation was significantly more prevalent among patients with PCI than that of controls.

The incidence of SNI was higher in active smokers and patients who had history of myocardial infarction (MI) (%31 versus %15, P=0.03 for active smokers and %25 versus %10, P=0.02 for history of MI, respectively) (See table). However, multivariate analysis failed to identify any independent predictor of NSE elevation after elective PCI.

Conclusions: The use of sitagliptin in type 2 diabetic patients with recent ischemic stroke was not associated with increased or decreased risks of adverse cardiovascular outcomes.

P5615 | BEDSIDE
Clinical and angiographic characteristics of silent neuronal ischemia (+) and (-) patients in PCI group
C. Erol. Ankara University, Cardiology Department, Ankara, Turkey

Introduction: Increased plasma levels of neuron specific enolase (NSE) is related to damage of neurons and neuroendocrine cells. We aimed to investigate elevation of NSE after elective percutaneous coronary intervention (PCI) on the prediction of silent neuronal ischemias (SNIs).

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Clinical and angiographic characteristics of silent neuronal ischemia (+) and (-) patients in PCI group

**Variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>SNI(+)</th>
<th>SNI(-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>69.8±8.9</td>
<td>63.9±7.0</td>
</tr>
<tr>
<td>Gender</td>
<td>57%</td>
<td>57%</td>
</tr>
<tr>
<td>Diabetes</td>
<td>97%</td>
<td>87%</td>
</tr>
<tr>
<td>DM duration (y)</td>
<td>12.1±6.7</td>
<td>10.3±5.8</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>96%</td>
<td>89%</td>
</tr>
</tbody>
</table>
Conclusion: For patients undergoing elective PCI, NSE levels after procedure increases. Invasive coronary procedures have risk of SNSLs, even in patients with normal coronary arteries. Increased recognition of SNSL May facilitate therapies aimed at preventing their occurrence and decrease the risk of adverse neurological outcomes.

CARTOID DISEASE

P5616 | BEDSIDE Cardioid artery stenting prior to the cardiac surgery - a hybrid treatment strategy in the extended TARGET-CAS study population

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Purpose: To evaluate safety and feasibility of a less-invasive hybrid strategy for patients with severe cardioid and cardiac disease - cardioid artery stenting (CAS) immediately followed by an open heart surgery.

Methods: In the population of 1245 patients with severe/symptomatic internal carotid artery (ICA) stenosis enrolled in the TARGET-CAS (Cardioid Artery Stenting With Patient- and Lesion-Tailored Selection of the Neuroprotection System and Stent Type) study in 2009–2014: 42 subjects (3.4%; age 70.5±7.1; 74% male) required urgent cardiac surgery. Those with CCS class III/instable angina/NSTEMI (n=40) and multivessel coronary artery disease or left main stenosis underwent coronary artery bypass grafting (CABG) immediately after CAS. The others (n=2) with severe aortic stenosis and recent pulmonary oedema or NYHA class III symptoms had hybrid CAS and aortic valve replacement. Symptomatic ICA stenosis (stroke/transient ischaemic attack within 6 preceding months) was present in 15 (36%) patients. Mean angiographic ICA stenosis rate was 85±11% (range 60–99%). The selection of neuroprotection devices (NPD) and stent type was done according to the TARGET-CAS study algorithm. Proximal NPD was used in 19 (45%) cases and closed cell stent was implanted in 39 (93%) patients (with high risk or symptomatic ICA lesions). Each patient was assessed by an independent neurologist pre- and post-CAS, before transfer to the cardiac surgery operating room. Operation risk according to euroSCORE was 2.6±1.1% (range 1.15–4.3%). CAS was performed on acetylsalicylic acid and unfractioned heparin only. Clopidogrel (loading dose of 300 mg) was administered in the 6th – 10th postoperative hour, after surgical bleedings were excluded and continued at daily dose of 75 mg for at least a month. Most procedures (27, 64%) were done on normothermic cardiopulmonary bypass; 6 (14%) patients had off-pump CABG.

Results: No neurological complications (stroke, transient ischaemic attack) in hospital or on 30-day observation were noted. Three (7.1%) major complications in the early postoperative period occurred: one myocardial infarct (successfully treated by percutaneous coronary intervention and glycoprotein of right coronary artery) and two deaths as a result of multi-organ failure.

Conclusion: Our findings indicate that the treatment strategy by CAS simultaneously and stent type was done according to the TARGET-CAS study algorithm. Proximal NPD was used in 19 (45%) cases and closed cell stent was implanted in 39 (93%) patients (with high risk or symptomatic ICA lesions). Each patient was assessed by an independent neurologist pre- and post-CAS, before transfer to the cardiac surgery operating room. Operation risk according to euroSCORE was 2.6±1.1% (range 1.15–4.3%). CAS was performed on acetylsalicylic acid and unfractioned heparin only. Clopidogrel (loading dose of 300 mg) was administered in the 6th – 10th postoperative hour, after surgical bleedings were excluded and continued at daily dose of 75 mg for at least a month. Most procedures (27, 64%) were done on normothermic cardiopulmonary bypass; 6 (14%) patients had off-pump CABG.

Conclusion: Despite a higher risk profile for cerebrovascular events older patients (age >70) did not show any stroke during a follow-up of up to 12 years in the overall cohort. In case of asymptomatic carotid artery stenosis older patients seem to be at an increased risk for stroke in the acute phase after CAS. These findings underline the results of the CREST trial and the meta-analysis of the Cochrane Stroke Group in a real world setting and a far longer follow-up.

P5618 | BEDSIDE The clinical relevance of myocardial injury after carotid endarterectomy

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Purpose: Myocardial infarction (MI) is a frequent complication of carotid endarterectomy (CEA), yet the majority of events are silent. Routine monitoring of postoperative cardiac troponin was implemented in our center to facilitate timely driven AID of silent myocardial injury and improve subsequent diagnostic and treatment strategies. We aimed to evaluate the incidence of myocardial injury after CEA and its association with adverse cardiovascular events.

Methods: This analysis included patients >60 years old who underwent CEA between January 1st 2011 and December 31th 2012, whose Troponin-I levels were monitored the first three postoperative days and were included in an observational longitudinal cohort study that assessed adverse cardiovascular events. Myocardial injury was defined as a troponin concentration >60 nanogram per liter. Endpoints were myocardial infarction, stroke, coronary revascularization and cardiovascular death during follow-up.

Results: 240 consecutive patients were included in the analysis. Indications for CEA were stroke (30%), transient ischemic attack (39%), ocular symptoms (21%) and asymptomatic (10%). Postoperative myocardial injury occurred in 35 patients (15%) and was associated with age, preoperative renal insufficiency, postoperative pericardial effusion (9%) and contralateral carotid occlusion and >100% increase in postoperative transcranial doppler velocities. After a median follow-up of 1.8 years (IQR 1.0–2.6), MI occurred in 24% vs 1.6% (RR 15.0, 95% CI 4.2–56), stroke in 5.9% vs 0.6% (RR 4.2, 95% CI 1.0–17), renal dysfunction in 4% versus 0.0% (RR 9.1, 95% CI 1.0–93) and cardiovascular death in 5.9% vs 0.5% (RR 11.2, 95% CI 1.0–121) in patients with vs without postoperative myocardial injury, respectively. All MIs in patients with myocardial injury occurred within 30 days after surgery vs 4 months in other patients.

Conclusion: Myocardial injury after CEA occurred in 15% of patients and was associated with multiple patient- and procedure-specific factors. After a median follow-up time of 1.8 years, the incidence of MI was significantly higher in patients with myocardial injury, which was attributable to silent NSTEMIs that occurred in the early postoperative phase. Also, a higher incidence of cardiovascular death was observed in patients with myocardial injury.

P5619 | BEDSIDE Patients with carotid artery stenosis and recent cerebral ischemic event are less likely to have a well-developed cerebral collateral pathways, which should prompt early carotid intervention

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Background: Cerebral collateral pathways are of utmost importance in the occurrence of the first cerebral ischemic event (CIE), as well as CIE recurrence in patients with internal carotid artery stenosis (CAS).

Purpose: To assess collateral pathways in the cerebral arteries associated with severe carotid artery stenosis (CAS) in patients who suffered from cerebral ischemic event (CIE) within 1 month, 3 months, distant (over 3 months), and no history of CIE.

Methods: Study group included 316 subjects in mean age 65±8.28±24, 71% (97/334663) of the CREST trial and the meta-analysis of the Cochrane Stroke Group in a real
men, who were referred to carotid artery stenting, including 54 subjects who had CIE during last 1 month, 33 with CIE between 1 and 3 months, 149 with distant CIE (over 3 months) and 80 patients who had no history of CIE. Transcranial color-coded Doppler ultrasound (TCCD) was performed prior to carotid artery stenting in the test groups. The prevalence of collateral pathways via the anterior communicating artery (AcoA) and posterior communicating arteries (PCoAs) was evaluated.

**Results:** Any cerebral collateral pathway (through the AcoA or PCoA) was identified in 39 (72%) out of 54 subjects with CIE below 1 month, 18 (54%) with CIE between 1 and 3 months, 131 (88%) with distant CIE and 72 (90%) with asymptomatic ICAS.

The AcoA was found in 53%, 36%, 80% and 86% of subjects with CIE below 1 month, between 1 and 3 months, over 3 months and asymptomatic, respectively. While PCoA was found in 46%, 39%, 50% and 35% of cases in respective groups. Functioning collateral pathways were more often encountered in asymptomatic subjects as compared to subjects with CIE below 1 month (p<0.007) and between 1 and 3 months (p<0.001), respectively.

Similarly, collateral pathways were more prevalent in subjects with distant CIE as compared to patients with CIE below 1 month (0.007) and between 1 and 3 months (<0.001), respectively.

Interestingly, there was no statistical difference in the frequency of collateral cerebral circulation between asymptomatic and distant symptomatic patients (90% vs 89%; p=0.636).

Analyses revealed that subjects with recent (below 3 months) CIE were less likely to develop cerebral collateral flow (57 out of 87 subjects, 66%), as compared to subjects with CIE more distant than 3 months (p<0.001) and asymptomatic ICAS (<0.001).

**Conclusions:** There is lower prevalence of collateral flow in patients with recently untreated hypertension. Measuring of carotid intima-media thickness (cIMT) and carotid plaques allows sensitive assessment of the underlying burden of the atherosclerosis.

**Methods:** We analysed cross-sectional data on 25,000 randomly selected individuals in the 2nd re-survey in 2013–14 of the China Kadoorie Biobank study that had screening of their extracranial carotid arteries performed using automated B-mode ultrasound. Measurements of cIMT were recorded as the mean of 3 measurements over a 1-cm region in the far wall of the common carotid artery at end-diastole on each side. The presence of plaque (focal IMT >1.5 mm), number of plaques and size of maximum plaque were combined in a plaque score.

**Results:** The mean values of the left and right carotid arteries were highly correlated for both cIMT (r=0.60) and plaque scores (r=0.62) and each measure was strongly correlated with the other (r=0.55). Figure shows that the mean cIMT (left panel) and plaque score (right panel) increased linearly with age. Mean cIMT levels were 0.59 cm, 0.74 cm and 0.85 cm and the proportions with plaque were 4%, 39% and 49%, in those with mean age of 45, 65 and 85 years, respectively. At each age group, the mean cIMT and the mean plaque scores were also positively related to the severity of hypertension. Individuals with SBP ≥160 mmHg or SBP ≥140–159 mmHg and those with SBP ≥120 mmHg had age-equivalent differences of 11 and 7 years for cIMT and 11 and 6 years for carotid plaque scores, respectively.

**Conclusions:** The high prevalence of untreated hypertension results in a high burden of atherosclerosis, suggesting that the high rates of stroke are likely to persist, or even rise further, in China over the next decade.

**Acknowledgement/Funding:** Medical Research Council, Wellcome Trust and British Heart Foundation
Progression of atherosclerotic carotid plaque in hypertensive patients: the Campania-Salute Network

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Background: Carotid atherosclerotic plaques (CAP) progression affects prognosis in hypertensive patients. Experimental and clinical studies have shown that various anti-hypertensive agents exert anti-atherosclerotic action that is partly independent of the blood pressure-lowering effect. There is little information on the possible CAP progression during anti-hypertensive treatment.

Purpose: We evaluated the factors associated with CAP progression in a large hypertensive registry.

Methods: We assessed CAP progression in 2261 hypertensive patients with baseline intima-media thickness (IMT) >1.5 mm, defining clear-cut presence of CAP (age 59±10 years, 59% male) with ≥1 year follow-up. Assessment of changes in IMT was done at the time of the last available control visit. Annual IMT increase was expressed as absolute change in thickness normalized by the duration of follow-up [change in thickness / follow-up time in years]. CAP progression was defined as an annual IMT increase >0.1 mm. Mean systolic and diastolic blood pressure (BP) were computed as the average values of all control visits during follow-up. Medications were considered in the model of logistic analysis when prescribed in more than 50% of the control visits during follow-up, as previously reported.

Results: At a median follow-up period of 50 (interquartile range: 12–201) months, CAP progression occurred in 554 patients (24%). Among all demographic clinical and laboratory characteristics, patients with CAP progression at the time of the last available visit exhibited older age (60.5±8.6 years) than patients without CAP progression (58.0±9.5 years; p<0.0001) and higher mean systolic BP during the follow-up (139±20 vs 123 mmHg; p<0.003). Classes of anti-hypertensive medications in patients with and without CAP progression including diuretics, ACE-inhibitors, angiotensin receptor blockers, CA++-channel blockers, beta-blockers, cholesterol lowering agent and antplatelet agents were prescribed with similar frequency in both groups.

Conclusions: In a registry of treated hypertensive patients, the risk of CAP progression was associated with older age and less effective systolic BP control during follow-up, and is independent of the type of prescribed medications. These results suggest that only more aggressive and effective anti-hypertensive therapy but not specific anti-hypertensive medications could prevent CAP progression.

Investigating the mechanism of action of statins in carotid plaque stability in patients undergoing endarterectomy

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Background: Oxidative stress and macrophage infiltration are associated with atherosclerotic plaque formation and instability, through endothelial dysfunction and inflammation. Statins are well known to show benefits in atherosclerosis besides lipid lowering, including the endothelial function improvement potentially by enhancement of eNOS expression and activity, but the underlying mechanisms remain unclear. We sought to elucidate the underlying signaling pathways in atherosclerotic plaques, including changes in eNOS expression during follow-up, and is independent of the type of prescribed medications. These results suggest that only more aggressive and effective anti-hypertensive therapy but not specific anti-hypertensive medications could prevent CAP progression.

Methods: We collected carotid atherosclerotic plaques specimens from 62 patients having undergone endarterectomy for internal carotid artery stenosis. Patients were divided into four groups: symptomatic unstable patients not receiving statins (u/nost group, n=22), symptomatic unstable patients on statin (u/st group, n=11), asymptomatic stable patients not receiving statins (s/nost group, n=9) and asymptomatic stable on statin (s/st group, n=20). Samples were examined by histopathology for plaque morphology (stable vs unstable) by immunohistochemistry for p-eNOS/eNOS, p-Akt/Akt, iNOS and NOX-4 determination and for detection of oxidative stress biomarkers, malondialdehyde (MDA) and nitrotyrosine (NT).

Results: Stable plaques were found in 66% of patients on statins versus 33% of those not receiving statins (p=0.02). Immunohistochemistry revealed that iNOS was mainly expressed in macrophages and vascular smooth muscle cells and its expression was attenuated only in s/t group. NOX-4 expression was higher only in macrophages and reduced in both groups treated with statins. Western Blot analysis confirmed the decreased iNOS expression in the s/t group, while along with the increased p-eNOS expression in the same group. P-Akt/Akt ratio was significantly increased in s/nost and s/st groups and NOX-4 expression was increased in u/nost and u/st groups. MDA and NT were not different among groups.

Conclusion: Akt phosphorylation and NOX-4 expression were associated with atherosclerotic plaque stability independently of statin therapy, while p-eNOS/iNOS expression was favorable only in patients with stable plaques on statins. Oxidative stress biomarkers level did not differ among groups. p-eNOS activation with parallel decreased iNOS expression seems to be a potential mechanism for atherosclerotic plaque stabilization by statin therapy.
Methods: Consecutive patients with recent acute anterior circulation ischemic stroke due to large artery atherosclerosis were included in the study. Patients with history of paroxysmal or permanent atrial fibrillation were excluded. Carotid arteries of patients were evaluated within 24 hours from symptoms onset by: 1) carotid ultrasound and 2) microwave radiometry (MWR). During ultrasound study, maximum thickness of carotid plaques (maxPTA) was evaluated. Only patients with bilateral carotid plaques were included in the study. During MWR measurements, temperature difference (ΔT) was defined as the maximal temperature recorded along the carotid artery minus minimum. The ipsilateral to the cerebral intact carotid arteries, assumed to be causant the symptoms, were defined as culprit. Results: In total 100 carotid arteries of 50 patients were analyzed. Culprit carotid arteries had higher maxPTA compared to nonculprit carotid arteries (3.76±2.03 versus 2.53±1.99 mm, p<0.001). Culprit carotid arteries had also higher temperature differences, compared to nonculprit in both vessel and patient based analysis (0.93±0.58 versus 0.58±0.35°C, p<0.01 and 0.98±0.59 versus 0.52±0.26°C, p<0.001, respectively). In multivariate logistic regression analysis, ΔT was independently associated with the culprit carotid artery, causing the symptoms, when adjusted to sex, age, vascular risk factors and maxPTA (OR: 5.94, 95% CI: 1.56–22.63, p<0.01). By ROC curve analysis the optimal cutoff point of ΔT for predicting the symptomatic carotid artery was >0.60°C with a sensitivity of 72% and a specificity of 60% (AUC=0.726, 95% CI: 0.626–0.827, p<0.001). Conclusions: Microwave radiometry can recognize the culprit and nonculprit carotid artery based on their differences in temperature. However, the ident ΔT display high temperatures in asymptomatic patients with intermediate but bilateral carotid artery stenosis could better guide intensive medical treatment or intervention.

CORONARY SURGERY

PS5629 | BEDSIDE
Sex specific trends in 4-year survival in 94 328 patients who underwent a first isolated coronary artery bypass graft procedure 1987-2006
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Purpose: The aim of the present study was to examine trends in age-and sex-specific 4-year survival after a first isolated coronary artery bypass surgery (CABG).

Methods: We used the National Inpatient register to identify 94,328 (74,113 men and 20,215 women) who survived the first 30 days after CABG during 1987–2006. The cohort was divided into two age groups (18–54 years, ≥ 55 years) and stratified into four periods (1987–1991; 1992–1996; 1997–2001; 2002–2006) with a 4-year follow-up for each five year period.

Results: A continuously decreasing trend in mortality risk was observed with a HR of (0.63, 95% CI, 0.46–0.88) in men ≤55 years and (HR 0.69, 95% CI, 0.63–0.76) in men aged ≥55 years in the last period (2002–2006). Among women aged <55 years there was a non-significant difference in HR during the periods (HR 1.02–1.05) in 2000–2006. However, the HR of ≤55 years displayed a favorable decreasing trend from the first to the last period (HR 0.62, 95% CI, 0.52–0.75).

Conclusions: During the 20 year study period there was an overall favourable trend in survival after CABG in both men and women, except for women below 55 years of age.

PS5629 | BEDSIDE
Current off-pump coronary artery bypass grafting with multiple skeletonized arterial conduits can improve clinical outcome for diabetic patients
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Background: Diabetes mellitus is a strong risk factor for worsened clinical outcome in CABG surgery. In Japan, off-pump CABG has achieved widespread application in last decade, with up to 60% of CABG cases performed via the off-pump technique. Following the development of off-pump CABG, the current trend in revascularization strategy is toward in-situ all-arterial grafting. We were interested in whether application of the current off-pump technique using multiple skeletonized arterial conduits could improve outcome for diabetic patients.

Methods: From January 2002 to December 2013, a total of 1,064 patients underwent isolated off-pump CABG. Of these 1,064 patients, 551 had diabetes (DM) and 513 did not (nDM). We compared the clinical results between the two groups using maximum thickness of carotid plaques (maxPTA) was evaluated. Only patients with bilateral carotid plaques were included in the study. During MWR measurements, temperature difference (ΔT) was defined as the maximal temperature recorded along the carotid artery minus minimum. The ipsilateral to the cerebral intact carotid arteries, assumed to be causant the symptoms, were defined as culprit. Results: In total 100 carotid arteries of 50 patients were analyzed. Culprit carotid arteries had higher maxPTA compared to nonculprit carotid arteries (3.76±2.03 versus 2.53±1.99 mm, p<0.001). Culprit carotid arteries had also higher temperature differences, compared to nonculprit in both vessel and patient based analysis (0.93±0.58 versus 0.58±0.35°C, p<0.01 and 0.98±0.59 versus 0.52±0.26°C, p<0.001, respectively). In multivariate logistic regression analysis, ΔT was independently associated with the culprit carotid artery, causing the symptoms, when adjusted to sex, age, vascular risk factors and maxPTA (OR: 5.94, 95% CI: 1.56–22.63, p<0.01). By ROC curve analysis the optimal cutoff point of ΔT for predicting the symptomatic carotid artery was >0.60°C with a sensitivity of 72% and a specificity of 60% (AUC=0.726, 95% CI: 0.626–0.827, p<0.001). Conclusions: Microwave radiometry can recognize the culprit and nonculprit carotid artery based on their differences in temperature. However, the ident ΔT display high temperatures in asymptomatic patients with intermediate but bilateral carotid artery stenosis could better guide intensive medical treatment or intervention.

PS5630 | BEDSIDE
Effect of warfarin use in patients with new-onset atrial tachyarrhythmia after isolated coronary artery bypass graft
K.W. Hwang1, G.B. Nam2, C.H. Kwon2, W.S. Lee2, Y.G. Kim3, H.O. Choi4, J. Kim2, K.J. Choi5, Y.H. Kim1. 1Pusan National University Yangsan Hospital, Division of Cardiology, Department of Internal Medicine, Vansan, Korea, Republic of; 2Asan Medical Center, University of Ulans College of Medicine, Seoul, Korea, Republic of; 3Ulsan University Hospital, cardiology, Ulans, Korea, Republic of; 4Soochunhyang University Hospital, Cardiology, Bucheon, Korea, Republic of; 5Background: New-onset atrial fibrillation (AF) has been shown to affect late mortality after isolated coronary artery bypass graft surgery (CABG). Little is known about the need for long-term warfarin therapy in patients with newly diagnosed post-CABG AF.

Methods: We evaluated long-term survival data in 4,368 patients who underwent isolated CABG from 2000 through 2011. All-cause mortality data were obtained from Korea National Registry of Vital Statistics. A Multivariable Cox proportional hazards regression model was constructed to determine the independent impact of new-onset AF after isolated CABG (POAF) on long-term survival after adjusting for several covariates.

Results: After excluding 133 patients with prior AF or atrial flutter, 4,235 consecutive patients with isolated CABG was enrolled. New-onset POAF was identified in 756 patients (17.9%) and 479 patients (63.3%) received a cardioversion or amiodarone infusion for restoration of POAF. POAF independently predicted long-term mortality (hazard ratio [HR]: 1.27; 95% confidence interval [CI]: 1.02 to 1.59) with a median follow-up duration of 6.0 years (interquartile range, 3.4–8.9 years). However, treatment with warfarin for >3 months in POAF patients did not significantly reduce long-term mortality compared with POAF patients receiving no warfarin or warfarin for <3 month (Figure).

Conclusion: Symptomatic POAF is significantly associated with poorer long-term survival. However, long-term treatment of warfarin after POAF does not provide survival benefit compared with no or short-term treatment of warfarin.
of cardiac troponin (p<0.03). Post-operative major organic dysfunctions (cardiac, respiratory and renal) were similar between groups. Group B presented a longer post-operative hospital stay (median 5 days, IQR 4–7, p<0.05). Extracorporeal circulation during surgery was significantly associated with a decrease in post-operative complications (OR 0.32, 95% confidence interval (CI) 0.13–0.74, p<0.01).

With a mean follow-up of 11.0±6.8 months, overall mortality was 3.1%. After multivariate logistic regression analysis (adjusted for age and cardiovascular risk factors), left main disease was a determinant of increased post-operative complications, acute myocardial infarction (AMI) and long-term mortality (OR 2.84, 95% CI 1.12–7.23, p<0.03). Time from admission to CABG was not a risk factor for post-operative complications, AMI or long-term mortality (group A: OR 0.76, 95% CI 0.29–2.02, p=0.58; group B: OR 1.63, 95% CI 0.70–3.75, p=0.25; group C: OR 0.65, 95% CI 0.24–1.77, p=0.40).

Conclusion: In this group of patients after ACS, critical left main disease, but not time from admission to CABG, was a predictor of short and long-term adverse outcomes.

Our findings emphasize the importance of early surgery in patients with left main disease, whereas in those with larger infarct extension (higher troponin values), delay in surgery may reduce the risk of post-operative adverse events. Ultimately, the optimal surgical timing remains an individualized decision.

P5632 | BEDSIDE
Role of HDL-C in patients undergoing coronary artery bypass grafting
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Background: Previous studies showed that high-density lipoprotein cholesterol (HDL-C) functionality may be impaired under certain conditions, affecting its beneficial effects. We previously reported about the lack of protective role of HDL-C among patients who underwent coronary artery bypass grafting (CABG).

Purpose: To further investigate the protective role of HDL-C in the settings of CABG patients.

Methods: A consecutive series of 2016 patients undergoing first-time elective CABG at one institution between 2004 and 2011 was studied. According to the ATPIII criteria, pre-operative HDL-C values were used to identify patients with high (Group A) vs. low (Group B) HDL-C. To eliminate biased estimations, a propensity score model was built and two cohorts of 1:1 optimally matched patients were obtained. Cumulative survival and major adverse cardiovascular events (MACE) were analyzed by means of Kaplan–Meier method, and Cox proportional-hazards regression models were used to identify independent predictors of MACE and death.

Results: Propensity matching identified two cohorts of 711 patients each. At a median follow-up time of 34 months, mortality was 60/711 (8.4%) in Group A, and 49/711 (6.9%) in Group B (p=0.26). Three-year survival free from MACE was 58.3±4.1% for Group A vs. 68.6±5.5% for Group B (Chi-squared 17.6, p<0.02). Regression analysis showed that pre-operative HDL-C levels were associated with increased MACE occurrence during follow-up (HR 1.76, p=0.04).

Conclusion: Higher HDL-C levels are not associated with reduced risk of vascular events in patients undergoing coronary artery bypass grafting (CABG). Present findings may encourage efforts to improve HDL-C functionality rather than arbitrary increasing their levels.

P5633 | BENCH
Should bilateral internal thoracic artery grafting be used in patients with left main disease?
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Objective: Left main (LM) disease is a severe form of coronary artery disease. Coronary artery bypass grafting (CABG) is the standard of care for patients diagnosed with complex lesions of the left main (LM). Improved survival of patients treated with internal thoracic artery (ITA) grafts used to bypass the left anterior descending (LAD) artery is believed to be related to their better long-term patency compared to saphenous vein grafts (SVGs). Survival is further improved when left-simultaneous ITA (SIMA) grafting.

Methods: Seven hundred and forty seven patients with LM who underwent BITA grafting between 1996 and 2008 were compared with 352 LM patients who underwent SITA. Euroscore of BITA patients was significantly higher (8.97 + 3.73 vs. 6.23 + 4.51 p<0.01). Operative mortality (3.5% vs. 3.9% in BITA and SITA) and sternal wound infections (2.4% vs. 3.1%) were not significantly different between groups. Mean follow-up was 11.5±2 years. Ten-year survival (Kaplan-Meier) of the BITA group was significantly lower than that of the BITA group (50.0±2.8% vs. 69.1±1.7%, P<0.001, Log Rank test). However, assignment to the BITA group was poorly associated with better COX-adjusted survival (HR 0.988, 95% CI 0.822–1.188, P=0.588).

Conclusion: This large cohort study does not support routine use of BITA in all patients presented with LM disease. Similar long term survival can be achieved with SITA. Largers studies of subsets of LM patients that had better Kaplan-Meier survival are required.

P5634 | BEDSIDE
Do diabetic patients benefit from bilateral internal mammary artery grafting?
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Introduction: Bilateral internal mammary artery (BIMA) grafting has been associated with better long-term survival in the setting of bilateral internal mammary artery (BIMA), but its benefit on diabetic patients remains controversial.

Purpose: To compare long-term survival following BIMA versus SIMA grafting between diabetic and non-diabetic patients.

Methods: We retrospectively reviewed all the patients who underwent isolated CABG and received two or more grafts with at least one IMA graft between 2004 and 2013. Kaplan-Meier analysis was used to compare long-term survival between BIMA and SIMA in both groups (diabetic vs. non-diabetic). Propensity score matching with 2:1 and 1:1 pairing was used to adjust for treatment selection bias.

Results: 1259 out of 3045 eligible patients were diabetic (19% insulin-dependent and mean follow-up was 4 years. In unadjusted analysis, BIMA was less common in diabetic patients (29.7% vs. 37.6% for diabetic vs. non-diabetic patients). Although diabetic patients had a higher Euroscore II (median 1.78 vs. 1.38 for diabetics vs. non-diabetics), hospital mortality was similar (1.1% vs. 1.0% for diabetics vs. non-diabetics). Sternal wound infection was more prevalent in diabetic patients (0.9% vs. 0.2% for diabetics vs. non-diabetics). BIMA was associated with better long-term survival than SIMA in both groups (cumulative survival of 87% vs. 70% in diabetic patients and 89% vs. 79% in non-diabetic patients, respectively). After propensity score matching, BIMA was associated with increased survival in the diabetic cohort (Hazard Ratio: 0.570 CI95%: 0.342–0.950), but there was no statistically significant difference in the diabetic cohort (Hazard Ratio: 0.850, HR: 0.774 CI95%. 0.447–1.339). In-hospital mortality and sternal wound infection were low in matching cohorts irrespective of the number of IMA grafts.

Conclusions: BIMA grafting was associated with better long-term survival in non-diabetic patients without increasing hospital mortality or sternal wound infection regardless of diabetes status. BIMA grafting appears to be safe for diabetic patients, despite the apparent lack of significant survival advantage.

P5635 | BEDSIDE
BIMA versus SIMA in coronary artery bypass grafting surgery: long-term survival: retrospective cohort with propensity matched analysis
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Introduction: It remains controversial whether long-term outcomes and post-operative complications favour bilateral internal mammary artery (BIMA) grafting vs. single internal mammary artery (SIMA) grafting in coronary artery bypass grafting surgery (CABG).

Purpose: Our main aim was to compare long-term survival following BIMA versus SIMA grafting in our tertiary care centre.

Methods: Retrospective cohort including consecutive patients from 2004 to 2013 who underwent isolated CABG and received two or more bypasses with at least one IMA graft. Data were obtained from the Department of Cardiothoracic Surgery database. Mean follow-up was 4 years, maximum of 10. Kaplan–Meier analysis was used to compare long-term survival between BIMA and SIMA. Propensity score matching with 2:1 pairing was also employed to adjust for treatment selection bias. Secondary end-points were hospital mortality and sternal wound infection.

Results: BIMA was performed in 1050 (34%) out of 3080 eligible procedures. BIMA was more likely to be used for patients who were younger (58.5±16 vs. 66.5±8.8), men (86.1% vs. 77.2%), more frequently active smokers (27.1% vs. 14.9%) and dyslipidemic (77.3% vs. 72.1%). On the other hand, BIMA was less frequently used for patients with diabetes (35.7% vs. 44.3%), hypertension (68.7% vs. 74.8%) and severe renal impairment (CC-50mL/min: 5% vs. 17.0%). Hospital mortality was 1.1%. All-cause mortality at the end of follow-up was 11.1%. BIMA was associated with longer survival on unadjusted analysis.
Discussion and conclusion: (70xULN) did not meet our criteria for significance. A patient cohort that is currently recruiting will allow derivation of a more precise criterion is neither sensitive nor specific. Our results suggest that a clinically relevant finding. This threshold was associated with an adjusted HR for 30-day mortality of 7.8 (95% CI: 9.02±21.6 vs. 95.20±23.9; p=0.006). During surgery both groups respectively had similar cardiopulmonary bypass times in minutes (60.9±45.1 vs. 64.4±42.3; p=0.004) and similar ICU stay in hours (41.3±36.1 vs. 40.0±45.0; p=0.965). The peak postoperative cardiac enzymes CKMB/ (74±104.8 vs. 80±62.8; p=0.567) and peak Troponin I (1±3.2 vs. 3±1.4; p=0.209) were similar in the two groups. The postoperative median serum creatinine umol/l was significantly higher in the non-metformin users (90.1±127.7 vs. 107.6±81.7; p=0.004). The median transfusion volume in the non-metformin users ALT U/l (47.6±17.9 vs. 66±77.9; p=0.010) and AST U/l (38.1±26.0 vs. 51.9±50.9; p=0.012) were significantly higher in the non-metformin users. All clinical endpoints including: death, myocardial infarction, stroke, renal failure, and readmission were similar.

Conclusion: The patients who are taking metformin prior to CABG and who continue its use after surgery seem to have a reduced surgery in the transaminase enzymes. This novel finding may suggest that metformin may exhibit some liver protective properties. Further experimental studies are warranted to verify this finding.

Background: Coronary surgery 997

Does metformin exhibit liver protective properties in diabetic patients undergoing CABG? R. Nazer, M. Abaibassan, D. Sharma, H. Attaradi, F. Alyaboyi, A. Alsadique, M. Fouda, T. Kashour. King Saud University, King Fahad Cardiac Center, Riyadh, Saudi Arabia

Background: Metformin is an oral antidiabetic drug belonging to biguanide class. It is considered as the first line of treatment in diabetes especially for those who are obese. Recent studies have demonstrated some cardioprotective properties of metformin in patients with acute coronary ischemia. Other end organ effects are yet to be validated.

Methods: At a single center, a total of 200 consecutive diabetic patients under- went on-pump isolated CABG from July 2013 to July 2014. All patients on met formin prior to surgery continued taking the drug until the day of surgery and -unlesstrained- metformin was restarted the next day after surgery. All clinical parameters including cardiac, kidney and liver function test were serially collected until discharge.

Results: At the time of CABG, 68 patients were taking metformin (34%) and 132 patients were taking other antidiabetic agents (66%) respectively. Both groups were comparable in the following years (52±10.9 vs. 57±10.9; p=0.544) body mass index kg/M2 (28.4±5.6 vs. 27.7±4.4; p=0.388), pre-operative left ventricular ejection fraction of <40% (17.6% vs. 15.2%; p=0.546), and viral hepatitis (1.5% vs. 0.8%; p=0.631). Prior to surgery, the metformin users had a slightly higher glycosylated hemoglobin HbA1C% (8.8±1.6 vs. 7.8±1.9; p=0.001) but a significantly lower serum creatinine umol/l (85.0±21.6 vs. 95.20±23.9; p=0.006). During surgery both groups respectively had similar cardiopulmonary bypass times in minutes (60.9±45.1 vs. 64.4±42.3; p=0.004) and similar ICU stay in hours (41.3±36.1 vs. 40.0±45.0; p=0.965). The peak postoperative cardiac enzymes CKMB/ (74±104.8 vs. 80±62.8; p=0.567) and peak Troponin I (1±3.2 vs. 3±1.4; p=0.209) were similar in the two groups. The postoperative median serum creatinine umol/l was significantly higher in the non-metformin users (90.1±127.7 vs. 107.6±81.7; p=0.004). The median transfusion volume in the non-metformin users ALT U/l (47.6±17.9 vs. 66±77.9; p=0.010) and AST U/l (38.1±26.0 vs. 51.9±50.9; p=0.012) were significantly higher in the non-metformin users. All clinical endpoints including: death, myocardial infarction, stroke, renal failure, and readmission were similar.

Conclusion: The patients who are taking metformin prior to CABG and who continue its use after surgery seem to have a reduced surgery in the transaminase enzymes. This novel finding may suggest that metformin may exhibit some liver protective properties. Further experimental studies are warranted to verify this finding.

P5639 | BEDSIDE

The anemia conundrum in cardiac surgery: does it enhance risk assessment? L.S. De Santo1, G.P. Romano2, S. De Notaris3, M. Mangio4, L. Savarese5, F. Iorio6, M. Miele6, F. Nurnis7, S.M. Caparroti8, 1 University of Foggia, Foggia, Italy; 2 AO dei Colli-Monaldi Hospital, Cardiovascular surgery and transplant, Naples, Italy; 3 Montevergine Cardiology Clinic, Cardiovascular Surgery, Mercogliano, Italy; 4 Centro Montevergine, Cardiac Surgery, Mercogliano, Italy.

Objective: Preoperative anemia is a well-known predictor of morbidity and mortality after cardiac surgery procedures. Nevertheless, the European System for Cardiac Operative Risk Evaluation (EuroSCORE), even in its most recent version, ignores this feature. This study explored whether adding anemia to conventional scoring could enhance risk assessment.

Methods: Data on 1765 consecutive patients (age: 67±10.3; female: 33%; anemic: 33.8%; preoperative creatinine clearance: 75.6±21.2 ml/min; mean euroSCORE: 9.8±2.9; urgent/emergent: 12.9%; redo: 6.2%; isolated CABG: 40.1%; valve procedures: 35.4%; combined: 11.2%; aortic: 13%), who under went on-pump procedures in a single centre from 2011 to 2013, were retrieved from Puglia Adult Cardiac Surgery Registry. Logistic regression analysis of mortality predictors was performed forcing anemia and additive euroSCORE into the model. The c-statistic of a predictive model encompassing both anemia and euroSCORE was calculated and confronted to that inherent to isolated euroSCORE.

Results: Overall observed mortality rate was 2.6%; the medium risk group (eu rosCORE 3–5) had 544 patients with 1.8% observed mortality (1% vs 3.7% in non anemic vs anemic patients; p = 0.044), the high risk group (EuroSCORE 6 plus) had 874 patients with 3% observed mortality (2.7% vs 5.3% in non anemic vs anemic patients; p = 0.027). Both anemia (β =2.13; 95% CI: 1.14–3.98; p = 0.018) and EuroSCORE (β =1.34; 95% CI: 1.21–1.48; p < 0.0001) proved predictors of mortality. The area under the ROC curve of the model encompassing both anemia and euroSCORE was 0.71±0.03, while c-statistic of the isolated EuroSCORE was 0.736; 95% CI: 0.663–0.809.

Conclusions: Preoperative risk stratification is enhanced when taking into ac count preoperative anemia.
gender was an independent predictor of better long-term survival (HR 0.682 95% CI 0.510–0.912). Moreover, women had a lower risk of hospital mortality (OR 0.384 95% CI 0.157–0.935) and a lower incidence of post-operative low cardiac output syndrome (OR 0.756 95% CI 0.601–0.952). Female gender, BIMA CABG (HR 0.584 95% CI 0.371–0.917) was also associated with better long-term survival. On the other hand, age (HR 1.036 95% CI 1.022–1.049), PAD (HR 1.827 95% CI 1.392–2.404), NYHA III-IV (HR 1.919 95% CI 1.372–2.699), and no mammary artery graft (HR 1.925 95% CI 1.241–2.986) were independently associated with worse long-term survival.

Conclusions: In this patient population, women undergoing CABG showed lower long-term mortality, even if they had more risk factors and received a lower number of grafts and less frequently BIMA.

Acknowledgement/Funding: FCT

## P5642 | BEDSIDE

Impact of gender on long-term outcomes following surgical versus interventional revascularization

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### Background:
Coronary artery bypass grafting (CABG) has historically had a higher mortality in women than men. Data regarding the impact of gender on outcomes for percutaneous coronary interventions (PCI) have been heterogeneous. Our study aimed to evaluate sex-specific differences in outcomes between CABG and PCI.

### Methods:
Patients undergoing CABG (1489 PCI) and PCI (991 women) were compared. Cox regression models were used to analyze the impact of gender on mortality, major adverse cardiac events (MACE), and all-cause mortality.

### Results:
The incidence of major adverse cardiac events (MACE) was lower for CABG versus PCI (28.6% vs. 41.8%, p<0.001). On the other hand, female patients showed no difference between CABG and PCI (39.1% vs. 42.6%, p=0.496). Overall MACE for men was lower than that for women (33.4% vs. 40.5%, p=0.016) and appeared to be related to improved outcomes following CABG in men compared with women. However, when matched groups were used to account for differences in risk factors between male and female patients, MACE was comparable between men and women for both CABG (male vs. female, 25.1% vs. 30.6%, p=0.167) and PCI (37.1% vs. 39.3%, p=0.041).

### Conclusions:
In an unselected cohort of patients undergoing CR in a contemporary community hospital setting, comparable male patients appear to benefit from CABG vs. PCI. However, female patients appear to have equivalent outcomes with either procedure. Further analysis suggests that it is the difference in risk factors between the sexes, rather than gender itself, that accounts for this difference, emphasizing the critical importance of accounting for gender differences in evaluating outcomes following CR.

Acknowledgement/Funding: Cardiopulmonary Research Science & Technology Institute; Florida Heart Research Institute

## P5643 | BEDSIDE

Reduced benefit of delayed coronary artery bypass graft surgery after acute coronary syndromes


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### Background:
In patients with acute coronary syndromes (ACS), early myocardial revascularization is increasingly used, but the optimal timing remains uncertain, especially in patients eligible for coronary artery bypass graft surgery (CABG). Many patients submitted to coronary angiography and with a suitable coronary anatomy do not proceed to CABG during the initial hospitalization and are discharged with a planned surgical procedure.

### Objective:
To evaluate the benefit of this unselected delayed CABG (cases – planned CABG at discharge), in comparison with the patients referred for CABG immediately after acute coronary syndromes.

### Methods:
We studied 408 consecutive patients admitted for non-ST-segment elevation acute coronary syndromes (NSTEMACS) with obstructive coronary disease referred for CABG since 2009. Our study population included 55 cases and 353
controls. Patients with cardiogenic shock or mechanical complications were excluded. The study endpoint was the incidence of death at 1 year.

Results: CABG was performed in 89% of cases with a median time delay of 105 days and in 99% controls (2 patients died before surgery) with a median time delay of 7 days after admission (p=0.026). The cumulative incidence of death at 1 year was 21.8% in cases and 11.5% in controls (p=0.033). Cox proportional hazard models identified delayed CABG (HR 1.96; 95% CI 1.03–3.73), left ventricular ejection fraction <50% (HR 2.58; 1.46–4.56) and GRACE score ≥158 (HR 2.12; 1.20–3.74) as independent predictors of mortality at 1 year.

Conclusion: In our population, a post-discharge surgical coronary revascularization practice was associated with increased mortality at 1 year.

P5644 | BEDSIDE
Sleep apnea is associated with new-onset atrial fibrillation after coronary artery bypass grafting: Results from SABOT study
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Background: Previous studies using questionnaire as a surrogate for sleep apnea have produced conflicting findings on the relationship between sleep apnea and occurrence of post-coronary artery bypass grafting (CABG) AF.

Methods: We retrospectively reviewed patients who underwent CABG and evaluated the incidence of sleep apnea by using questionnaires. The diagnosis of sleep apnea was defined as Apnea-Hypopnea Index ≥5. Primary endpoint is new-onset AF during in-hospital stay.

Results: Among the 160 patients who completed the study, those in the sleep apnea group (n=128, 80%) had larger left atrial diameter (40.4±5.4 versus 38.4±6.0 mm, p=0.03) and left ventricular end-diastolic diameter (52.6±7.9 versus 49.2±8.6 mm, p=0.03) than those in the non-sleep apnea group. Patients in the sleep apnea group had a higher body mass index and waist circumference. The incidence of post-CABG AF (adjudicated independently) was higher for the sleep apnea than non-sleep apnea groups (24.8% versus 9.7%, p<0.007).

The AF occurred on an average of 75±92 and 45±39 hours after the CABG in the sleep apnea and non-sleep apnea groups, respectively (p=0.60). There was no in-hospital death and two acute renal failure requiring dialysis after CABG in the sleep apnea group. None of the patients developed in-hospital stroke. Length of hospital stay was similar between the two groups (8.3±3.9 versus 7.8±3.6 days, p=0.4).

Multiple logistic regression analysis showed the sleep apnea was an independent predictor of post-CABG AF (OR 4.8, 95% CI 1.1–18.1, p=0.004).

Conclusion: The incidence of post-CABG AF for patients in the sleep apnea group was nearly five times as high as that for patients in the non-sleep apnea group, probably related to atrial and ventricular remodeling.

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P5645 | SPOTLIGHT
Hospital-acquired pneumonia increases risk of mediastinitis associated with cardiac surgery
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Background: Mediastinitis after heart surgery prolongs in-hospital stay, and increases morbidity by 50% and mortality by 14 to 47%. In Mexico, its incidence has been reported to be 0.34%, and worldwide, 0.6%–4%. Postoperative pneumonia has not been reported as an established risk factor for mediastinitis, however it is linked with a high mortality rate.

Materials and methods: We retrospectively reviewed patients who underwent cardiac surgery (n=1339) from May 2009 to May 2014, diagnosed with mediastinitis according to clinical 2014 CDC criteria were selected and compared with a control group. Healthcare-associated pneumonia was identified in patients with and without mediastinitis and its relationship analysed with multivariate chi square test, and was also performed for other epidemiologic characteristics. The statistical analysis was made using the Stata software.

Results: Forty-nine patients fulfilled the CDC criteria for mediastinitis. Mean age was 53.6±16.2. Both groups were well balanced. Staphylococcus epidermidis was the leading microorganism at the surgical wound. There was a prevalence of 18.8% for in-hospital pneumonia, 42.5% were related to mediastinitis, finding the same germ in 45% of the cases. The presence of Pneumococcus confers an OR=6.3 (CI: 2.7–14.34) P<0.01, for developing mediastinitis, obesity conferred an OR of 2.5 (CI: 1.2–5.4) p<0.01 and diabetes confers an OR of 2.6 (CI: 1.2–5.6) p<0.05. Our data suggest that the risk of in-hospital pneumonia after CABG is significantly higher in patients with mediastinitis. A total of 14 (28.6%) deaths were attributable to pneumonia, and 3.0% due to mediastinitis.

Conclusions: Mediastinitis after open heart surgery is an overwhelming complication. Among different risk factors pneumonia, obesity and diabetes stand out. Future research should focus in evaluating temporal relationship with pneumonia and mediastinitis and implementing measures to prevent this dreadful complication.

P5646 | BEDSIDE
Comparison of quality of life among patients with multivessel coronary artery disease treated with CABG or hybrid coronary revascularization
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Background: Even though CABG is still a gold standard for treatment of patients with multivessel coronary artery disease (MVCAD), hybrid coronary revascularization (HCR) strategy consists of minimally invasive direct coronary artery bypass (MIDCAB) LIMA-LAD grafting using endoscopic LIMA harvesting and catheter-based techniques with implantation of DESS in non-LAD vessels, is a new accepted method of revascularization in this group of patients. There is a lack of data comparing those two methods in terms of quality of life.

Aim: The aim of this study was to assess the quality of life (QoL) in patients with multivessel coronary artery disease according to the method of revascularization: standard coronary artery bypass grafting (CABG) or hybrid coronary revascularization (HCR) with the use of the generic SF-36 questionnaire.

Methods: From a total of 200 patients with MVCAD enrolled to the POLMIDES study (Prospective randomized pilot study evaluating the safety and efficacy of hybrid revascularization in Multi-vessel coronary artery Disease) randomly assigned to undergo CABG or HCR (in a 1:1 ratio) we analyzed 199 patients (75 from HCR and 84 from CABG group) who completed correctly SF-36 questionnaire before revascularization procedures and during follow-up visit at 12 months. The differences between second and first score in both HCR and CABG groups were assessed.

Results: Most of the baseline clinical characteristics were similar in HCR and CABG groups. In both groups significant improvement in QoL was seen at follow-up visit. Patients from HCR group had both at baseline (51.3 vs. 59.2; p=0.006) and 12 months follow-up (67.57 vs. 73.7) improvement in QoL than patients from CABG group. The differences between scores at 12-month follow-up and at baseline were not statistically significant between the groups. Additionally significant clinical improvement had been noted in Social Functioning (SF) and Role Emotional (RE) role scores. The differences between scores at 12-month follow-up and at baseline were not statistically significant between the groups. Additionally significant clinical improvement had been noted in Social Functioning (SF) and Role Emotional (RE) role scores. The differences between scores at 12-month follow-up and at baseline were not statistically significant between the groups.

Conclusion: Both methods of revascularization in multivessel coronary artery disease (CABG surgery and Hybrid Coronary Revascularization) are associated with improvement in quality of life at 1 year after the procedures. We did not find any clear evidence on the advantage of one method over the other in terms of the quality of life.

P5647 | BEDSIDE
Aortic coronary bypass graft outcomes predicted by the distal vessel quality score: optimization of revascularization strategy
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Introduction: Coronary bypass graft (CABG) is recommended by the guidelines in several scenarios. However, it is not uncommon the early occlusion of the grafts. Some clinical factors have been described as predictors of this early dysfunction but the impact of the grafted distal vessel on outcomes is poorly understood.

Aims: We aimed to create an easily applicable score to depict the quality of the distal vessel and evaluate its impact on the outcomes of aorto-coronary grafts.

Methods: We created a score to assess visibility, diameter, and size of the vessel-dependent myocardial territory as angiographically evaluated for each vessel. Each variable was quantified from 0 (worst) to 3 (best). The final Distal Vessel Quality (DVQ) score was the result of the cumulative score for all distal vessels.
that were grafted divided by the number of vessels. Two independent cardiologist blind to the outcomes calculated the DVQ score with low interobserver variability. **Results:** We evaluated a total of 116 consecutive patients who underwent single CABG, with a mean follow-up of 6.5±3.1 yrs (available for all patients, all with > 6 yrs of follow-up). Mean age was 66±9.9 yrs, 82% were males and risk factors included hypertension in 46.2%, diabetes in 30.8%, and dyslipidemia in 48.7%. Each patient received a mean of 2.8 bypass grafts, up to a total of 337 grafts, specially to left anterior descending artery (34%), and obuse marginal artery (29.1%). A total of 235 (69.7%) venous and 102 (30.3%) grafts were implanted. In the follow-up 14.5% of the patients were admitted due to NTEACS (1.7%), unstable angina (4%), and stable angina (3%). Occulsion of 32 grafts was angiographically demonstrated at a median time from surgery of 1.2 (IQR 0.5–2.5) yrs, specially affecting those sutured to the obuse marginal artery (40.3%). Occulsion was more frequent in women (18 vs. 9%, p=0.036), venous grafts (12.3 vs. 2.9%, p=0.007), and patients with lower single vessel (5.7±1.6 vs. 6.4±1.3, p=0.006) and mean (5.8±1.0 vs. 6.3±2.0, p=0.019) DVQ score. Multivariate analysis demonstrate that the use of arterial grafts (OR=0.217, 95% CI [0.064–0.737], p=0.014) and higher values of mean DVQ score (OR=0.555, 95% CI [0.370–0.832], p=0.004) were related to longer patency duration of the grafts. **Conclusions:** The DVQ score is a new simple tool to accurately predict good outcomes of coronary artery bypass grafts. Therefore, lower values of this score ought to preclude from grafting specific vessels. Percutaneous or hybrid strategies could be used to optimize outcomes. External validation of the DVQ score is warranted.

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**Sleep apnoea screening in patients scheduled for coronary artery bypass surgery**

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**Objectives:** Although it has been recognised as a cardiovascular risk factor, data on sleep apnoea screening before coronary artery bypass grafting (CABG) are scarce. This study sought to determine the prevalence, predictors and effects of sleep apnoea on re-admission in patients undergoing CABG.

**Methods:** We prospectively recruited 152 patients to undergo an overnight sleep study before CABG. Sleep apnoea was defined as an apnoea-hypopnoea index of ≥ 15. Data on unscheduled re-admission due to cardiovascular events were adjudicated.

**Results:** Among the 138 patients who completed the sleep study, sleep apnoea was diagnosed in 69 (50%). The patients who had sleep apnoea had a lower LVEF (p=0.029), a larger left atrial diameter (p=0.014) and a larger left ventricular end-systolic dimension (p=0.019) than those who did not. Angiographic SYNTAX and Gensini scores were similar in patients with and without sleep apnoea. The genetic analysis and structural equation model revealed that hypertension, a high body mass index and chronic renal failure were independent predictors of sleep apnoea (p=0.05). After an average follow-up of 6±3 months, 12 patients with sleep apnoea (17.3%) and three patients without sleep apnoea (4.3%) were involved in unscheduled re-admission due to cardiovascular events. Patients with sleep apnoea were five times more likely to have an unscheduled re-admission due to cardiovascular events (adjusted odds ratio: 4.63, 95% CI: 1.24–17.31, p=0.023) than those without sleep apnoea. As depicted in the Kaplan-Meier curves, patients with sleep apnoea had a poorer prognosis in terms of time to re-admissions (log-rank test, p=0.01) (Figure).

**Conclusions:** Sleep apnoea was prevalent and predictive of unscheduled re-admissions in patients scheduled for CABG.

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**The forgotten variable of shear stress in saphenous venous graft disease: whole blood viscosity**

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**Purpose:** We included prospectivelyPts with ACS on DAPT undergoing CABG. Platelet aggregation assessed with VerifyNow P2Y12 assay (California). Result reported in Platelet Reaction Units (PRU) and % of platelet inhibition (% Inh), calculated as [(Baseline-PRU)/Baseline] x 100. In allPts. %Inh was measured.

**Background:** Dual antiplatelet therapy (DAPT) is the gold standard treatment in acute coronary syndromes (ACS). Patients (Pts.) with ACS on DAPT undergoing coronary artery bypass grafting (CABG) should expect a washout period of 5-day for clopidogrel (C) and ticagrelor (T). Some guidelines support the use of platelet function tests (PFT) for timing CABG.

**Methods:** We prospectively recruited 152 patients undergoing coronary artery bypass surgery

Discussion: The well-known but neglected determinant of endothelial shear stress, WBV, especially at LSR was an independent predictor of SVGD. With bedside extrapolation of WBV with this simple calculation, may contribute to the evaluation of patients more comprehensively.
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daily after deciding CABG (basal); When <15% Inh was reached, CABG was scheduled. Primary end point: intraoperative and 24 hrs bleeding after CABG. Secondary endpoint: 24 hrs blood consumption and reinterventions. Excessive bleeding: >200 ml/h (or 100 ml/h) in the first 4 hrs.

Results: We studied 11 Pts, 5 T and 6 C. Pharmacodynamic showed in fig. T greatest %Inh and faster reversibility. T Pts. were operated in 3.610±5 days vs C 3.8±1.17 days, p<0.006, in both groups CABG performed in less than recommended 5-day, p=0.0001. Surgical bleeding: T 325±253 ml vs C 433±261 ml, p=NS. 24 hrs bleeding: T 470±710 ml vs C 560±245.5 ml, p=NS. No differences in packed red blood cells consumption or platelepheresis. No one Pts met excessive bleeding criterion and 0% of reinterventions.

Conclusions: In our study, PFT guiding CABG allowed 25% reduction in waiting time than recommended in the current guidelines without increase in bleeding or blood transfusion requirements. Security and benefit of this stategy must be confirmed in large scale trails.

COMORBIDITIES

P5651 | BEDSIDE
Additive positive effect of the reversion of depression and physical capacity improvement on the sympathovagal balance in the course of heart failure patients

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Autonomic nervous system (ANS) dysfunction appears in the course of both heart failure (CHF) and depression. Comprehensive cardiac rehabilitation (CCR) apart from improving physical capacity, can reduce depressive symptoms and leads to the restoration of ANS function among CHF patients.

Purpose: To evaluate the influence of the reversion of depression (measured by BDI score) and the physical capacity improvement (measured by peak oxygen consumption [pVO2; ml/kg/min]) on the sympathovagal balance (measured by low/high frequency ratio [LF/HF]) after CCR in CHF patients.

Methods: The study group comprised 111 CHF patients (NYHAII-III;EF ≤ 40%). Patients were randomized (2:1) to 8-week CCR based on Nordic walking training (five times weekly) at 40–70% of maximal heart rate, training group (TG) n=77, or to control group (CG) n=34. The effectiveness of CCR was assessed by changes - delta (Δ) in LF/HF, BDI score and pVO2, as a result of comparing these parameters from the beginning and the end of the program.

Results: Eventually, 46 patients in TG and 23 patients in CG were eligible for simultaneous ANS and psychological status analysis. Only in TG the LF/HF decreased 2.06±1.14 vs 1.19±0.80 (p=0.0001) and pVO2 increased 16.83±3.72 vs 19.14±4.20 ml/kg/min (p<0.0001). Favorable results in CG were not observed. The differences between TG and CG were significant: ΔpVO2 (p=0.0001); ΔLF/HF (p=0.0001). Depressive symptoms (BDI score) were substantially reduced in both groups (TG, p=0.0006; CG, p=0.0049). Nevertheless, the greatest improvement of sympathovagal balance was observed in patients whose depression was reversed thanks to the CCR in comparison to other patients from TG and the entire CG (Kruskal-Wallis test; p=0.0003).

Conclusion: Positive effect of the sympatho-parasympathetic balance obtained during the home CCR based on Nordic walking training results from the additive effects of the reversion of depression and physical capacity improvement in CHF patients.

Acknowledgement/Funding: The study was supported by the National Science Centre, Poland - grant number NN404 107936.

P5652 | BEDSIDE
Value of renal vascular Doppler sonography in management of cardioirenal syndrome type 1

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Introduction: Recent studies have demonstrated the relief of the congestion has demonstrated to improve renal functions in decompensated heart failure.

Purpose: The current trial was set up to investigate the changes of renal venous impedance and renal arteriolar resistance indices with diuretic therapy, in patients with congestive renal failure.

Methods: A total of 64 patients who presented with acute cardiorenal syndrome type 1 were enrolled. Daily measurements of renal arteriolar resistivity indices, renal venous impedance indices and serum creatinine levels were obtained.

Results: Thirty of the patients had improvement of serum creatinine levels along with diuretic therapy. Table shows the comparison of the renal Doppler parameters on admission and at time of creatinine nadir stratified according to those who had improvement of creatinine with diuresis and those who did not. Multi-variable regression model revealed that only high arterial resistance index which was obtained on admission might be a predictor of the creatinine drop along with diuretic therapy among patients with congestive renal failure (OR: 6.25, 95% CI 1.84–14.3, p=0.003).

Table 1. Renal arterial and venous Doppler parameters on admission and at time of creatinine nadir.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Improvement of creatinine with diuresis (n=30)</th>
<th>No improvement of creatinine with diuresis (n=34)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine, mg/dl</td>
<td>1.68±0.45</td>
<td>1.59±0.36</td>
<td>0.28</td>
</tr>
<tr>
<td>Median V (min–max)</td>
<td>0.86 (0.34–1)</td>
<td>0.66 (0.3–1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pulmonary venous waveform, (%)</td>
<td>19 (63)</td>
<td>8 (24)</td>
<td>0.002</td>
</tr>
<tr>
<td>Non-pulmonary venous waveform, (%)</td>
<td>11 (37)</td>
<td>26 (76)</td>
<td>0.002</td>
</tr>
<tr>
<td>Median arterial RI (min–max)</td>
<td>0.78 (0.6–1)</td>
<td>0.65 (0.54–0.78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time of creatinine nadir</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine, mg/dl</td>
<td>1.29±0.43</td>
<td>1.51±0.29</td>
<td>0.04</td>
</tr>
<tr>
<td>Median V (min–max)</td>
<td>0.69 (0.4–1)</td>
<td>0.44 (0.32–1)</td>
<td>0.005</td>
</tr>
<tr>
<td>Pulmonary venous waveform, (%)</td>
<td>4 (13)</td>
<td>2 (6)</td>
<td>0.31</td>
</tr>
<tr>
<td>Non-pulmonary venous waveform, (%)</td>
<td>26 (87)</td>
<td>32 (94)</td>
<td>0.31</td>
</tr>
<tr>
<td>Median arterial RI (min–max)</td>
<td>0.65 (0.45–0.87)</td>
<td>0.7 (0.48–0.78)</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Conclusions: High renal arteriolar resistance index may indicate the patients with congestive renal failure who benefit diuretic therapy in regard to improvement of kidney functions.

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The reverse remodeling of left atrium in patients after renal transplantation - the value of left atrium volume index

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Background: Cardiovascular diseases compose a kind of continuum initiated by cardiovascular risk factors in consequence leading to the development of atherothrombotic and secondary heart failure. Research concerning reverse process, which can be present due to disappaearence of causative factors is not numerous and but rather incomplete. The main aim of study is the assessment of left atrium (LA) reverse remodeling in patients with end-stage renal disease (ESRD) after renal transplantation (RT).

Materials and methods: Study group consisted of 42 patients after RT from non-related renal transplant donors; age 43.3±12.6 years, including 19 women 49.9±10.9 years old and 23 men 41.5±12.91 years old. The study protocol has been consisted of 5 stages: 1 week after RT, 3 months after RT, 6 months after RT, 1 year after RT, 3 years after RT. The echocardiographic examination was performed and following measurements were done: LAmax, LAmIn, LApWavep, LAshortm, LAshortmp, LAlongmp, LAlongmp, LAcrossmax, LAarea max. On the base of obtained parameters according to adequate formulas the following indices were calculated: left atrium volume (LAV), LAV index (LAI) and hemodynamic indices of LA (LAEF, LAAE, LAPE, LAIE, LAFS).

Results: The exact analysis of parameters concerning LA showed significant and progressive reduction either planimetric and volumetric LA dimensions. The LAV value measured after RT was – 34.63±10.34 ml/m2, 3 months after RT – 32.24±9.59 ml/m2, 6 months after RT – 31.36±2.90 ml/m2, 1 year after RT – 28.29±8.32 ml/m2, 3 years after RT – 27.57±8.40 ml/m2. The progressive decrease of LA size was the most marked during early stages of observation after RT and subsequently the slow down of this process was observed in the end of observation. Simultaneously with continuous decreasing of LA size its contractility was improved which was expressed by progressive and statistically significant improving of indices such as LAEF, LAFS, LAAE, and LAIE.

Conclusions: Disappearance of causative factors of unfavourable changes in cardio-vascular system allows to initiate the reparative processes leading to at least partial restitution of LA structure and function, which is called reverse remodeling. Reduction of LA volume improvement due to uremic atrial cardiomyopathy in patients after RT.
P5654 | BEDSIDE
Cardiac involvement in hemoglobin SC disease compared to homozygous sickle-cell anemia
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Background: Hemoglobin SC (HbSC) disease and homozygous sickle-cell anemia (SCA) are the most frequent genotypes (accounting for respectively 25% and 70%) of sickle-cell disease. Although the SCA cardiac involvement was well studied, the cardiac remodeling associated to HbSC has never been specifically investigated.

The aim of the study was to describe the HbSC cardiac remodeling versus SCA.

Methods: Using a case-control design, 61 HbSC (mean age 31.3±10.0 years, 36 women) patients underwent a comprehensive echocardiography and were compared to 61 SCA patients in stable conditions.

LV end diastolic volume index and LV ejection fraction were measured by Simpson method. LV mass index, left atrial volume index, septal E/e' ratio, peak tricuspid regurgitation velocity (TRV) and cardiac index were also measured as recommended. All the parameters were the average of three measures.

Results: Both LV morphological and diastolic functional parameters differed dramatically between the two groups of patients (table, mean ± SD). Moreover, the pulmonary artery systolic pressure as estimated by TRV was lower in HbSC patients.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HbSC patients (n=61)</th>
<th>SCA patients (n=61)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)</td>
<td>70±11</td>
<td>72±10</td>
<td>0.26</td>
</tr>
<tr>
<td>LV mass index (g/m²)</td>
<td>103±26</td>
<td>171±16</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV end diastolic volume index (m³/m²)</td>
<td>92±19</td>
<td>64±15</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiac index (L/min/m²)</td>
<td>4.2±1.0</td>
<td>3.1±1.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>60±5</td>
<td>61±6</td>
<td>0.88</td>
</tr>
<tr>
<td>Septal E/e' ratio</td>
<td>10.9±2.4</td>
<td>7.2±1.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Left atrial volume index (m³/m²)</td>
<td>51±11.9</td>
<td>33±8.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tricuspid regurgitation velocity (m/s)</td>
<td>2.57±0.26</td>
<td>2.26±0.23</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tricuspid regurgitation velocity &gt;2.5m/s, n (%)</td>
<td>34 (56)</td>
<td>4 (7)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusions: Cardiac remodeling is very different in HbSC compared to SCA. Clinical interpretation of echocardiography data should be adjusted to each variant of the disease. Moreover, this study is further evidence that the both genotypes of sickle-cell disease have different organ involvements and should not be pooled in clinical studies.

P5655 | BEDSIDE
Lack of association between central chemosensitivity and disease severity in optimally treated patients with mild heart failure
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Background: Previous studies reporting the association between augmented central chemosensitivity and severity of heart failure (HF) are conflicting. The aim of this study was to test this hypothesis in optimally treated patients with mild heart failure (NYHA II-III) and to determine whether a relationship is present in the entire cohort or only in subgroups.

Methods: A total of 47 patients (32% men; 78.2±9.7 years) with mild-to-moderate HF were prospectively recruited from a cardiology clinic. The primary endpoint of the study was the change in disease severity over 6 months. Chemosensitivity was estimated by the difference between end-tidal partial pressure of carbon dioxide (EtCO₂) and arterial pH at the end of apneic period. HF severity was assessed according to the New York Heart Association (NYHA) classification.

Results: The chemosensitivity was significantly higher in patients with NYHA class II (age: 57±10 y, LVEF: 34±17%, all receiving ACE-inhibitor and beta-blocker) in comparison to NYHA class III (17±7, 68±10, 60±11, respectively). Multivariate Cox regression analysis was applied to investigate whether each PH-LHD predict death or heart failure (HF) readmission after adjusting for other variables.

Conclusions: PH-LHD with PVD classified by DPG was significantly associated with death or HF readmission as compared to TN group (hazard ratio: 3.27 [95% CI: 1.20 to 8.89], P=0.02), while FP group did not reach statistical significance (hazard ratio: 1.96 [95% CI: 0.82 to 4.69], P=0.13).

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Pulmonary hypertension due to left heart disease: comparison between transpulmonary pressure gradient and diastolic pulmonary vascular pressure gradient
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Background: As compared to transpulmonary pressure gradient (TPPG), diastolic pulmonary vascular pressure gradient (DPG) may be more sensitive and specific indicator for pulmonary hypertension (PH) due to left heart disease (LHD) with significant pulmonary vascular disease (PVD). The aim of this study was to investigate the incidence and clinical features of PH-LHD with PVD classified by DPG and TPPG.

Methods: We analyzed 410 patients admitted for symptomatic heart failure (NYHA II-III) and underwent right heart catheterization (RHC) at compensated stage between 2007 and 2012. Patients with PH-LHD was divided into 3 groups according to the value of DPG and TPPG (True negative (TN) group: DPG<7mmHg and TPPG<12mmHg; False positive (FP) group: DPG<7mmHg and TPPG≥12mmHg; True positive (TP) group: DPG≥7mmHg). Multivariate Cox regression analysis was applied to investigate whether each PH-LHD predict death or heart failure (HF) readmission after adjusting for other variables.

Results: PH-LHD was observed in 164 patients (40%) in symptomatic heart failure. Thirteen patients (3%) were allocated into TP group, while 24 patients were allocated into FP group (6%). TP group was significantly associated with death or HF readmission as compared to TN group (hazard ratio: 3.27 [95% CI: 1.20 to 8.89], P=0.02), while FP group did not reach statistical significance (hazard ratio: 1.96 [95% CI: 0.82 to 4.69], P=0.13).
a total of 47 worsening HF events, changes in MCV were positively correlated with the changes in body weight (r=0.31, P=0.034), serum sodium (Na) (r=0.42, P=0.0036), and chloride (Cl) (r=0.457, P=0.0012), and negatively correlated with the changes in BUN (r=−0.389, P=0.0069) and creatinine (r=−0.494, P=0.0004). Multivariate logistic regression analysis demonstrated independent association between the increase in serum Cl concentration and the increase in MCV from stability to worsening of HF (OR: 6.02, 95% CI: 1.09−33.2, P=0.039). At recovery from worsening HF after decongestive therapy, MCV decreased to 94.9±15.6 fl (P<0.001). The incidence of an increase, no change, or decrease in MCV was 94.7±10.47 (21%), and 29±47 (80%), respectively. No correlation was detected between the change in MCV and blood tests upon recovery, though change in MCV was positively correlated with the change in body weight (r=0.323, P=0.027).

Conclusions: We observed serial changes in MCV according to the transition of HF status, which might reflect changes in cellular hydration status. Changes in MCV were significantly associated with changes in the serum Cl, indicating a role for this solute as an important osmoregulator in the regulation of MCV. Whether MCV changes in HF patients actually reflect the cellular hydration status of the whole body warrants further research.

P5660 | BEDSIDE
Chronic kidney disease and community-acquired acute kidney injury are associated with cardio-hepatic syndrome in patients with decompenated heart failure
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Objective: Cardiological syndrome is a common and serious problem with negative impact on outcomes in patients with acute decompenated heart failure (ADHF). Over the last several years prevalence and prognostic value of cardio-hepatic syndrome in this population has been discussed. The aim of the study was to assess possible relationship between renal and hepatic abnormalities in patients with ADHF.
Methods: In 200 patients with ADHF (male 72.9±10.7 years (M±SD), arterial hypertension 79%, ischemic heart disease 65%, myocardial infarction 43%, atrial fibrillation (AF) 62%, diabetes mellitus 36.5%, chronic kidney disease (CKD) 38%, chronic anemia 23.5%, chronic obstructive lung disease 23.5%, ejection fraction (EF) 45±12%, EF<35% 25%, chronic hepatic diseases 9.5%) alanine transaminase (ALT) and aspartate transaminase (AST) were measured baseline. Transaminases (TA) were considered abnormal when levels exceeded 50 U/L (local upper normal limit (UNL)). CKD and acute kidney injury (AKI) were diagnosed based on KDIGO 2012 Guidelines. Mann-Whitney test and multivariate logistic regression analysis were performed. P<0.05 was considered statistically significant.
Results: Mean baseline ALT and AST values in patients with versus without increase of TA were 95±36 vs 21±14U/L and 87±26 vs 25±11U/L respectively (p<0.001). Increase of ALT and/or AST occurred in 29 (14.5%) patients (alone ALT/ alone AST) in both TA in - 42.3, 19.2, 38.5% respectively). Community-acquired AKI occurred in 36 (18%) patients. Patients with versus without community-acquired AKI had higher levels of ALT (38±37 vs 21±18U/L, p<0.001) and AST (41±31 vs 25±14U/L, p=0.001). Incidence of cytolsis was higher in patients with versus without community-acquired AKI (20 vs 2%, p<0.001). Incidence of patients with community-acquired AKI and RV dysfunction (EF<35%) was higher in patients with community-acquired AKI (70 vs 17.3%, p<0.001). Combination of cytolsis with CKD or AKI was revealed in 10 (5%) patients. The independent predictors of cytolsis were AF at admission (odds ratio (OR) 1.1, 95% confidence interval (CI) 2.6–48.4), community-acquired AKI (OR 1.12, CI 4.1–30.3), CKD (OR 4.2, CI 1.6–11.0), chronic anemia (OR 2.7, CI 1.1–6.4), EF<40% (OR 2.4, CI 1.1–5.7).
Conclusions: Cardiohepatic syndrome occurred in 14.5% of patients with ADHF. Community-acquired AKI was diagnosed in 18% of patients. Different phenotypes of cardiorenalhepatic interrelations were revealed in 5% of patients. CKD and AKI along with AF at admission, chronic anemia, and EF<40% were the independent predictors of TA increase.

P5661 | BEDSIDE
Sleep-disordered breathing is of high prevalence in patients with acute cardiac decempanation
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Background and purpose: Most recently, sleep-disordered breathing (SDB) was identified as left ventricular independently associated with poor outcome (mortality and rehospitalization) in patients with acute decompenated heart failure (ADHF). This study investigated the prevalence of SDB in patients presenting with acute cardiac decempanation in a large cohort of these patients.
Methods and results: 233 consecutive patients (age 70.6±10.3 years, and 624±24.4 ±17.3% BMI 27±3.4 kg/m², NYHA class III/IV, age, increased pulmonary systolic pressure and moderate/severe FTR (OR: 1.5, 95% CI: 1.0–2.3, p=0.03) were associated to RD, but not the RV dysfunction (OR: 1.1, 95% CI: 0.6–2.0, p=0.7). At the multivariate analysis, neither moderate/severe FTR nor RV dysfunction were independent determinants of RD, whereas the interaction between moderate/severe FTR with RV dysfunction was an independent determinant of RD (OR: 1.2, 95% CI: 1.1–1.5, p=0.04). Kaplan–Meier analysis showed significant lower event-free survival rates in patients with moderate/severe FTR compared with absent/mild FTR (at 9 years, 43% vs 63%; Log-rank test 10.8, p<0.001). At multivariate Cox analysis, no interaction with RD of FTR was present (HR: 1.3, 95% CI: 1.2–2.7, p=0.02), RV dysfunction (HR: 3.9, 95% CI: 1.0–3.7, p=0.01) as well as interaction of moderate/severe FTR with RV dysfunction (HR: 1.5, 95% CI: 1.2–1.8, p<0.001) were significantly related to HF episodes. Kaplan–Meier analysis showed a lower survival rate in patients with moderate/severe FTR compared with absent/mild FTR (at 9 years, 22% vs 47%; Log-rank test 8.6, p=0.003). The multivariate Cox regression analysis showed that RD dysfunction (HR: 1.3, 95% CI: 1.1–1.8, p<0.03) and the interaction of moderate/severe FTR with RV dysfunction (HR: 1.5, 95% CI: 1.1–1.7, p=0.02) but not FTR were significantly related to the outcome.
Conclusions: The combination of significant FTR and RV dysfunction, but not FTR and RV dysfunction alone, is independently associated with RD, and both factors portend worse prognosis.

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tion. None of the patients was treated with ventilation therapy and all patients were naïve to ventilation therapy. The prevalence of SDB (apnea-hypopnea index $[AHI] \geq 5$) was 59.1% (AHI $\geq 15$) was 51.3% and AHI $\geq 15$ was 32.2%. Mean AHI was 35.3±23.9/h, mean ODI (3%) was 36.2±25.4/h, mean oxygen saturation was 91.4±3.1%, lowest oxygen saturation 78.8±9.4%, mean oxygen desaturation 6.4±3.3%. Average oxygen saturation time under 90% was 28±33%. 

**Conclusions:** SDB is of high prevalence in ADHF patients with 50% of these patients demonstrating moderate to severe SDB. Whether treatment of SDB in the setting of ADHF is of any benefit, is currently investigated in a randomized controlled study (CAT-HF).

**P5664 | BEDSIDE**

The effects of Baduanjin exercise on fatigue and quality of life in patients with heart failure

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**Background:** Fatigue is a common symptom in patients with heart failure due to reduced cardiac output which caused activity intolerance and reduced quality of life. Exercise was found to be safe and beneficial for heart failure patients, specifically regarding exercise capacity and quality of life. Baduanjin is a traditional Chinese exercise programme (Baduanjin exercise) on fatigue and quality of life of patients with heart failure.

**Methods:** The study used randomized control trial research design. Subjects were recruited using convenience sampling from two medical centers in northern Taiwan. Participants were randomly assigned to the Baduanjin group (n=41) or control group (n=41). Patients in the intervention group performed a 12-week Baduanjin exercise program, three times per week. A 35 min Baduanjin exercise demonstration videotape, a picture-based educational brochure, and a performance record form were provided. The control group had no any intervention. Data were collected by a structured questionnaire including demographic information, the modified Piper Fatigue Scale, Minnesota Living with Heart Failure Questionnaire at four time points: baseline, 4 weeks, 8 weeks, and 12 weeks after intervention.

**Results:** Subjects in the Baduanjin exercise group had significantly improved fatigue (F=5.083, p<0.01) and quality of life (F=9.108, p<0.001) from week 4 to week 12 after intervention. Those in control group showed significantly worse in fatigue (F=3.464, p=0.05) and no significant changes in quality of life (F=0.701, p=0.5). Generalized estimating equations revealed that compared to the control group, exercise group had significantly greater improvement on fatigue (p<0.01) and quality of life (p<0.01) at 4 weeks, 8 weeks, and 12 weeks. Overall adherence rate for exercise was 85%, and there were no reported adverse events.

**Conclusions:** These results support the effects of Baduanjin exercise on fatigue and quality of life of patients with heart failure. We recommend application of this simple traditional exercise in patients with heart failure to improve their fatigue and quality of life.

**Acknowledgement/Funding:** Ministry of Science and Technology

**P5655 | BEDSIDE**

Three-year experience of the left sided radiofrequency ablation in patients with long-standing persistent atrial fibrillation and rheumatic mitral valve disease


**Background:** In patients with long-standing persistent atrial fibrillation (AF) associated with rheumatic mitral valve (MV) disease, the results of left atrial ablation are controversial. The aim of this study was to evaluate the effectiveness of the left sided radiofrequency ablation (RFA) for long-standing persistent AF added to mitral valve procedures.

**Methods:** Between 2011 and 2015 187 patients in our Center underwent RFA. Of those, 63 patients had left atrial ablation for long-standing persistent AF added to surgery for rheumatic mitral valve disease. The saline-irrigated cooled-tip monopolaural ablating device was used in all cases. Mean age was 54 years (±12.4), 40 men (53.4%). AF duration was 58 months (±15.4). Primary indications for surgery were: rheumatic mitral stenosis (75%), mitral insufficiency (25%). Mean left ventricular ejection fraction was 46.5%. Clinical follow-up, 24-hour Holter, echocardiogram were done at 1, 6, 12, 24 up to 38 months post surgery.

**Results:** After a mean follow-up of 28 months (±9.3), 62 patients (98.4%) remained alive and 32 (50.8%) were in sinus rhythm. 27 patients did not represent signs of heart failure, and 5 (8%) were in NYHA class I. Of those who had AF, 19 (70%) patients were in NYHA class 0–I, 7 (29%) were in NYHA class II, and 4 (14%) NYHA class III. Peace-maker implantation was indicated in 2 cases (3.1%). In patients with prosthetic valve, patient died before the intervention (n=39) or control group (n=41). Patients in the intervention group performed a 12-week Baduanjin exercise program, three times per week. A 35 min Baduanjin exercise demonstration videotape, a picture-based educational brochure, and a performance record form were provided. The control group had no any intervention. Data were collected by a structured questionnaire including demographic information, the modified Piper Fatigue Scale, Minnesota Living with Heart Failure Questionnaire at four time points: baseline, 4 weeks, 8 weeks, and 12 weeks after intervention.

**Results:** Subjects in the Baduanjin exercise group had significantly improved fatigue (F=5.083, p<0.01) and quality of life (F=9.108, p<0.001) from week 4 to week 12 after intervention. Those in control group showed significantly worse in fatigue (F=3.464, p=0.05) and no significant changes in quality of life (F=0.701, p=0.5). Generalized estimating equations revealed that compared to the control group, exercise group had significantly greater improvement on fatigue (p<0.01) and quality of life (p<0.01) at 4 weeks, 8 weeks, and 12 weeks. Overall adherence rate for exercise was 85%, and there were no reported adverse events.

**Conclusions:** These results support the effects of Baduanjin exercise on fatigue and quality of life of patients with heart failure. We recommend application of this simple traditional exercise in patients with heart failure to improve their fatigue and quality of life.

**Acknowledgement/Funding:** Ministry of Science and Technology
Introduction: In chronic heart failure (CHF), symptoms reduce the level of patients’ usual activities, impacting negatively on quality of life.

Purpose: To record the effect of ivabradine on symptoms, NYHA classification and quality of life, in patients with CHF (NYHA II-IV) and left ventricular systolic dysfunction (LVSD) (the left ventricular ejection fraction <35%).

Methods: In this non-interventional study, 1245 patients with CHF and LVSD were prospectively studied in 102 cardiology hospital clinics/private cabinets. Data were recorded at baseline, at 1 and 4 months after inclusion. In all visits, patients’ quality of life (QOL) was assessed by means of the Left Ventricular Dysfunction (LVD) 36 questionnaire. The effect of treatment was assessed by the patient and by the treating physician at the 2nd and 3rd visit, using the Patient and the Physician Global Assessment questionnaire (PaGA/PhGA).

Results: During the total study duration, 81.3%, 77.9%, 53.6% of patients were receiving β-blockers, ACE inhibitors/ARBs, diuretics and mineralocorticoid antagonists respectively. Ivabradine administration decreased the number of patients in NYHA III/IV from 52.7% to 18.9%, while increased the number of patients in NYHA II from 0.0% to 4.7% to 18.2% to 6.2% respectively (from inclusion to 4 months, P < 0.001). Additional symptoms improved markedly, since 47% fewer patients reported dyspnea, 31.8% less orthopnea, 28.5% less ankle edema, 28.5% less fatigue, 25.7% less aniga and 24.2% less reduced exercise capacity. As a consequence, QOL was improved by 29 points, while 75.9% of patients reported a >10-point improvement, which is considered significant (P < 0.001). 23%~20.7% of patients and physicians respectively reported mild improvement and 67%~69.7% reported a moderate/significant improvement after a 4-month ivabradine administration (P < 0.001). Mean heart rate (HR) was reduced by 16.4 bpm at study completion, while this reduction was related to baseline HR level; patients with HR >80 bpm, 70–80 bpm, <70 bpm presented a mean HR reduction of 21.3 bpm, 11.7 bpm, and 4.7 bpm respectively (P < 0.001). 98.8% of patients received ivabradine “every day” or “quite often”, while at the 1st month almost 75% of patients received 7.5 mg bid, a dosage maintained by study completion.

Conclusions: Treatment with ivabradine significantly improves symptoms, NYHA classification and QOL in patients with CHF and LVSD. The abovementioned results are confirmed by both patients’ and treating physicians’ assessment.

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P5669 | BEDSIDE

Guidelines implementation in different populations - summarizing from CIBIS ELD and CIBIS ELD 24 Months FUP studies

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Introduction and aims: Data of recent Registries are collected from the western developed countries. This study gives us the insight into the basic differences of the patients’ characteristics and implementation of Guidelines for treatment of chronic heart failure (HF) in patients from Germany and South-Eastern Europe (SEE).

Results: We included 297 patients from Germany (age 74 years, 46% male, 37% with systolic HF, LVEF 51.5%, 45% on beta-blocker therapy) and 579 patients from SEE – 532 from Serbia, 30 from Slovenia and 17 from Montenegro (age 72 years, 71% male, 89% with systolic HF, LVEF 36.6%, 68% on beta blocker therapy) in CIBIS ELD study. 68.4% did not consume alcohol from SEE and 59.3% from Germany, p <0.01. 60.1% of patients from Germany never smoked, 31.8% were ex-smokers and 8.1% were smokers. Among patients from SEE 55.9% never smoked, 39.6% ex-smokers and 4.5% smoked (p=ns). BMI in patients from Germany was 29.4 vs. 26.9 (P <0.05), 13.5% from Germany suffered from depression vs. 3% of patients from SEE.

After 24 months of follow up, 17.2% of patients from Germany and 23.2% from SEE (p <0.05) died. 82% of patients from Germany continued to use beta blocker, 43.8% had ACE inhibitor and 27.3% had AT1 blocker and 34% loop diuretic in therapy. However, 92.7% of patients from SEE continued with beta blocker, 86.8% had ACE inhibitor and 9.7% AT1 blocker and 66% had loop diuretic in therapy.

Conclusions: Roughly taken, patients from developed Germany with HF were older, more often females with diastolic HF, overweight alcohol consumers, more likely depressed and less likely smokers, compared to those from developing countries from SEE who had more often beta blockers, ACE inhibitors, loop diuretics and expensive AT1 blockers in therapy. Patients from Germany and SEE have different profiles of cardiovascular characteristics, co-morbidities, and risk factors. Data suggest that use of medication is possibly better adapted to the patients’ needs and economic status in different European regions. Having so different socio-economic, environmental milieu in this HF patients we must pose the question are the Guidelines for diagnosis and management for cardiovascular diseases suitable for all and how could we bring them closer to clinical practice? Should we start with the new plan for controlled, randomized studies so that we include environmental factors, as well?

Acknowledgement/Funding: The study was funded by Ono Pharmaceutical Co., Ltd.
ilar trends were seen in mortality (n=28, 10%). Self-care scores, low at baseline, improved significantly in the maintenance and confidence scales (all p<0.0). Significantly more participants in the usual care group needed health care facilities than in the intervention group (n=24 (23%) vs. n=12 (11%) respectively, p<0.05).

Conclusion: Involving the family in self-care of heart failure is a new approach in the Lebanese context. Significant improvement is noted when this care is structured through a family-centred educational intervention.

P5670 | BEDSIDE
Audit and clinical service evaluation for acute heart failure patients dying within 48 hours of admission

Purpose: In the United States, better outcomes for acute heart failure (AHF) are found in higher spending hospitals with more intensive Treatment Unit (ITU) and High Dependency Unit (HDU) resources. The National Heart Failure Audit shows that in-patient mortality for AHF is lower when care is delivered in cardiology than in general medicine.

Despite lower than the National average inpatient mortality, we reviewed all cases dying within 48 hours of non-elective heart failure admission to this Trust, to assess potential for improving service delivery.

Methods: Medical records were reviewed from July 2012 to June 2014 for all patients dying within 48 hours of non-elective admission to our hospital with HF in the primary diagnosis code (n=24).

Results: For 55% (n=13) this was the first ever presentation with heart failure. Respiratory failure was documented in 88% (n=21) on arterial blood gas (63% type 1, 25% type 2), and acute renal failure in 83% (n=15). Only 21% (n=5) were cared for in a Level 2 (ITU/HDU) area (13%, n=3 in Cardiac Intensive Care, 8%, n=2 in General ITU). Only 3 patients (13%) received invasive ventilation (non-invasive ventilation in 34% - CPAP 21%, BiPAP 13%).

Most (51%) died in medical general wards (38%, n=9, acute medical unit, 13%, n=3, medical ward). Care was delivered in cardiology for 21%. The majority died without senior cardiology review (13%, n=3 received HF Consultant review, 16%, n=4, non-HF Consultant Cardiologist review).

Left bundle branch block was present in 17% (n=4). Acute triggers for decompenation included infection in 42%, suspected acute coronary syndrome in 28% and arrhythmia in 13%. One patient received palliative care input (4%).

Conclusions: This audit of acute heart failure patients dying within 48 hours of admission demonstrates that despite multi-organ failure at presentation, most do not receive level 2 care or above and most die without senior cardiology review. Inpatient mortality is well below the national average at this Trust, indicating that the potential to improve acute heart failure management within the first 48 hours may be widespread. The data provides supportive evidence for investment in level 2 care capacity to manage these complex patients and to streamline care delivery to specialist heart failure teams.

P5671 | BEDSIDE
Chronic vagus nerve stimulation improves baroreflex sensitivity assessed by heart rate turbulence in heart failure patients
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Introduction: Autonomic regulation therapy (ART) by chronic vagus nerve stimulation (VNS) improves ventricular function in heart failure (HF) patients, but its impact on CRT outcome. CMR is superior to gated SPECT in detection of scar burden. Global and lateral scar burden of the left ventricle have unfavorable correlation to LV remodeling. Applying ROC curve for CMR examination data for LV scar analysis showed that a cutoff value of 38.5% for global LV scar burden correlated to LV remodeling. Applying ROC curve for CMR examination data for LV scar analysis showed that a cutoff value of 38.5% for global LV scar burden correlated to LV remodeling.

Conclusions: Both temperature and PM2.5 predicted readmissions among patients not taking beta-blockers (p<0.002), but not among those taking beta-blockers (Figure 1).

Acknowledgement/Funding: Cyberonics Inc., Houston USA

P5672 | BEDSIDE
The effects of temperature and air pollution on heart failure incidence and readmissions: is beta-blocker protective?
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Background: The effects of seasonal variation on heart failure (HF) incidence and readmissions are uncertain. We measured factors associated with seasonal variations (temperature and air pollution), and investigated their relationships with HF incidence and readmission.

Methods: This Tasmanian statewide data linkage included all patients with a first-ever HF admission and their subsequent readmissions during 2009–2012. Daily temperature and particulate matter -2.5μm (PM2.5) in Tasmania were also recorded. Poisson regression was used, with adjustment for time trend, public and school holidays, day of week, flu infections and relative humidity.

Results: There were 1727 HF incidences (average 1.5±1.4/day) and 3355 readmissions (average 3.1±3.1/day). Greater HF incidences and readmissions (p<0.001) occurred in winter than other seasons. While higher average temperature was protectively associated with HF incidences (RR=0.60 [0.53, 0.67]) and readmissions (RR=0.70 [0.64, 0.77]), PM2.5 was detrimentally associated with HF incidences (RR=1.32 [1.21, 1.44]) and weakly so with readmissions (RR=1.08 [1.01, 1.16]). The effects of temperature and PM2.5 had a four-day and one-day lagging period respectively. In multivariable analyses, while both temperature (RR=0.67 [0.57, 0.79]) and PM2.5 (RR=1.14 [1.03, 1.27]) predicted HF incidences, only temperature (RR=0.76 [0.67, 0.87]) predicted readmissions. Stratified analyses showed that exposure to PM2.5 predicted readmissions among patients not taking beta-blockers (p<0.002), but not among those taking beta-blockers (Figure 1).

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P5673 | BEDSIDE
Impact of evaluation of left ventricular dys-synchrony and scar burden upon outcome of cardiac resynchronization therapy
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Methods: Thirty patients underwent CRT implantation. Pre-implantation CMR was done to document scar burden and lateral wall involvement. Degree of dysynchrony was assessed through LV phase analysis.

Results: Thirty patients received CRT (mean age 58.7±9.0, 24 males). CRT implantation had a favorable prognosis on cardiac function (LVEF pre-implantation: 30±5% versus 37±7% post-implantation; P=0.017). Echocardiographic response, defined as relative decrease in LVES by >15%, was documented in 19 patients (63.3%). After adjusting for CMR scar burden, neither HbA1C nor SNR was correlated to LV remodeling. Applying ROC curve for CMR examination data for LV scar analysis showed that a cutoff value of 38.5% for global LV scar burden had a sensitivity of 72.7% and specificity of 68.4%. A cutoff value of 12% for lateral wall scar burden had a sensitivity of 81.8% and specificity of 68.4%.

Conclusions: Global and lateral scar burden of the left ventricle have unfavorable impact on CRT outcome. CMR is superior to gated SPECT in detection of scar burden and providing acceptable predictors for potential CRT non-responders. Mechanical dysynchrony depends largely on underlying LV scar substrate.

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Background: Left ventricular hypertrophy (LVH) is common in patients with type 2 diabetes mellitus (T2DM) and a strong independent predictor of heart failure. Left ventricular (LV) mass is highly heritable. The Kruppel like factor 15 (KLF15), a transcriptional factor, is highly expressed in the heart and regulates cardiac hypertrophy.

Purpose: We investigated the association of two KLF15 single nucleotide polymorphisms (SNPs) with LVH and heart failure hospitalisations in patients with T2DM.

Methods: We recruited 347 ambulatory Caucasian patients with T2DM for a transhormochromatic echiogram. Patients with moderate/severe valvular dysfunction or valvar replacement/repair (n=28) were excluded. No patients had a previous history of heart failure. Two KLF15 SNPs (rs9838915 and rs6918698) were genotyped in 319 patients. LVH was defined as LV mass (indexed to body surface area) of >115 g/m² in men and >95 g/m² in women. Data are presented as mean ± SD and medians [25, 75th quartile] for non-parametric variables.

Results: The mean age of the cohort was 64±12 years (male = 54%) with a body mass index (BMI) of 31.7±6.1 kg/m² and median diabetes duration of 10 years [5, 16]. LVH was present in 35% of patients. The KLF15 SNP rs9838915 A allele was significantly associated with increased LV mass (GA + AA genotype vs. GG genotype: 105.8±28.3 vs. 95.9±25.5 g/m², p=0.001), interventricular septum thickness (1.11±0.15 vs. 1.05±0.15 cm, p=0.001) and posterior wall thickness (1.08±0.15 vs. 1.04±0.15 cm, p=0.003) in a co-dominant genetic model independent of age, gender, BMI and hypertension. There were no significant associations between the KLF15 SNP rs9818698 and LV mass before and after adjustment for the same covariates. Over a 6–yr period, patients with LVH and who carried the rs9838915 SNP A allele had a 4-fold increase in heart failure hospitalisations compared to those without LVH and who were GG homozygotes (hazard ratio 4.7 [95% confidence intervals, 1.3 to 16.9], p=0.018). This association was independent of age, gender, BMI, hypertension, systolic blood pressure and renal function.

Conclusion: In patients with T2DM, the KLF15 SNP rs9838915 A allele is associated with increased LV mass and heart failure hospitalisations. Our findings suggest that genetic variation in KLF15 may contribute to LVH, and studies are now required to identify the mechanisms by which SNP rs9838915 contributes to cardiac hypertrophy.

P5675 | BEDSIDE

Echocardiographic myocardial scar during left ventricular assist device support

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Purpose: The aim of this study was to determine the radial strain and radial strain rate values by Speckle Tracking Echocardiography in patients receiving continuous flow LVADs. The calculation of radial strain and strain rate measurements were performed offline on digitally archived images using commercially available software (GE HC, Buckinghamshire, UK).

Results: Speckle-tracking was feasible from at least one short axis view in all 20 patients. The calculated radial strain mean value was 12.6±7.6%, median value was 10.8% (IQR 6.9%, 16.7%). The radial strain rate mean values were 1.2±0.07 s⁻¹, median values was 1.08 s⁻¹ (IQR 0.79 s⁻¹, 1.7 s⁻¹). With the LVAD speeds reduced, the calculated radial strain and strain rate mean values did not significantly change. Reduction of LVAD speed was associated with a significant increase in LV size in systole (27±13 mm vs 22±12 mm, p=0.03) and a trend towards increase in systole. However, LV function assessed by LVF (25±14 vs 27±10, p=0.50) did not change significantly.

Conclusions: This study demonstrate that strain values can be easily derived and provides added value to existing measures, such as LVF, and may provide insight into the mechanical LV function in LVAD patients. Performing strain measurements routinely in stable LVAD patients may better evaluation of the underlying LV function and monitor for temporal changes.

P5676 | BEDSIDE

Depressive symptomatology accompanies impaired ventricular diastolic function, detected by Doppler imaging, in patients with chronic systolic heart failure

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Introduction: Short-term depressive symptoms have been associated with worsened prognosis of heart failure patients; although the involved mechanisms have not well understood. The aim of the present work is to evaluate any relationship between depressive symptoms and left ventricular systolic and diastolic function in patients with chronic heart failure.

Methods: We enrolled 202 males (mean age 63±13 years) and 39 females (mean age 65±13 years), all consecutive patients with chronic heart failure due to ischemic or dilated cardiomyopathy, under optimal medical treatment. At the echocardiographic assessment pulsed tissue Doppler imaging (TDI) of the systolic and diastolic function of mitral annulus was characterized by the systolic wave Smv, and the diastolic waves: Emv and Amv. Furthermore the ratio E/Emv was also calculated; where E is the rapid mitral filling wave, detected by pulse Doppler. Detailed information regarding their medical records, anthropometric data, physical activity, nutrition and smoking habits were recorded; while short term depressive symptoms were evaluated using the Zung depressive scale (0–88).

Results: Patients in the lower tertile in Zung scale showed compared to those in the lower tertile, higher E/Emv, lower ejection fraction and lower Smv ratio (all p <0.05). Linear regression analysis, after adjustment for left ventricular ejection fraction, arterial hypertension and total cholesterol, revealed that depressive symptoms were independently associated with lower E/Emv ratio (b=1.719, 95% CI: 0.86–2.59, p<0.001) Conclusion: This study reveals that depressive symptomatology is associated with more advanced left ventricular diastolic and systolic dysfunction, in patients with chronic heart failure.

P5677 | BEDSIDE

Scar burden and mechanical dyssynchrony assessment with SPECT-myocardial perfusion imaging as a potential tool to predict responsiveness to cardiac resynchronization therapy

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Introduction: QRS morphology and duration on the electrocardiogram (ECG), are the best predictors of response to cardiac resynchronization therapy (CRT). A considerable number of patients (pts) who meet the criteria for CRT do not improve (~30–35%) and additional criteria for best selection are needed. Assessment of scar burden and left ventricular mechanical dyssynchrony (LVMD) by phase analysis of gated SPECT myocardial perfusion imaging (MPI), may be useful tools for improving the prediction of CRT response. Methods: We retrospectively evaluated heart failure (HF) pts with LV function fraction (EF) <50% who underwent SPECT-MPI. We obtained parameters of dyssynchrony by phase analysis of SPECT-MPI: histogram bandwidth (HB – a measure of the time dispersion of the onset of systolic contraction between regional LV function) and standard deviation (sd) for each patient. The presence of myocardial scar (persistent perfusion defect) was defined as a “summed stress score (SSS) > 3 with a “summed difference score (SDS) > 3, and the presence of ischemia was defined as a SSS – 3 with an SDS -3.

Results: Ninety-four patients (74 males; mean age 63±9 years) underwent SPECT-MPI with phase analysis. Thirty-seven (39%) were classified as having ischemic cardiomyopathy (ICM) and 57 pts (60.6%) were classified as having non-ischemic (nICM). Mean QRS duration was 139±32ms (134±35ms for ICM and 143±30ms for nICM, p=0.128), and LBBB was present in 51 pts (69%) with a higher frequency in nICM (38 vs 13 pts; p<0.003). Mean EF was 29±9±12%, with no significant difference between ICM VS nICM (P=0.06). Mean HB and SD values were 162±77 and 52±21 in ICM and 99±65 and 33±19 in nICM (normal values of ~38° for HB and 14° for SD; p<0.001 and p<0.001 respectively). In patients SSS-3 and SDS-4 (scar), increasing values of SSS are correlated with higher HB and sd values (r=0.57, p<0.001), suggesting that increasing scar burden is associated with increasing mechanical dyssynchrony. Myocardial scar was present in both populations of pts, although, as expected, was more frequent in ICM (p=0.004).

Conclusions: Extensive myocardial scar is a predictor for non-response to CRT. Although mean EF and mean QRS duration were not different between groups, LVMd assessed with SPECT-MPI phase analysis is significantly higher in patients with ICM compared to nICM, and this was related to a higher scar burden. These findings suggest that LVMd assessed with phase analysis of SPECT-MPI may be a surrogate marker of the extent of myocardial scarred area and may be a useful predictor of CRT response, in addition to ECG parameters.
P5678 | BEDSIDE
Relationship between transmural myocardial mechanical and acute heart failure in STEMI patients treated with primary percutaneous coronary intervention
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In patients with ST segment elevation myocardial infarction (STEMI) treated by primary percutaneous coronary intervention (pPCI) post-procedural acute heart failure (HF) has important impact on prognosis. Contemporary echocardiographic techniques offer possibility to comprehensively explore left ventricular (LV) systolic dysfunction, based on ejection fraction (EF), measuring myocardial deformation by strain and strain rate.

Aim: Aim of this echocardiographic study was to analyze relation between LV myocardial mechanics and postprocedural HF (Killip class ≥2) in STEMI pts treated with pPCI.

Methods: In 35 consecutive STEMI patients treated with pPCI early echocardiography was done including conventional echo parameters as well as longitudinal (L), radial (R) and circumferential (C) peak global strain (%S), and peak systolic strain rate (SR;1/s) on endocardial (endo), medial (mid) and epicardial (epi) level. Transmural gradients of LS (LSgrad) and CS (CSgrad) were calculated as difference between endocardial and epicardial echo values. Echo studies were done on VIVID 9-GE echo machine and EchoPac was used for speckle tracking analysis.

Results: 20% of all pts had HF. HF pts had significantly lower peak global LS on endo (r=-0.36, p<0.05) and mid (r=-0.34, p<0.05) levels, LSgrad in groups, plasma and PF. L-L Arg levels were higher than that of non-HF pts. Plasma L-Arg level was significantly (p<0.05) higher in CABG than VR (75.7±4.6 μmol/L vs. 58.1±4.9 μmol/L), whereas PF L-Arg level was significantly higher in VR than CABG (0.39±0.0 μmol/L vs. 0.7±0.0 μmol/L). L-Arg/ADMA ratio was significantly lower (the VR group) compared to CABG (p=0.001). Plasma L-Arg level was significantly (p<0.05) higher than CABG and VR. LFADMA levels were higher than CABG and VR.

Conclusions: ADMA levels in plasma and PF and plasma L-Arg level were significantly higher in the VR group than CABG and PF respectively. Plasma L-Arg precursor of, and ADMA false substrate of NOS are present in PF of cardiac patients and their altered levels may contribute to altered cardiac morphology.

P5679 | BEDSIDE
Stress cardiomyopathy - 10 years’ experience at a tertiary care hospital

Background: Stress cardiomyopathy (SC) is an entity recognized since the 1990s. Frequently mimicking the presentation of myocardial infarction (MI), it demands differentiation to coronary atherothrombosis, although its pathophysiology still isn’t fully clear. We present a description of SC cases identified at our hospital in the last 10 years.

Methods: We made a descriptive analysis of retrospectively gathered data on patients (pts) presenting to our hospital and diagnosed with SC, according to the Mayo Clinic diagnostic criteria, between 2005 and 2014.

Results: We identified 58 pts (55 women and 3 men) with a mean age of 64 years (ranging from 33 to 84 years). A precipitating factor was found in 45 cases (78%). The most common were cardiogenic shock and acute pulmonary oedema, in 6 cases (10%). Associated myocardial dysfunction in 55 cases (95%), the majority with apical hypokinesia (51 pts, 88%). Echocardiographic evaluation revealed left ventricular systolic dysfunction (13.2±4.3 mm vs. 7.4±3.6, p=0.005) and higher WMSI (1.9±0.23 vs. 1.43±0.34, p=0.002). Cardiogenic shock is frequently associated with severe clinical complications, but has nonetheless a very good short and long-term prognosis. We expect country-wide information, as the current national registry on SC starts being analysed.

P5680 | BENCH
Asymmetric dimethylarginine (ADMA) in the pericardial fluid may contribute to the development of cardiac hypertrophy
A. Koller1, Z. Nemeth2, S. Szabados2, B. Biró1, S. Kek1, A. Czirik1. 1University of Physical Education, Dept of Physiology, Budapest and Valahia, Hungary; 2University of Pecs, Medical School, Department of Pathophysiology and Geront and Szientagatho R.C., Pecs, Hungary; 3University of Pecs, Medical School, Institute of Pathophysiology, Pecs, Hungary; 4University of Debrecen, Department of Applied Chemistry, Debrecen, Hungary.

Background: Pericardial fluid (PF) contains several biologically active substances, which may play a role in modulation of cardiac function and morphology. Nitric oxide (NO) has been implicated in cardiac function and remodeling.

Methods: Levels L-Arg and ADMA in plasma and PF, and echocardiographic parameters of patients undergoing coronary artery bypass graft (CABG, n=28) or valve replacement (VR, n=25) were determined.

Results: In VR patients 39.7% and in CABG 80% demonstrated LV hypertrophy (HFrEF). The asymmetric dimethylarginine (ADMA) has been shown to inhibit NO-synthase (NOS).

Purpose: To test the hypothesis that L-arginine (L-Arg) precursor of, and ADMA a false substrate of NOS are present in PF of cardiac patients and their altered levels may contribute to altered cardiac morphology.

Methods: Levels L-Arg and ADMA in plasma and PF, and echocardiographic parameters of patients undergoing coronary artery bypass graft (CABG, n=28) or valve replacement (VR, n=25) were determined.

Conclusions: We suggest that elevated levels of ADMA in the pericardial fluid of cardiac patients indicate a reduced bioavailability of NO, which can contribute to the development of cardiac dysfunction, hypertrophy, and remodeling.

P5681 | BEDSIDE
Heart failure awareness is being increased in HF patients: TREAT-HF cohort
H. Kaya1, B. Yagmur2, B. Acar3, M. Demir4, K. Karaozum5, G. Acar6, A. Celik7, M. Ege8, I. Sarı9, M.B. Yilmaz10. 1Cumhuriyet University, Cardiology, Sivas, Turkey; 2Ege University, Izmir, Turkey; 3Turkey Yuksek Ihtisas Hospital, Ankara, Turkey; 4Ankara Numune Hospital, Ankara, Turkey; 5Kocaeli University, Kocaeli, Turkey; 6Kahramanmaras Sutbu Imam University, Kahramanmaras, Turkey; 7Mersin University, Mersin, Turkey; 8Koru hospital, cardiology, ankara, Turkey; 9Marmara University, Istanbul, Turkey.

Purpose: Herein, results of campaigns between 2013 and 2014 to increase awareness was tested.

Methods: TREAT-HF (Turkish Research Team-Heart Failure) is a network of 16 HF centers in Turkey. Herein, a direct comparison between TREAT-HF-2013 cohort (n=503) and TREAT-HF-2014 cohort (n=437, complete records by 12th Feb 2015) were presented.

Results: Mean age of whole group was 60.7±13.8 years (670 males, 270 females). Mean age was lower in the 2014 cohort than 2013 cohort (59±14.3 vs. 62.6±12.9 years, p<0.001). Gender distribution was similar in both cohorts (p=0.615). There were less patients with an index diagnosis of HF more than 5 years in the 2014 cohort than in the 2013 cohort (28.9% vs 36.7%, p=0.011). Distribution of NYHA Class I-II-III-IV was different in 2014 cohort and 2013 cohort (8.3%, 41.6%, 44.7%, 5.4% vs 15.7%, 49%, 31.4%, 3.9%, p<0.001). Patients in the 2014 cohort more frequently stated that patients in the 2013 cohort that they were adequately informed by their physicians (78.2% vs 68.4%, p=0.001). There were more patients reaching target dose of ACEI or ARBs in the 2014 cohort than in the 2013 cohort (27.8% vs 13.4%, p<0.001). Patients in the 2014 cohort were more likely to keep dietary advice than patients in the 2013 cohort (66% vs 49.8%, p<0.001). Patients in the 2014 cohort were more likely to enjoy exercise programs than patients in the 2013 cohort (93.6% vs 89.7%, p=0.033) In the 2014 cohort, patients responded more frequently than 2013 cohort that “their relatives have adequate information with regard to their disease” (83.3% vs 77.6%, p=0.029). There were more patients reaching target dose of β-blockers in the 2014 cohort (13.4% vs 9.3%, p=0.033). In the 2014 cohort, patients
responsible more frequently than 2013 cohort that relatives of the HF patient knew what to do in case of an emergency (79.7% vs 71%, p=0.002). Patients in the 2014 cohort less likely to rely on alternative medicine than patients in the 2013 cohort (18.5% vs 23.4%, p=0.07). Patients were asked “when they admit hospital except for regular visits”, and it was noticed that patients in 2014 cohort responded more frequently as “when my dyspnea worsens” than patients in the 2013 cohort (64.7% vs 33.3%, p<0.001). Patients in the 2014 cohort visit “more than one physician after index diagnosis of HF” more frequently than patients in the 2013 cohort (88.6% vs 79.6%, p<0.001). It seems, HF patients in Turkey seek for another medical opinion quite frequently, and their number is increasing.

Conclusion: Heart failure awareness is being improved in HF patients by various campaigns in Turkey.

P5682 | BEDSIDE
Impact of sociodemographic and clinical risk factors on hospitalization rates among ambulatory patients with heart failure and preserved ejection fraction
V. Georgiopoulos1, G. Burkhart1, T. Lebes1, K. Farooq1, R. Al-Anbari1, M. Yazdani1, L. Papadimitriou2, A. Smith1, J. Butler1, A. Kalogeropoulos1
1Emory University School of Medicine, Atlanta, United States of America; 2Stony Brook University Medical Center, Stony Brook, United States of America

Background: There are limited quantitative data on the impact of concomitant conditions on hospitalization rates among patients with heart failure and preserved ejection fraction (HFpEF).

Methods: We evaluated 333 outpatients with HFpEF (age 72±13 years: 58% women; 49% white, 46% black; median EF 55%) over 2 years of follow up. We calculated the attributable risk conferred by sociodemographic and clinical factors for all-cause, cardiovascular (CV), and HF-related admissions using negative binomial regression models.

Results: Mortality was 10.2% at 2 years. Of 506 total admissions, 147 (29%) were HF-related, 73 (14%) due to other CV causes, and 286 (57%) non-CV. Table 1 presents factors that attained attributable risk with P<0.05.

<table>
<thead>
<tr>
<th>Factor</th>
<th>CV admissions AR (%)</th>
<th>P</th>
<th>HF admissions AR (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital status non-married</td>
<td></td>
<td>-0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td>0.002</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>0.005</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Age ≥75 years</td>
<td></td>
<td>0.001</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>NYHA II/III</td>
<td></td>
<td>0.002</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>NYHA IV</td>
<td></td>
<td>0.001</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Non-married status</td>
<td></td>
<td>0.001</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Poor renal function</td>
<td></td>
<td>0.001</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Functional class</td>
<td></td>
<td>0.001</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>History Hx noncoronary intervention</td>
<td></td>
<td>0.001</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Hx coronary revascularisation</td>
<td></td>
<td>0.001</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Hx noncoronary intervention, cancer, RRT</td>
<td></td>
<td>0.001</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Serum K+ ≥4.0 mmol/L</td>
<td></td>
<td>0.001</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Non-modifiable ARH</td>
<td></td>
<td>-0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total ARH</td>
<td></td>
<td>-0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Results showed that in HF patients with SH as isolated etiology, HFpEF was the most frequent HF phenotype, while one-third of cases presented LV systolic dysfunction. Among different LVF strata, HFpEF showed the worst outcome.

P5684 | BEDSIDE
Proposed diagnostic algorithm for patients with heart failure and sleep disordered breathing
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1Hospital de Sao Francisco Xavier, Unidade de Insuficiencia Cardiaca, Lisboa, Portugal; 2Hospital de Sao Francisco Xavier, Servico de Pneumologia, Lisboa, Portugal; 3Hospital de Sao Francisco Xavier, Servico Medicina, Lisboa, Portugal

Sleep Disordered Breathing (SDB) is a highly prevalent comorbidity in heart failure (HF) patients, that weighs on HF high morbidity/mortality. Both HF and SDB overlap of symptoms and difficulty in scheduling a laboratory for the diagnostic gold standard, the polysomnography (PSG), are responsible for the underdiagnosis of SDB in HF patients. The use of a validated type 3 home sleep testing diagnostic device, allows an early intervention and initiation of treatment, aiming towards better outcomes.

Objective: To compare the diagnostic accuracy of the portable diagnostic device as a screening test for SDB in stabilized inpatients “versus” outpatients with HF, previously validated against PSG, and to propose a diagnostic algorithm. Hospitalization period is a crucial moment for treatment optimization in HF.

Methods: Observational, prospective study of consecutive patients discharged from an HF unit of a central university hospital during one year. The diagnostic test was performed just before discharge, on stable optimized treatment and repeated while outpatient. Outpatient diagnostic test has previously shown a good correlation with PSG. Specificity (Sp), Sensitivity (S), positive predictive value (PPV) and negative predictive value (NPV) for both central apneas (CA) and obstructive apneas (OA) diagnosis were obtained to validate inpatient diagnostic test in order to take advantage of the hospitalization period, a precious moment for treatment optimization.

Results: 38 patients were included, 23 women, age 71±10.2 years, avg BMI 27.6±5.1kg/m2. For an apnea-hypopnea index (AHI)–15 as cut-off, the portable diagnostic test at discharge had NPV of 0.92 and Sp of 0.88 for CA and NPV of 0.95 for Cheyne Stokes respiration. PPV for OA was 0.89.

Objective: Using the AHI–15 as cut-off, the portable diagnostic test applied to inpatients with stabilized HF and drug treatment revealed to be a trustworthy method for detecting SDB and, therefore, allowing early treatment, dismissing the PSG.

P5685 | BEDSIDE
Heart failure patients in Germany: mortality and morbidity in a claims database analysis
C. Bakogiannis1, F. Calado2, J. Walker3, S. Hupler1, S. Klebs1, R. Handrock3
1Novartis Pharma GmbH, Nuernberg, Germany; 2Novartis AG, Basel, Switzerland; 3Elsevier, Berlin, Germany

Background: Heart failure (HF) is one of the most important causes of morbidity

Abstract P5682 – Table 1. Attributable risks

<table>
<thead>
<tr>
<th>Factor</th>
<th>CV admissions AR (%)</th>
<th>P</th>
<th>HF admissions AR (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marital status non-married</td>
<td></td>
<td>-0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood urea nitrogen (mg/dl)</td>
<td>19.4% (5.9–30.1)</td>
<td>0.006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting glucose &gt; 125 mg/dl</td>
<td>17.0% (5.5–27.2)</td>
<td>0.005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>16.2% (2.5–27.9)</td>
<td>0.022</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NYHA Class III or IV</td>
<td>16.6% (10.0–26.4)</td>
<td>0.010</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin ≥3.5 g/dl</td>
<td>14.3% (3.8–23.9)</td>
<td>0.017</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hx coronary revascularisation</td>
<td>13.2% (2.5–22.7)</td>
<td>0.017</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hx noncoronary intervention, cancer, RRT</td>
<td>17.5% (8.3–25.8)</td>
<td>0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum K+ ≥4.0 mmol/L</td>
<td>18.7% (3.7–31.3)</td>
<td>0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-modifiable ARH</td>
<td>53.6% (37.4–65.5)</td>
<td>-0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total ARH</td>
<td>80.4% (71.4–89.5)</td>
<td>-0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1Marital status and history. 2Attributable risks are not additive. 3AR, attributable risk; BUN, blood urea nitrogen; HF, heart failure; Hx, history of; NYHA, New York Heart Association; RRT, renal replacement therapy.
Acute heart failure (AHF) accounts for 101,000 hospital admissions per year in Spain, being the 2nd most frequent DRGs in patients over 75. The Table 1 shows results by service according to different metrics. Solid co-

Table 1. Results

<table>
<thead>
<tr>
<th>Service</th>
<th>Discharges (%)</th>
<th>Cost per patient (€)</th>
<th>In-hospital stay (days)</th>
<th>Readmissions (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiology</td>
<td>121 (22)</td>
<td>2695</td>
<td>6</td>
<td>8,6</td>
<td>5.8</td>
</tr>
<tr>
<td>Geriatric Medicine</td>
<td>221 (43)</td>
<td>2499</td>
<td>7.5</td>
<td>15.1</td>
<td>12.2</td>
</tr>
<tr>
<td>Internal Medicine</td>
<td>185 (35)</td>
<td>2936</td>
<td>&lt;0.001</td>
<td>9.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Results: 123.925 (4%) of the patients already had an existing HF diagnosis in 2011 (55% women, 45% men). 113,868 of these patients (92%) were at least 60 years old. For 79% severity of HF was not coded. In 3%, 9%, 6%, and 3% severity was coded as NYHA I, II, III and IV, respectively.

26,368 newly identified HF cases were documented in the study population in 2011 (51% women vs. 49% men). More than 88% of newly identified patients were 60 years of age or older. In 63% of the patients () the index diagnosis was coded by an office based physician, and for 37% by a hospital-based physician. There were 48,159 hospitalizations in the 2-year period after initial identification of the patients, and HF was found to be the most common cause for hospital admission. Overall mortality rate within two years after initial identification was 23% without differences between women and men. For NYHA I, II, III and IV, two-year mortality rate was 15%, 17%, 31%, and 53%, respectively.

Conclusion: The results underline the relevant HF disease burden in Germany. It has to be considered that the ICD-10 codes used as the basis for the analysis do not reflect the severity between HF with preserved and reduced ejection fraction – each of them usually represents about 50% according to literature. The overall mortality rate of 23% in the newly identified patients in the following 2 years highlights the medical need given in this indication.

P5686 | BEDSIDE

Acute heart failure management at a secondary hospital in Spain: consequences and opportunities for improvement based on the best available evidence

L. Molina Blazquez1, R. Mata1, J. Pais1, J. Gorriz1, R. Casado1, A. Rodriguez-Chavero1, L. Goicoela1, A. Fraile1, V. Hernandez1, J. Saavedra1,1 University Hospital of Getafe, Cardiology, Getafe, Spain;2 University Hospital Rey Juan Carlos, Cardiology, Mostoles, Spain

Introduction: Acute heart failure (AHF) accounts for 1,100,000 hospital admissions per year in Spain, being the 2nd most frequent DRGs in patients over 75. The British National Institute for Clinical Excellence and for 37% by a hospital-based physician. There were 48,159 hospitalizations in the 2-year period after initial identification of the patients, and HF was found to be the most common cause for hospital admission. Overall mortality rate within two years after initial identification was 23% without differences between women and men. For NYHA I, II, III and IV, two-year mortality rate was 15%, 17%, 31%, and 53%, respectively.

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P5687 | BEDSIDE

High prevalence of asymptomatic left ventricular dysfunction despite excellent risk factor control in a diabetic cohort

S. James1, J. Gallagher2, C. Kenny3, D.F. Waterhouse4, J. Mc Cambridge4, T. Murphy5, E. O’Connell5, M. Ledwidge5, V. Harkins6, K. McDonald7, St Vincent’s University Hospital, Cardiology, Dublin, Ireland; 2HSE, Dublin, Ireland; 3Blackrock Clinic, Cardiovascular Magnetic Resonance Centre, Dublin, Ireland; 4University College Dublin, School of Medicine, Dublin, Ireland; 5Heart Beat Trust, Dublin, Ireland

Introduction: Diabetes mellitus is an established cause of left ventricular dysfunction and a strong independent predictor of new onset heart failure. The STOP-HF Midlands project is a screening programme utilizing NT-proBNP and collaborative care to detect left ventricular dysfunction in an asymptomatic diabetic cohort.

Purpose: We sought to assess the prevalence of asymptomatic left ventricular dysfunction in this diabetic population.

Methods: 612 diabetic patients attending the STOP-HF Midlands were included in this analysis. The demographic characteristics and biomarkers of traditional risk factor control in diabetics were recorded, including NT-proBNP. Doppler-echocardiography was performed if the NT-proBNP was >250pg/mL. Left ventricular systolic dysfunction (LVD) was defined as left ventricular ejection fraction of <50%. Left ventricular diastolic dysfunction (LVDV) was defined by an office based physician, and for 37% by a hospital-based physician. There were 48,159 hospitalizations in the 2-year period after initial identification of the patients, and HF was found to be the most common cause for hospital admission. Overall mortality rate within two years after initial identification was 23% without differences between women and men. For NYHA I, II, III and IV, two-year mortality rate was 15%, 17%, 31%, and 53%, respectively.

Conclusion: There seems to be a minor difference in the profile of heart failure among diabetic patients seen in a specialized cardiac facility compared to reports from Teaching Hospitals. In the same environment the profile of heart failure among study participants. Control of risk factors, early identification remains a major way to reduce the burden of heart failure among Nigerians.

P5688 | BEDSIDE

High prevalence of asymptomatic left ventricular dysfunction despite excellent risk factor control in a diabetic cohort

S. James1, J. Gallagher2, C. Kenny3, D.F. Waterhouse4, J. Mc Cambridge4, T. Murphy5, E. O’Connell5, M. Ledwidge5, V. Harkins6, K. McDonald7, St Vincent’s University Hospital, Cardiology, Dublin, Ireland; 2HSE, Dublin, Ireland; 3Blackrock Clinic, Cardiovascular Magnetic Resonance Centre, Dublin, Ireland; 4University College Dublin, School of Medicine, Dublin, Ireland; 5Heart Beat Trust, Dublin, Ireland

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Competence Network for Heart Failure.

M. Lainscak2, F. Edelmann1, G. Loncar 3, C. Herrmann-Lingen 4 on behalf of
(CVK), Berlin, Germany; 2 University Clinik Golnik, Division of Cardiology, Golnik, Slovenia; 3 Medical Hospital Center Zvezdara, Cardiology department, Belgrade, Serbia; 4 Georg-August University, Department of Psychosomatic Medicine and Psychotherapy, Göttingen, Germany

Purpose: To examine whether patient backgrounds and in-hospital outcomes of TTC were different between four seasons.

Methods: Using the Diagnosis Procedure Combination inpatient database in Japan, we identified patients who were admitted to acute-care hospitals with TTC and underwent coronary angiography without any revascularization procedure between 2010 and 2013. The patients were classified into the four sea- son groups [I, autumn [September-November], and winter [December-February]] according to their admission dates. Patient backgrounds including 16 relevant coexisting diseases at admission and in-hospital outcomes were compared between the groups.

Results: The study population consisted of 3300 patients (mean age, 73.5±11.2 years; male, 22.4%). The incidence of TTC was highest in the summer group (114 patients/month) and lowest in the spring group (87 patients/month). There was no significant difference in age between the four groups (p=0.534). The winter group showed a higher proportion of males (24.7% vs. 20.8%, p=0.026). The summer group showed a higher proportion of psychiatric disease than the others (7.9% vs 4.6–5.8%, p=0.020), while the autumn group showed a lower proportion of cerebrovascular disease at admission (2.6% vs 4.3–4.7%, p=0.058). In-hospital mortality was highest in the winter group (6.2%), followed by the summer (5.8%), spring (4.8%), and autumn (4.6%) groups. There was no significant difference in survival between the four groups (p=0.391 for log rank test).

Conclusions: This study suggested that there was a significant seasonal varia- tion in patient backgrounds and in-hospital outcomes of TTC.

Acknowledgement/Funding: This study was supported by a grant from the Ministry of Health, Labour and Welfare, Japan (Grant Number: H26-Policy-011).

Purpose: To examine if weather conditions are associated with the incidence of cardiovascular disease, the influence of climatic conditions in the onset of acute heart failure remains unknown.

Methods: The Acute Heart Failure Kyoto registry is a physician-directed multi-center registry in Japan enrolling consecutive patients hospitalized for AHF. Between April 2013 and March 2014, 194 patients were admitted for AHF in our hospital. Among 365 days, we identified 141 days transferred for AHF and investigated the association between the local weather parameters obtained from Japan Meteorological Agency.

Results: On the AHF admission days, minimum temperature (11.7±8.7 °C vs. 9.6±8.4 °C, p=0.02) and average temperature (15.7±8.8 °C vs. 13.9±8.4 °C, p=0.04) were significantly low. While maximum temperature (20.5±9.5 °C vs. 18.8±7.2 °C, p=0.09) tended to be lower. On the previous days, maximum temper- ature (20.5±9.5 °C vs. 18.4±9.0 °C, p=0.01), minimum temperature (11.7±8.2 °C vs. 9.6±8.4 °C, p=0.02) and average temperature (15.8±8.8 °C vs. 13.7±8.4 °C, p=0.02) were significantly lower. Compared with the previous days, maximum temper- ature was increasing (−0.26±3.15 °C vs. 0.42±3.28 °C, p=0.04), diurnal temper- ature range was extended (−0.31±3.56 °C vs. 0.49±3.57 °C, p=0.03) and minimum humidity was decreasing (1.67±14.73% vs. −2.72±15.71%, p=0.007). A mean at- mospheric pressure on the AHF admission days tended to be high (1012.1±7.1 hPa vs. 1013.4±4.6 hPa, p=0.10). Interestingly, the maximum instantaneous wind speed tended to rise (−0.24±3.37 m/sec vs. 0.44±3.99 m/sec, p=0.08) on the previous days.

The wind direction showed a trend toward south and west based on the geographical features. There were no significant differences in sunshine duration. After adjustment for other factors, the difference from the pre-
vicious day of minimum humidity [odds ratio (OR), 0.97; 95% confidence interval (CI), 0.96–0.99] and averaged maximum precipitation during previous 2 days [OR, 0.82; 95% CI, 0.67–0.97] were demonstrated as the independent risk factors for the onset of AHF syndrome. The difference from the previous day of the maximum instantaneous wind speed [OR, 1.04; 95% confidence interval (CI), 0.98–1.11] and averaged maximum temperature on the previous day [OR, 0.98; 95% CI, 0.95–1.00] showed a trend toward predicting the admission for AHF.

**Conclusions:** Not only low temperature but rapid wind velocity, little rain and lower minimum humidity contributed to increase the onset of AHF syndrome.

**PROGNOSTIC MARKERS IN HEART FAILURE**

**P5686 | BESIDE**

Increased heart rate at hospital discharge augments 1-year rehospitalization rates, but does not affect two and three year rehospitalization rates in heart failure patients

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**Purpose:** Increased heart rate is a marker for adverse cardiovascular outcomes in heart failure patients. But the value of heart rate at hospital discharge in heart failure patients admitted, is not very well so. We decided to identify the value of heart rate in this setting on rehospitalization rates of heart failure patients.

**Methods:** We collected information from 210 consecutive heart failure patients hospitalized in our hospital between December 2010 and December 2011 who survived and had a hospital discharge heart rate record in their files. The heart rate values, laboratory measurement values, demographic and echocardiographic parameters were recorded. One hundred and twenty-nine (61%) of the patients were male and 21 (10%) had diastolic heart failure, 31 (15%) had right heart failure and 29 (14%) had heart failure due to valve disease. The mean age of the patients was 72. One hundred and ten patients (52%) were men and 100 (48%) patients were women. The patients were divided into two groups according to their heart rate at hospital discharge: the patients in the first group had heart rate >75 beats/minute and the ones in the second group had heart rate ≤75 beats/minute.

**Results:** The patients in the first group who had discharge heart rate >75 beats/minute had higher ejection fraction, lower serum uric acid values and had been given inotropic treatment more commonly than the patients in the second group. According to Spearman’s correlation analysis, discharge heart rate was positively correlated with ejection fraction and the use of inotropic therapy. Fifty-eight patients were rehospitalized during the first year follow-up. The rehospitalization rates in the first group was significantly higher than in the second group (43 vs. 15, p value<0.03). At the end of second year follow-up 73 patients were rehospitalized, (52 vs. 21, p value=0.07) At the end of third year, a total of 78 patients were rehospitalized due to heart failure, (54 vs. 24, p value=0.33)

**Conclusion:** Increased heart rate augments early 1-year rehospitalization rates, but its effect disappears in two and three years follow-up period.

**P5684 | BESIDE**

Clinical profile and prognosis of the combination of diabetes mellitus and heart failure in ambulatory patients


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**Background:** The prevalence of concomitant diabetes mellitus (DM) and heart failure (HF) is increasing. This relation has a worse prognosis due to a different response to treatment in hospitalized patients as seen in recent clinical trials. Therefore, the impact of DM on HF outcomes remains unclear.

**Purpose:** To analyze the clinical profile and prognosis of DM in HF ambulatory patients.

**Methods:** A cohort of 2,4986 patients with chronic HF recruited between 2007 and 2011 from 18 tertiary centers of HF Spanish Network was prospectively followed for a median of 40 months. Clinical, echocardiographic, ECG, and biochemical parameters were used in a competing risk model to determine the effect of DM on mortality.

**Results:** The prevalence of DM was 42.4%. DM patients were older, had more cardiovascular risk factors, previous myocardial infarction (MI) and comorbidities.

After a multivariable analysis, the presence of concurrent DM and HF was independently related with aging, previous MI, cardiac risks factors, peripheral artery disease and anemia. After adjusting by a propensity score including previous significant variables, DM patients showed a higher HF mortality (sHR 1.22, CI 1.02–1.47), cardiac mortality (sHR 1.47, CI 1.30–1.66), and all-cause mortality (sHR 1.40, CI 1.24–1.59).

**Conclusions:** Coexistence of DM and HF in outpatients is very frequent, is associated with a higher risk profile, and has a very unfavorable long-term prognosis in spite of optimal medical treatment.

**P5685 | BESIDE**

The prevalence of sleep-disordered breathing and the predictors of the increased apnea-hypopnea index in patients with chronic heart failure

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**Background:** Sleep-disordered breathing (SDB) is a widespread co-morbidity in patients with chronic heart failure (HF) that not only leads to a poor quality of life, but also a shorter life expectancy.

**Methods:** A total of 132 patients with chronic HF (mean age: 67±11 y, 23% female, left ventricular ejection fraction [LVEF] 37±13%, body mass index [BMI] 28.9±5.2 kg/m², New York Heart Association [NYHA] class 2.2±0.7 underwent polysomnography screening between 2011 and 2014. Patients were screened for SDB using the Embletta portable diagnostic system. SDB was defined as an apnea-hypopnea index ≥5. Patients with LVEF<40% were categorized as HF with reduced ejection fraction [HFrEF], LVEF<40% as HF with preserved ejection fraction [HFpEF].

**Results:** A total of 58 (44%) patients were diagnosed to have SDB and showed an increased apnea-hypopnea index. Patients with SDB (mean age: 68±10 y, 17% female, LVEF 33±12%, BMI 28.9±5.9 kg/m², NYHA class 2.3±0.7) showed lower LVEF compared to patients without SDB (33±12% vs 40±13%, p<0.05). In patients with HF/HFpEF (n=47, 81%) SDB was more common than in patients without SDB (n=11, 19%). Logistic regression analysis showed that reduced LVEF and higher creatinine level were predictive (both p<0.05) for increased apnea-hypopnea index.

**Conclusion:** In patients with chronic HF, predictors of SDB include reduced LVEF and high level of creatinine. This fact emphasizes the view that patients with more advanced HF are more likely to develop SDB. Screening for SDB provides an easy tool to identify patients with this co-morbidity.

**P5684 | BESIDE**

Predictors of cytosis in patients with acute decompensated heart failure

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**Objective:** The impact of acute decompensated heart failure (ADHF) on hematological parameters has been described as cardio-hepatic syndrome that may reflect severity of HF. The aim of this study was to evaluate predictors of liver transaminase (TA) increase in patients with ADHF.

**Methods:** In 200 patients with ADHF (48 male, 72±10.7 years, M±SD), arterial hypertension 79%, ischemic heart disease 65%, myocardial infarction 43%, diabetes mellitus 35%, chronic kidney disease (CKD) 38%, chronic anemia 23.5%, chronic obstructive lung disease 23.5%, ejection fraction (EF) 51±5%, EF <35%, 25% chronic heart diseases 9.5% alanine transaminase (ALT) and aspartate transaminase (AST) were measured. Patients were considered abnormal when levels exceeded 50 U/L (upper normal limit (UNL)). Mann-Whitney test and multivariable logistic regression analysis were performed. P<0.05 was considered statistically significant.

**Results:** Increase of ALT and/or AST occurred in 29 (14.5%) patients (alone ALT/AST in 4 patients, both TA – in 42.3, 19.2% respectively). The baseline ALT and AST values in patients with versus without increase of TA were 95±36 vs 21±14 U/l and 87±26 vs 25±11 U/l respectively (p<0.001).

Patients with vs without increased TA had lower weight (78±15 vs 87±11kg, respectively).
Main independent predictors of cytolysis were AF on admission, (OR 1.102–6.368, p<0.05), lower GRFCKD-EPI (34±10 vs 57±18ml/min/1.73m², p<0.001), higher heart rate (115±25 vs 92±25 minute, p<0.001), left ventricular mass index (LVMi) (194±40 vs 174±48g/m², p<0.01), lower EF (40±11 vs 45±12%, p<0.05), higher rate of comorbidity – CKD (11 vs 2.8%, p<0.05), chronic anaemia (83 vs 24%, p<0.05), AF (11 vs 1%, p<0.001), higher rate of signs of congestion: echo-hydropericardium (72 vs 32%, p<0.001), jugular venous distension (55 vs 21%, p<0.001).

Liver cytolysis was also associated with community-acquired acute kidney injury (AKI) (70% vs 17.3%, p<0.001) in patients with vs without increased TA.

Main independent predictors of TA increase were AF on admission (odds ratio (OR) 11.25, 95% confidence interval (CI) 2.59–48.89), community-acquired AKI (OR 11.17, CI 4.11–30.32), hydropericardium (OR 5.58, CI 2.12–14.64), jugular venous distension (OR 4.47, CI 1.86–10.75), CKD (OR 4.208, CI 1.605–11.036), echo-hydropericardium (OR 3.71, CI 1.32–10.47), chronic anaemia (OR 2.65, CI 1.32–5.34), and comorbidities (other than AKI) (OR) 11.25, 95% confidence interval (CI) 2.59–48.89), community-acquired AKI (OR 11.17, CI 4.11–30.32), hydropericardium (OR 5.58, CI 2.12–14.64), jugular venous distension (OR 4.47, CI 1.86–10.75), CKD (OR 4.208, CI 1.605–11.036), echo-hydropericardium (OR 3.71, CI 1.32–10.47), chronic anaemia (OR 2.65, CI 1.32–5.34), and comorbidities (other than AKI).

Conclusions: Main independent predictors of cytolysis were AF on admission, AKI, CKD, signs of congestion, chronic anaemia, EF<40%.

P5697 | BEDSIDE

Predictors of heart failure in patients with diabetes mellitus: insights from an observational study over 20 years

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Background: Diabetes mellitus (DM) may cause or worsen congestive heart failure (CHF) regardless of the known CHF predictors.

Purpose: We aimed to study the clinical presentation, predictors and outcomes of CHF among DM patients over a 20-year period.

Methods: A retrospective observational study was conducted for all CHF patients who were admitted in the heart hospital in Qatar between 1991 and 2010. Patients were divided into 2 groups: Group I (CHF plus DM) and Group II (CHF without DM). Patients' demographics, clinical presentation, predictors and in-hospital outcomes were analyzed and compared.

Results: A total of 7068 patients presenting with CHF, of them 57% were diabetic; Group I had more advanced age, female gender, Arabs, old MI, ACS at presentation and co-existing dyslipidemia, hypertension, and obesity (p<0.001 for all). Whereas Group II were more Arabs, and more likely to have prior myocardial infarction, renal impairment, dyslipidemia, hypertension, and obesity (p<0.01) in Group I. Non-ST-elevation acute coronary syndrome was more evident in Group II. On univariate analysis, predictors of CHF in diabetic patients were advanced age, female gender, Arabs, old MI, ACS at presentation and co-existing valvular insufficiency.

Conclusions: DM is highly prevalent among CHF patients regardless of the underlying cause of CHF. Age, gender and ethnicity play important prognostic role among diabetic patients.

P5698 | BEDSIDE

Investigation of incidence, etiology, prognosis, and predictors of ischemic stroke during hospitalization for congestive heart failure

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Background: Heart failure (HF) increases the risk of ischemic stroke. Data regarding the incidence of ischemic stroke during hospitalization for HF are limited.

Methods: The study population of this retrospective cohort study consisted of patients with congestive HF, consecutively admitted to our center from October 2010 to April 2014. We excluded patients complicated with acute myocardial infarction, and those with dialysis or mechanical circulatory support. We investigated the incidence, etiology, and prognosis of ischemic stroke during hospitalization for HF.

Results: A total of 560 patients (mean age: 76.8 years, female sex: 244 patients, 272 with atrial fibrillation (AF), and 288 without AF) were enrolled. The mean ejec tion fraction was 47±3.16±6. The oral anticoagulants were prescribed in 149 patients (140 with AF, 9 without AF). During the hospitalization (median length of hospitalization 18 days), symptomatic ischemic stroke (excluding catheter-related) occurred in 15 patients (2.7% of the total, 7 with AF, 8 without AF). Among 7 ischemic stroke patients with AF, 6 were caused by cardioembolism, and 1 by undetermined etiology according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria. Meanwhile, 2 were caused by cardioembolism, and 6 by undetermined etiology in 8 patients without AF. Patients complicated with ischemic stroke during hospitalization for HF showed worse prognosis than those without it (hazard ratio: 3.11, 95% confidence interval: 1.21–6.52).

Conclusions: The incidence of ischemic stroke during hospitalization for HF was high, even in patients without AF. Previous stroke was significantly associated with the incidence of ischemic stroke. Considering its frequency and poor prognosis, further studies are needed to determine predictors or risk markers of ischemic stroke.

P5699 | BEDSIDE

Left bundle branch block by Strauss criteria predicts outcome of cardiac resynchronisation therapy

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Background: QRS morphology is associated with outcomes from cardiac resynchronisation therapy (CRT). However, left bundle branch block (LBBB) has been variably defined. We hypothesized that patients with LBBB (as defined by Strauss and colleagues) are associated with better clinical outcomes with CRT, compared to LBBB-type pattern (LBBB-p).

Methods: We studied 179 advanced heart failure patients with CRT. Median follow-up assessment was 311 (267–494) days. LBBB was defined as (i) a QS or rS QRS morphology in ≥ 2 leads; (ii) mid-QRS notch or slurring in ≥ 2 leads among I, AVL, V1, V2, V5, and V6 (n=100). Patients with QS or rS morphology in V1–V2, but QRSd less than 130ms or 140ms (men and women respectively) and/or lacked the notching/slurring in at least 2 leads were classified as LBBB-p (n=79). Right bundle branch block was excluded. Echocardiography (left ventricular end systolic volume index, LVESVi; tricuspid annular plane systolic excursion, TAPSE) and cardiac catheter assessment were undertaken. Clinical outcomes were defined as survival, free from transplantation and mechanical circulatory support.

Results: The characteristics of both groups were comparable except QRSd (Table 1). QRSd was further prolonged in both groups post-CRT. There was a significant increase in LVESVi, reduction in TAPSE and increase in right atrial pressure (RAP) in the non-LBBB group. The clinical outcome was significantly worse in the LBBB-p group (LBBB vs LBBB-p: number of patients with adverse outcome 27/100 vs 48/79, log rank p<0.001).

Table 1

<table>
<thead>
<tr>
<th>LBBB (n=100)</th>
<th>Non-LBBB (n=79)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRSd baseline (ms)</td>
<td>157 (147–170)</td>
<td>134 (127–141)</td>
</tr>
<tr>
<td>QRSd paced (ms)</td>
<td>168 (155–180)</td>
<td>151 (144–162)</td>
</tr>
<tr>
<td>LVESVi baseline</td>
<td>104±4</td>
<td>106±4</td>
</tr>
<tr>
<td>LVESVi paced (ml/m²)</td>
<td>107±5</td>
<td>115±5</td>
</tr>
<tr>
<td>TAPSE baseline (mm)</td>
<td>14 (12–15)</td>
<td>13 (11–15)</td>
</tr>
<tr>
<td>TAPSE paced (mm)</td>
<td>14 (12–15)</td>
<td>12 (10–14)</td>
</tr>
<tr>
<td>RAp baseline vs. paced (mmHg)</td>
<td>13±2</td>
<td>16±2</td>
</tr>
</tbody>
</table>

Conclusions: LBBB as defined by Strauss and colleagues is a stronger predictor of outcome following CRT compared to QRSd alone and should be used for the selection of patients for CRT.
Background: Galexin 3 (Gal-3) is a relatively new cardiac biomarker. It is reflecting cardiac and renal fibrosis and increased plasma concentrations are associated with a decreased glomerular filtration rate (GFR) and an increased risk of death and a re-admission in heart failure (HF). It is, however, unknown whether it is associated with myocardial function, and whether Gal-3 is associated with another cardio renal marker like 24 hrs urinary albuminuria excretion.

Purpose: This aim of this study was to evaluate the relationship of Gal-3 according to renal and myocardial function in systolic HF.

Methods: The CARDIO-REN study enrolled 149 patients referred to an outpatient HF clinic. Systolic HF was verified by echocardiography according to standard recommendation. Collected data included physical examination, blood samples and 24-hours urine sample. Baseline characteristics of the patients were median age 70 years, 26.5% female, median left ventricular ejection fraction was 33%, and 20% was in functional class III IV.

Results: GFR was significantly lower in patients with increased plasma concentrations of Gal-3. This association remained significant in linear regression analyses (β: -0.010; 95% CI: -0.012 to -0.008; P=0.001) adjusted for age and gender. Urinary albuminuria excretion was not associated to plasma concentrations of Gal-3 (β: 0.008; 95% CI: -0.028:0.045; P=0.652). There was no significant association between Gal-3 and myocardial function estimated by LVEF, E/E' or left ventricular global longitudinal strain. However, plasma concentrations of Gal-3 was significantly associated with cardiac function estimated by NT-proBNP (β: 0.049; 95% CI: 0.012:0.087; P=0.011) and MR-proANP (β: 5.79E-5; 95% CI: 0.000:0.000; P=0.002) in multivariate analyses adjusted for age, gender, and GFR.

Conclusions: Gal-3 is associated with myocardial function estimated by natriuretic peptides and it is closely and inversely associated with GFR. However, Gal-3 is not associated with 24 hrs urinary albuminuria excretion. Therefore, Gal-3 reflects other cardio renal aspects than Albuminuria. Further studies are needed to evaluate whether plasma concentrations of Gal-3 increase before GFR declines in HF.

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P5701 | BEDSIDE
Prognostic impact of syncope in patients hospitalized with heart failure: insights from the Gulf CARE registry

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Background: Heart failure (HF) patients show brain injury in autonomic and neuropsychological control sites, and such damage can change resting-state functional connectivity (rs-FC), temporal correlations between neuronal activities of distinct brain regions) that may lead to alteration in overall functional organization. However, rs-FC and whole-brain organization of these interactions in HF is unknown.

Purpose: To investigate the whole-brain functional interactions and network organization of these interactions in HF and control subjects.

Methods: We acquired rs-functional MRI (3.0-Tesla scanner) data from 27 HF (age, 55.3±7.9 yrs; BMI, 27.9±5.5 kg/m²; 20 male; LVEF, 28.0±9.2%) and 53 controls (52.7±6.2 yrs; 25±4.3±5 kg/m², 36 male). Data were processed using standard procedures, and group analyses were performed using ANCOVA (covariates, age and gender) and permutation tests.

Results: Decreased FC in HF (Fig. 1a, blue) were involved in the caudate, olfactory, vermis 10, and precentral gyrus, and increased FC in HF (Fig. 1b, red) were lateralized to the right hemisphere and involved in the middle frontal, superior parietal, inferior temporal, and fusiform gyri, vermis 6, and cerebellum 6. HF showed aberrant brain network organization in sites showing altered FC over controls.

Conclusions: These findings suggest that brain dysfunction in HF extends to resting conditions, and autonomic and neuropsychological deficits in HF may stem from altered FC and brain network organization that may contribute to higher morbidity and mortality in the condition. The outcomes likely result from the prominent structural changes in both axons and nuclear structures reported earlier in HF, and protecting neural tissue may improve FC integrity, and thus, reduce morbidity and mortality and improve quality of life.

Acknowledgement/Funding: This work was supported by National Institutes of Health R01 NR-013825 and R01 NR-014669.

HYPERTENSION HAEMODYNAMICS

P5702 | BEDSIDE
Ablant brain functional connectivity in patients with heart failure

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Purpose: Our study identified a history of syncope in the year prior to admission with AHF to be a marker of worse outcome. Further studies are required to confirm this observation.

Acknowledgement/Funding: HMC

P5703 | BEDSIDE
Long-term mortality in patients admitted with hypertensive crisis

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Background and introduction: Hypertensive crisis, formerly referred to as “malignant hypertension”, is a severe elevation in blood pressure >180/110 with or without end organ involvement. Small series have reported significant morbidity and mortality despite intensive management of these patients. There is limited data on the long term outcomes of patients admitted with hypertensive crisis in the modern era of antihypertensive therapy.

Purpose: We performed a retrospective cohort analysis of consecutive adult patients admitted with hypertensive crisis to determine long-term mortality.

Methods: Consecutive patients with a hypertensive crisis at a university medical center from 1/2000 through 12/2010 were retrospectively identified by International Classification of Diseases (ICD)-9 diagnosis codes (401.0, 405.0, 405.01, 405.09, 404.0, 403.0, 402.0) assigned during inpatient hospitalization. All available data were used to construct a database of patients and to determine long-term survival. Mortality was followed through the Social Security Death Index. The Kaplan-Meier survival model was used to determine long-term survival. Results: We identified 55 patients admitted with hypertensive crisis. The average age of patients was 55.3±11.6 years and 54% of patients were male. Average length of stay was 6.2±5.4 days. The mean systolic blood pressure at hospital admission was 235±27 mmHg. Cause of admission was malignant hypertension in 85% of patients. Mortality at 1 year was 48% (17/36 patients). The mortality rate increased in line with levels of blood pressure up to 265 mmHg at admission.

Conclusions: Mortality rates are alarmingly high in patients with hypertensive crisis despite optimal therapy and aggressive medical management. Further studies are required to evaluate long-term outcomes of patients with hypertensive crisis.
able demographics and baseline clinical data were obtained from the electronic medical record. Survival was ascertained using the Social Security Death Index (SSDI) database.

Results: A total of 955 subjects were identified with hypertensive crisis; 940 (98.4%) had survival data and were included in the analysis. Mean age at presentation was 60.9±17.8 years and 56.5% were female. Comorbidities included diabetes in 35%, coronary artery disease in 34.4%, heart failure in 25%, and kidney disease in 12.8%. Mean follow-up was 5.4±3.0 years following the index hospital admission. 597 (63.5%) had a repeat hospitalization; 181 (19.2%) had 5 or more hospitalizations. The average age at hospitalization occurred in 176 (18.7%), 223 (23.7%) subjects died during follow-up. Mortality at 1, 3, 5, and 10 years were 7.7%, 14.1%, 20.2%, and 31.8%, respectively. Using multivariable adjustment, age (HR 1.04, CI 1.03–1.05), a history of heart failure (HR 2.06, CI 1.55–2.75), stroke (HR 1.57, CI 1.09–2.27), and hypertensive crisis (HR 1.54, CI 0.84–2.88) were all significant risk factors for long-term mortality in patients with hypertensive crisis.

Conclusions: Despite modern pharmacologic treatment, hypertensive crisis was associated with high rates of morbidity and mortality. Subjects who died during long-term follow-up were older and had a higher prevalence of stroke and chronic kidney disease. Patients with hypertensive crisis may need intensive treatment after discharge to address their risk for future cardiovascular events.

P5704 | BEDSIDE
One-point carotid wave intensity in newly diagnosed untreated hypertensive patients
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Objective: Increased left ventricular (LV) contractility is described in hypertension. In the present study we assessed the LV contractility using the traditional echocardiographic parameters and the wave intensity (WI) parameters as ventricular-arterial coupling in newly diagnosed and never treated hypertensive patients.

Methods: Participants were 145 normotensives and 145 age–and sex-matched hypertensives (mean age 50±10 vs 51.9±12 years). Antropometric, office blood pressure (BP) measurements and echocardiography were performed. LV mass index, relative wall thickness, LV stress, LV ejection fraction (LVEF), midwall fractional shortening (MWFS), circumferencial end systolic stress (cESS) and the E/A ratio and E/Em as a measure of diastolic function were calculated. Wave intensity (WI) analysis was performed at the level of the common carotid artery as well non-invasive one-point measurement of pulse wave velocity (PWV), using a high definition echo-tracking system implemented in the echo-machine (Aloka).

Results: Hypertensive patients, after adjustment for weight and physical activity, had similar heart rate but significantly higher LVEF (62.9±6.5% vs 64.6±7.7%, p=0.016), cEES (121.9±39 vs 137.9±43 g/cm², p=0.006), LV stress (59.5±22.2 vs 65.9±23.4 kdyn/cm², p=0.048), one-point PWV (5.42±1.0 vs 6.51±1.6 m/s, p=0.0001) and WI (W1=308±47 vs 13.64±7.36 mmHg m/s, p=0.001). WI, cESS and cWFS were associated with higher BMI (p=0.003) negatively, MWFS (p=0.01), fractional shortening (p=0.007) significantly increased according to LVEF while the opposite was observed for cESS (p=0.004) and LV stress (p=0.003). Among the WI parameters W1 was significantly higher in the group with higher LVEF (11.93±4.836 group 2, 17.22±8.889 mmHg m/s3 group 3 p=0.0001).

Conclusions: In patients with new onset of hypertension LV structure was similar to normal subjects but they had higher LV performance represented by LVEF and higher LV performance combined with higher WI. Moreover, hypertensive patients with higher LVEF had the tendency of normal subjects but they had higher LV performance represented by LVEF and LV internal pressure-volume ratio. In patients with new onset of hypertension LV structure was similar to normal subjects but they had higher LV performance represented by LVEF and LV internal pressure-volume ratio.

P5705 | BEDSIDE
Renal artery anatomy as a new risk factor for resistant hypertension?
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Purpose: Implementation of renal denervation into clinical practice increased the proportion of resistant hypertensins patients proceeded to multidetector computer tomography (MDCT) angiography for confirmation of technical feasibility of the procedure. And the failure rates reported in different studies were really surpris- ing thus raising a question whether we’ve missed association between specific features of renal arteries anatomy and resistance to antihypertensive therapy. The aim of the present study was to compare renal arteries anatomy according to MDCT angiography results in resistant hypertensins patients referred to renal denervation and in control group consisting of subjects after MDCT performed for various reasons.

Material and methods: We examined 37 patients, selected for renal denervation after confirmation of true treatment resistance according to current guidelines with a mean age 51±12 years, 48.6% of patients (17) were male, 51.4% (18) female. Control group consisted of 32669 patients form the database, whom routinely underwent MDCT angiography with available data on renal arteries anatomy.

MDCT was performed in two centers with 128-slices CT Somatom Definition 128 (Siemens).

Results: In resistant hypertension group additional and multiple renal arteries were detected in 20 patients (54%), fibromuscular dysplasia in 2 (5.4%) patients, early proximal division in 3 (8.1%) subjects and the rest 12 (32%) had normal anatomy of the renal arteries. Bilateral additional renal arteries were present in 5 patients of the whole group with additional renal arteries, 9 patients (24.3% and 45%, respectively) had more than one additional renal artery. All arteries seemed intact with no hemodynamically significant stenosis. From the control group database shows that additional or multiple renal arteries were present only in 8331 subject (25.5%), and only 233 (2.8%) of them bilaterally. The frequency of additional renal arteries was higher in resistant hyper- tension population (p=0.0001), as well as the proportion of patients with bilateral additional renal arteries (p=0.00001).

Conclusion: The resistant hypertensins patients are characterized by higher incidence of additional renal arteries, both uni- and bilateral. Thus observation can indicate that renal anatomy might be of importance in resistant hypertension as an underestimated cause nowadays.

P5707 | BEDSIDE
Ankle-brachial index and brachial-ankle pulse wave velocity jointed to predict mortality in a community study
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Background: Pulse volume recordings and blood pressures at arms and ankles can be obtained automatically and simultaneously to allow fast measurements of the brachial-ankle wave velocity and the ankle-brachial index. We evaluated tracking echocardiography and coronary flow reserve (CFR) of the LAD after adenosine infusion using Doppler echocardiography c) perfusion boundary region (PBR- micrometers) of the sublingual arterial microvessels (ranged from 5–25 micrometers) using Sideview Darkfield imaging (Microscan, Glycocheck). The PBR in microvessels is the cell–poor layer which results from the phase separation between the flowing red cells (RBC) and plasma. The PBR includes the most luminal part of glyocalyx that does allow cell penetration.Increased PBR is considered an accurate index of reduced endothelial glyocalyx thickness because of adenosine RBC penetration in the glyocalyx. The functional consequences of these differences as assessed by increased PBR was related to increased clinic SBP (r=0.41), DBP (r=0.50), cSBP (r=0.36), AI (r=0.20) and reduced CFR (r=0.30) (p<0.05 for all associations). These associations were more prominent for PBR measured in the microvessels ranged from 20–25 micrometers. Increased PWV and cSBP were related with reduced GLS (r=0.35, r=0.40) and CFR (r=0.40 r=0.35) respectively (p<0.05 for all associations) while reduced CFR was also associated with impaired GLS (r=0.36) (p<0.05 for all associations).

Conclusion: Endothelial glyocalyx is impaired in newly diagnosed untreated hypertensive patients. Changes in the coronary microcirculatory function leading to impaired LV longitudinal deformation.

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ments of brachial-ankle pulse wave velocity and ankle-brachial index in 10 working days. By linking with the National Death Registry, we retrieved the dates and causes of death of all participants until December 31, 2012. The median follow-up durations was 10 years. The Cox proportional hazard model was used to es- timate the hazard ratios (HRs) of abnormal Ankle-ankle index (ABI < 0.9 or > 1.3) and high brachial-ankle pulse wave velocity (baPWV > 160 cm/sec) for total cardiovascular mortality.

**Results:** A total of 115 deaths occurred and 26 cardiovascular mortality during the 10-ys (median) follow period. The prevalence of abnormal ABI and high baPWV were 11.3% and 26.34%, respectively. The total mortality was 4.1 for 1000 persons for normal PWV and normal ABI, 20.6 for 1000 PYS for normal PWV and abnormal ABI, 19.6 per 1000 PYS for high PWV and normal ABI, and 48.3 per 1000 PYS for high PWV and abnormal ABI. The crude hazard ratio (95% CI) for death was 0.01 for normal PWV and normal ABI, 4.92 (3.30–7.32) for high PWV and normal ABI, and 5.16 (1.85–14.42) for normal baPWV and abnormal ABI, compared to those with normal ABI and normal PWV. The accumulation of PWV and ABI was observed at 2-5 cm/sec/year in both PWV and ABI. The comparison of PWV and ABI showed a larger PWV for abnormal ABI (p < 0.01).

**Conclusion:** Ankle-ankle index and brachial-ankle pulse wave velocity joined significantly to predict total and cardiovascular mortality in a general community cohort.

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**P5708 | BEDSIDE**

**Impact of myocardial deformation on exercise tolerance in patients with arterial hypertension**

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**Purpose:** The aim of the investigation was to assess the relation between exercise tolerance (ET) and myocardial deformation in patients with arterial hypertension and preserved left ventricle (LV) ejection fraction (LVEF).

**Methods:** We examined a cohort of 82 patients with arterial hypertension and preserved LV ejection fraction (Ees > 21%) and 58.3±2.5 years, who were divided depending on the severity of LV hypertrophy into 4 groups: without hypertrophy (n=28, 1st group), mild hypertrophy (n=17, 2nd group), moderate hypertrophy (n=18, 3rd group) and severe hypertrophy (n=18, 4th group). Group consisted of 30 healthy persons. By the use of speckle tracking echocardiography we studied the parameters of myocardial deformation, which were: in absolute values of strain in longitudinal direction of LV, circumferential and basal rotation. All patients were undergoing bicycle exercise stress test (BEST) in order to assess the possibility to achieve endpoint criteria of submaxi- mal BEST.

**Results:** There was no difference of LVEF among all groups, LGSS and RGSS in all groups were significantly reduced in patients of 4th and 3rd groups (p < 0.01 for other groups). Patients of 1st group had lower LGSS (14.3±0.1 vs 16.9±0.2%, p < 0.01) and lower TT (9.8±0.4 vs 11.2±0.2°, p < 0.05). Patients of 1st group had lower LGSS and LGSSR are the early markers of impair- ment of the LV systolic function in patients with arterial hypertension. In hyper- tension patients abnormal longitudinal mechanics and higher TT level and apical rotation were associated with impaired exercise tolerance.

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**P5709 | BEDSIDE**

**Echocardiographic assessment of longitudinal and radial left ventricular systolic function in hypertensive patients**


**Background:** Few data are available on the relationship between left ventricu- lar (LV) circumferential and longitudinal systolic function in hypertensive patients with preserved LV ejection fraction (EF). The aim of this study is to analyze LV circumferential and longitudinal systolic function and their main determinants in a group of hypertensive patients.

**Methods:** In 1285 hypertensive patients (547 female, mean age 57±13 yrs, 77% treated), a standard echocardiographic examination was performed, to assess LV anatomy and systolic function parameters, including EF, Midwall fractional shortening (MFSS) and MidFS adjusted for end systolic stress (ESS, ESSM). In ad- dition longitudinal systolic function was evaluated by the measurement of tissue Doppler, peak systolic velocity of the mitral annulus (Sm), a reduced systolic func- tion was defined in the presence of ESS, MidFS lower than 89% or Sm lower than 8cm/sec.

**Results:** A modest but statistically significant relationship between MidFS or ESS, MidFS and Sm (r=0.8, p < 0.001) was observed. MidFS was independently related to age, body mass index (BMI), LV mass index, relative wall thickness (RWT) and heart rate, while the main determinants of Sm were age, heart rate, systolic blood pressure and LV mass index. According to previously defined crite- ria a reduction of Sm and ESS, MidFS was observed in 47% and 26% of patients, respectively.

**Conclusions:** Longitudinal systolic function is impaired in a high percentage of hypertensive patients with preserved EF and identifies a higher number of pa- tients with impaired systolic function. The determinants of longitudinal and cir- cumferential systolic function are, at least in part, different.

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**P5711 | BEDSIDE**

**Testosterone levels in hypertensive patients with vascular organ damage**

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**Purpose:** Testosterone levels are decreased in hypertensive patients compared to normotensive subjects with similar age. Measurements of carotid IMT or aor- tic stiffness are reasonable for detecting vascular organ damage (OD) in patients with arterial hypertension. We investigated whether low testosterone concentra- tion is associated with vascular OD in hypertensive patients.

**Methods:** 178 consecutive asymptomatic hypertensive males (40–60 yo) were evaluated using exercise treadmill test and stress echocardiography. Men with positive one or both of the two tests were referred for coronary angiography in order to document coronary artery disease (CAD). All patients underwent carotid- femoral pulse wave velocity (PWV) and carotid IMT evaluation. Vascular OD was detected when IMT > 0.9 mm (or plaque) and/or PWV > 10 m/s. Total testosterone (TT) levels were measured in all participants. Testosterone deficiency (TD) was defined when TT levels were below 3.4 ng/ml.

**Results:** Coronary angiography revealed significant stenosis in 31 (17%) pa- tients. The prevalence of Grade II/III hypertension was not different between CAD patients and subjects without CAD. Subjects without CAD were further divided according to presence/absence of vascular OD. Patients with vascular OD had lower TT level (p < 0.001) and a greater prevalence of TD (p < 0.01) compared to hypertensive subjects without OD after adjustment for age and blood pressure (BP).

**Conclusion:** Total TT concentration is decreased in hypertensive patients with vascu- lar OD compared to subjects without OD. The findings of this study underscore the predictive value of TT in hypertensive males with OD.

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**P5711 | BEDSIDE**

**Oscillometric mean arterial pressure-derived, not systolic pressure-derived, central blood pressure better discriminates cardiac structural abnormalities**

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**Background:** Central blood pressure (CBP) independently predicts cardiovas- cular outcomes, but the calibration method to derive CBP noninvasively from brachial blood pressure (BP) affects its accuracy. Although standard CBP (Stan- CBP) and MAP-CBP measured from the lomar mean arterial pressure (MAP) and DBP (MAP-CBP) has been validated as a better estimate of invasive CBP.

**Purpose:** To examine which CBP method can discriminate cardiac structural abnormalities.

**Methods:** 349 community-based patients with stage A heart failure (71±5 years, 174 males) had CBP by two calibration methods: MAP-CBP and Stan-CBP. LV mass index and left atrial volume by echocardiography were compared with MAP-CBP significantly better discriminated LV hypertrophy (AUC 0.67) than Stan-CBP.
CBP better distinguished LA dilatation (LAVI ≥ cTnI measured because of suspected MI. The decision limit for an MI was 30 ng/L.

**Purpose:**
Cardiac troponin (cTn) elevations are commonly found in patients with myocardial injury. Both high and low blood pressure are among the proposed mechanisms for this occurrence. The aim of this study was to evaluate the feasibility, safety and 6 month outcomes of the Cardioband system enabling percutaneous implantation of an aortic band in patients for age, sex and BMI. Each patient performed a 24-hour blood pressure monitoring (ABPM), office blood pressure (OPB) measurement, Glomerular Filtration Rate (according to MDRD) assessment, echocardiography and carotid echo-color-Doppler ultrasoundography. We also estimated renal resistive index by Doppler sonography.

**Results:** OPB and ABP were higher in RH group in comparison with the RH4 and CH3 groups (OPB: 141±10/86±4 vs 122±8/73±6 mmHg, p<0.001; ABP: 141±10/86±6 vs 122±8/73±6 vs 121±8/72±6 mmHg, p=0.001). Office pulse pressure was higher in RH4 and CH3 groups (66±12 vs 53±10 vs 51±6 mmHg, p=0.001). Renal resistive index was similar in RH and RH4 (0.72±0.08 vs 0.70±0.07 vs 0.70±0.07, p=0.001; n.s.), as it was both higher than CH3 group (0.72±0.08 vs 0.70±0.07 vs 0.65±0.06, p=0.019). We also found a significant correlation between renal resistive index and age (r=0.421, p=0.0001), Glomerular Filtration Rate (r=−0.197, p=0.003), office pulse pressure (r=0.4 p 0.0001). We did not observe significant correlation between renal resistive index and left ventricular mass index and carotid intima-media thickness.

**Conclusions:** Renal resistive index is higher in patients with drug-resistant hypertension. The correlation between office pulse pressure and the renal resistive index confirms that the latter depends much more on systemic haemodynamics than on renal ones. These data need to be confirmed by larger and prospective studies.

**P5710 | BEDSIDE**

**Renal resistive index in resistant hypertension: a case-control study**

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**Background and aim:** Renal resistive index (RRI), assessed by Doppler sonography, has been classically considered as an expression of intrarenal vascular resistance. Recent studies, however, have showed that RRI is also influenced by arterial compliance, confirming its possible role as a marker of systemic vascular alterations. Our purpose was the evaluation of the renal resistive index in patients with uncontrolled hypertension with 3 or more antihypertensive drugs, including a diuretic (RH), in comparison with a group of patients with resistant drug hypertension controlled by 4 or more antihypertensive drugs (RH4) and patients with controlled hypertension by 3 antihypertensive agents (CH3). We also considered the correlation between renal resistive index and subclinical organ damage.

**Design and method**
We enrolled 120 patients (40 RH, 40 RH4, 40 CH3) without renal arterial stenosis and known nephropathy from our outpatient clinic for hypertension. We matched patients for age, sex and BMI. Each patient performed a 24-hour blood pressure monitoring (ABPM), office blood pressure (OPB) measurement, Glomerular Filtration Rate (according to MDRD) assessment, echocardiography and carotid echo-color-Doppler ultrasonography. We also estimated renal resistive index by Doppler sonography.

**Results:** OPB and ABP were higher in RH group in comparison with the RH4 and CH3 groups (OPB: 155±8/88±5 vs 130±7/79±5 vs 127±7/76±5 mmHg, p<0.001; ABP: 141±10/86±6 vs 122±8/73±6 vs 121±8/72±6 mmHg, p=0.001). Office pulse pressure was higher in RH4 and CH3 groups (66±12 vs 53±10 vs 51±6 mmHg, p=0.001). Renal resistive index was similar in RH and RH4 (0.72±0.08 vs 0.70±0.07 vs 0.70±0.07, p=0.001; n.s.) but was both higher than CH3 group (0.72±0.08 vs 0.70±0.07 vs 0.65±0.06, p=0.019). We also found a significant correlation between renal resistive index and age (r=0.421, p=0.0001), Glomerular Filtration Rate (r=−0.197, p=0.003), office pulse pressure (r=0.4 p 0.0001). We did not observe significant correlation between renal resistive index and left ventricular mass index and carotid intima-media thickness.

**Conclusions:** Renal resistive index is higher in patients with drug-resistant hypertension. The correlation between office pulse pressure and the renal resistive index confirms that the latter depends much more on systemic haemodynamics than on renal ones. These data need to be confirmed by larger and prospective studies.

**P5712 | BEDSIDE**

**Low systolic blood pressure is associated with increased mortality in patients with myocardial injury**

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**Background:** Cardiac troponin (cTn) elevations are commonly found in patients with myocardial infarction (MI), indicating myocardial injury. Both high and low blood pressure are among the proposed mechanisms causing myocardial injury. Both high and low blood pressure are among the proposed mechanisms causing myocardial injury.

**Purpose:** To assess the prognostic implications of high and low systolic blood pressure (SBP) in hospitalized patients (pts) with myocardial injury.

**Methods:** We prospectively studied unselected hospitalized patients who had cTnI measured because of suspected MI. The decision limit for an MI was 30 ng/L (CV <10%). Pts with evidence of myocardial injury but otherwise not fulfilling the MI diagnosis were classified into three groups according to SBP values: Group A: <100 mmHg, group B 100–140 mmHg and group C >140 mmHg. Pts were followed for 30 days with mortality as the end-point. Survival data were analyzed by using Kaplan-Meier curves and multivariate Cox regression analysis.

**Results:** During 2010 a total of 3762 consecutive pts were considered, 1089 of which had myocardial injury. The pts were categorized according to SBP: 143 pts (13%) had SBP <100 mmHg (group A), 389 pts (36%) had SBP 100–140 mmHg (group B) and 557 pts (51%) had SBP >140 mmHg (group C). After 30 days of follow-up 224 pts had died (21%). Mortality differed significantly between the three groups: Group A 63 pts (44%), group B 81 pts (21%) and group C 80 pts (14%). (P<0.0001, Figure). In the multivariate Cox regression analysis, the Hazard Ratio for group A vs pts was 3.18 (95% CI 1.33–7.58), compared with group B pts. Group C pts did not have significantly increased mortality compared with group B.

**Conclusions:** In hospitalized patients with myocardial injury those with hypoten- sion, particularly those with a non-dipper pattern. Additionally, this study indicates impaired sleep quality maybe helped diagnose of MHT, particularly those with a non-dipper pattern. Additionally, this study indicates impaired sleep quality maybe helped diagnose of MHT, particularly in the non-dipper group.
outcome of Cardioband in patients with functional mitral regurgitation (FMR) in a multicentre study.

**Methods:** Between February 2013 and November 2014, 30 high-risk patients with significant FMR were enrolled at 5 sites in Europe. After a Heart Team evaluation all patients were screened by echocardiography and cardiac CT to assess feasibility. Echocardiographic data were analysed by an independent core-laboratory.

**Results:** The mean age of the patients was 72±7 years, 25 were male (83%). Mean Log-EuroScore and median STS score were respectively 20±13% (2.2%-51%) and 7±8% (1.0%-33.8%). At baseline 97% of patients were in NYHA class III-IV with mean left ventricular ejection fraction of 35±10% (15%-57%). Device implantation was feasible in all patients (100%). Acute procedural success (device successfully implanted with acute reduction of MR -2/4+) was achieved in 28 patients (93%). After cinching of the device, an average of 20% reduction of the septo-lateral diameter was observed (from 36±4 mm to 29±5 mm; p<0.01). Thirty-day mortality was 6.7% (adjudicated as unrelated to the device). At 6 month follow-up (N=17), 81% of patients were in NYHA class I-II with significant improvement in quality of life (MLW-HFG from 38 to 18; p<0.05) and 88% of patients had MR≤2/4+

**Conclusions:** Transseptal direct mitral annuloplasty with an adjustable “surgical-like” ring is feasible, with a good safety profile. Effective reduction in MR severity is observed in most patients related to a significant septo-lateral dimension reduction. MR reduction is stable and consistent at 6 months, with clinical benefit.

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5785 | BEDSIDE

Predictors of left ventricular reverse remodeling and outcome in heart failure patients with severe mitral regurgitation treated with the MitraClip

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**Background:** Although percutaneous mitral valve repair using the MitraClip can successfully reduce the severity of mitral regurgitation (MR), clinical outcome is not consistent which might relate to a variable effect on left ventricular (LV) remodeling.

**Objective:** To identify predictors of LV reverse remodeling and outcome in heart failure (HF) patients (pts) with severe MR undergoing MitraClip implantation.

**Methods:** Study population consisted of 88 consecutive pts with advanced HF and severe MR (age 73±10y, 80% NYHA III-IV, LV ejection fraction 36±13%, left atrial dimension ≥60mm) as the only independent predictor of LV reverse remodeling with an optimal cut-off value of 60mm. LV reverse remodeling was present in 33% of pts with LVEDD >60mm and in 78% of pts with LVEDD <60mm. During a median follow up of 366 days (range 45–731), MACE occurred in 27 pts (31%). Cox regression analysis revealed that, beyond a high logistic EuroSCORE, a LVEDD≤60mm was independently associated with MACE (RR 4.3 (95% CI 1.3–14), see figure)

**Conclusions:** Extensive LV dilation impedes LV reverse remodeling and attenuates clinical outcome benefits after MitraClip implantation in HF pts with severe MR.

5786 | BEDSIDE

Prevalence and impact of atrial fibrillation in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation. A subanalysis of the SOURCE XT prospective multicentre registry

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**Background:** Atrial fibrillation (AFib) is a well-established predictor of adverse outcomes in patients with aortic stenosis. Previous studies have demonstrated increased risk of mortality due to AFib in patients undergoing valve surgery. Data on the impact of AFib in patients undergoing TAVI are scant.

**Purpose:** To assess prevalence, predictors and outcomes of patients treated by TAVI according to the presence of pre-existing or new onset AFib (AFib occurring within 30 days after TAVI).

**Methods:** We analysed the dataset of the SOURCE-XT study (Clinicaltrials.gov Identifier: NCT01238497), a multicenter prospective registry of patients treated by TAVI with the SAPIEN XT valve at 99 sites in 17 countries. Follow-up was scheduled at discharge, 1 month and 1 year.

**Results:** Of the 2688 consecutive TAVI patients, follow-up was complete in 98.7% at 1 year. AFib was reported in 24.6% (n=662) patients, while 5.1% (n=138) developed new onset AFib. Patients showed significantly worse 1-year outcome compared to patients without AFib in terms of all-cause mortality and the combination of all-cause mortality or stroke (Figure). In a multivariable analysis, total A-ib as well as new onset or pre-existing AFib alone remained independent predictors of 1-year mortality and of 1-year mortality or stroke. Independent predictors of new onset AFib were age (OR 1.1), non-transfemoral access route (OR 3) and balloon post-dilation (OR 1.6). No interaction was observed between paravalvular leak and occurrence of new onset AFib.

**Conclusions:** The presence of either pre-existing or new onset AFib is a major predictor of increased mortality and of mortality or stroke in patients undergoing TAVI. Non-transfemoral access route and balloon post-dilation are the strongest procedural predictors of new onset AFib after TAVI.

5787 | BEDSIDE

Mitraclip therapy in the setting of advanced heart failure with severe functional mitral regurgitation: pre-operative evaluation and implications in patients selection

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**Background:** Recurrence of high-grade mitral regurgitation after Mitraclip therapy may occur in patients with functional mitral regurgitation (FMR) and advanced left ventricular (LV) failure.

**Purpose:** We sought to investigate the pre-procedural predictors of FMR recurrence after Mitraclip in patients with advanced heart failure (HF) and importantly remedified left ventricle (LV).

**Methods:** From April 2012 and October 2014, 25 patients with advanced HF (NYHA III-IV), decreased LV function (median LV ejection fraction 29% [IQR 23–34%]) and FMR ≥3+ underwent Mitraclip implantation in our institution. FMR degree was systematically reassessed before discharge (median time 4 days, IQR 2–6) and at short-term follow-up (median time 2 months, IQR 1–6).

**Results:** At the time of procedure the median age was 77 years (IQR 60–76), 46% were ischemic, the median EuroSCORE II was 6 (3–11), 50% had CRT before Mitraclip. Study patients presented a significant LV remodeling (median LVEDV 214 ml; IQR 186–261) and high BNP values (406 pg/ml; IQR 294–1002);

**Conclusions:** The presence of either pre-existing or new onset AFib is a major predictor of increased mortality and of mortality or stroke in patients undergoing TAVI. Non-transfemoral access route and balloon post-dilation are the strongest procedural predictors of new onset AFib after TAVI.
46% had right ventricular (RV) dysfunction, median estimated systolic pulmonary pressure (sPAP) was 56 mmHg (OR 46–64). One patient died before the short-term evaluation. Clip implantation success was obtained in 24/25 patients (96%).

Acute procedural success (MR≤2+ before discharge) was obtained in 77% of patients. However MR=3+ was observed in 9/25 patients (39%) at short-term re-evaluation. Pre-implantation BNP (for 10 pg/ml increase OR 1.041, CI 1.001–1.0234, p=0.049), RV fractional area shortening (OR 1.077, CI 1.002–1.1058, p=0.045), sPAP (OR 1.09, CI 1.06–1.104, p=0.049), mitral annulus size (for 1 mm OR 1.49, CI 1.47–1.52, p=0.018) and vena contracta width (for 0.1 mm or 1.42–1.47, p=0.047) were significantly associated with short-term FMRI persistence/recurrence. BNP (AUC 0.827, p=0.014) and annulus dimensions (AUC 0.829, p=0.009) showed the best accuracy at the ROC analysis.

Conclusions: Valid predictors of Mitraclor efficacy in patients with advanced HF and LV dysfunction have not been identified yet. Pre-implantation information could help in the selection of patients eligible for Mitraclor therapy in this setting. Future prospective studies are warranted to test these findings on large populations.

5788 | BEDSIDE
Mortality in transfemoral transcatheter aortic valve implantation: impact of ejection fraction
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Introduction: Reduced LV ejection fraction (EF) is frequently seen in patients with severe aortic stenosis (AS). However, it is not clear to what extent this contributes to procedural risk and overall survival, as there has been conflicting data on clinical impact of EF reduction. The aim of the present analysis was to assess the clinical outcome when EF is consistently reflective of (LV) dysfunction in the setting of diastolic dysfunction typical for severe AS. We examined this issue in a large cohort of patients receiving transfemoral aortic valve implantation (TF-AVI) in our centre. Methods: EF determined by echocardiography was available in all 1570 patients (pts) receiving TF-AVI between 2006 and 2014. EF at 10 days after intervention was available in 1419 of these pts. Follow-up concerning 1-year-survival was available in 1502 of the pts. We analyzed survival at 30 days and at 1 year, as well as myocardial infarction (MI), bleeding, access site complications, stroke and kidney injury at 30 days, as defined by the Valve Academic Research Consortium (VARC).

Results: Of 1570 patients, 112 (7.2%) had an EF <30%. Mean STS-PROM was 8.5±6.1% with EF<30% versus 10.5±6.7% with EF≥30% (p<0.01). Mean logELFA score was 19.9±12.6% and 31.8±17.5%, respectively (p<0.01). However, 30-day mortality was 6.7% with EF<30% and 7.9% with EF≥30%, with no significant difference between groups (p=0.81). 1-year mortality did not differ significantly, either (21.0% vs. 23.9%, p=0.48). There were no significant differences concerning MI (0.7% in EF<30% vs. 1.1% in EF≥30%, p=0.72) or stroke (4.4% vs. 6.5%, p=0.37). There was also no significant difference concerning kidney injury (14.4% vs. 11.8%, p=0.70) or access site complications (27.7% vs. 18.3%, p=0.05). Life threatening (8.3% vs. 6.5%, p=0.54) or major (29.6% vs. 24.7%, p=0.32) bleeding were not different in incidence either. In patients with EF<30%, TF-AVI led to significant improvement of EF, from a mean of 24.9±5 to 37.5±5 % at 12.2 10 days after TF-AVI (p<0.01).

Conclusion: Although STS and EURO risk scores predicted a significantly higher risk in patients with severely impaired EF, we could not substantiate a significant differences in 30-day- or 1-year-mortality. Also, there were no significant differences in the VARC-defined endpoints MI, stroke, bleeding, access site complications or renal injury. These results, demonstrate that EF, even if severely reduced, is not a useful parameter in the preprocedural evaluation of TF-AVI patients, and patients with severely impaired EF should not be deemed unsuitable for TF-AVI.

5789 | BEDSIDE
Geometry of the aortoventricular annulus as a predictor of pacemaker implantation following transfemoral aortic valve implantation
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Background: One of the causes of conduction abnormalities associated with transcatheter aortic valve implantation (TAVI) is a disruption of aortoventricular (AV) conduction tissue caused by mural tension during positioning and expansion of the prosthetic valve. We sought to evaluate whether a higher difference between the long and short diameters of the elliptic AV annulus is a predictor of pacemaker (PM) need following TAVI.

Methods: We conducted a retrospective analysis of 104 consecutive patients who underwent TAVI during a 1 year period. All patients had the AV annulus geometry measured by multidetector cardiac computed tomography up to a month prior to valve implantation. The difference between maximal (DMax) and minimal diameters (Dmin) of the annulus was considered the elliptic factor (ELFA) which was analyzed using t-test to evaluate whether it significantly differs between the PM receiving group and the group without need for a PM. Then, using a univariate and multivariate model adjusted for other confounders predicting the need for a PM (age, gender, prior right bundle branch block, type of prosthetic valve implanted), we sought to evaluate whether the ELFA is a predictor of PM implantation within 1 month following TAVI.

Results: Mean age was 82±6 and 65% were women. The CoreValve prosthesis was implanted in 63% patients. Mean valve size was 27 mm. Average Dmax, Dmin and ELFA were 25.6 mm, 20.6 mm and 5 mm respectively. Thirteen patients (12.5%) underwent PM implantation. Those patients had an ELFA of 5.7 compared to 4.8 mm in those who did not get a PM (p=0.02). In multivariate analysis adjusted for known confounders, a higher ELFA still remained a statistically significant and independent predictor for the need of PM (p=0.04).

Conclusions: Our data shows that ELFA is an independent and significant predictor of the need for PM following TAVI and implantation of CoreValve prosthesis. Further investigation whether it should be considered as a factor in managing TAVI patients.

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5-year outcomes after transcatheter aortic valve implantation with the CoreValve prosthesis
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Little is known about long-term outcomes following TAVI. Previous reports of transcatheter aortic valve implantation (TAVI) have focused on short- and mid-term outcomes; however, long-term durability of transcatheter heart valves and long-term clinical outcomes (AUC 0.829, p=0.009) showed the best accuracy at the ROC analysis. Conclusions: Our study demonstrated favorable long-term outcomes after TAVI. Signs of prosthetic valve failure were observed in 2% of patients. Complications after procedure, notably acute kidney injury and severe P-PM, were associated with reduced long-term survival.

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Transfemoral aortic valve implantation of Edwards sapien 3 without premeditation
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Introduction: Transcatheter aortic valve implantation (TAVI) without premedication may have some advantages and has been demonstrated to be feasible with various transcatheter valves.

Purpose: We sought to investigate whether this concept also applies to transfemoral implantation of the Edwards SAPIEN 3 device.

Methods: Ninety-two consecutive patients from 2 centers with severe aortic stenosis undergoing transfemoral TAVI were enrolled in order to assess the feasibility and safety of TAVI with Edwards SAPIEN 3 device. The pre-balloon aortic valve implantation was performed without any premedication and balloon aortic valve implantation without significant difficulties while crossing the aortic stenosis with the wire or catheter. Patients requiring pre-balloon had significantly higher calcium-score and density of the aortic valve, higher age, and higher transvalvular gradients. The aortic valve area was...
**Methods:** Eight patients underwent TAVI with Dual-filter protection and additional Wirion filter in the left vertebral artery. After TAVI all filters were retrieved and sent for histopathologic evaluation.

**Results:** All filters were successfully deployed except for the Wirion left vertebral filter in one patient that was complicated by a dissection and required stenting of the proximal segment of the left vertebral artery. Seven Wirion left vertebral filters were available for histopathologic evaluation, which all showed traces of either native or foreign body material. The amount of encountered material per patient varied from two to forty-one separate fragments. Foreign body material was found in five patients, with diameters ranging from 0.04 to 0.65 mm. Thrombus and fibrin were found in four patients (size: 0.05 to 1.10 mm). In four patients tissue components were found, namely: endothelium, myocardial tissue, calcium fragments, collagen or multiple. Endothelium was found in three patients (size: 0.10 to 1.50 mm), myocardial tissue was found in two patients (size: 0.07 to 1.60 mm), calcium fragments were found in one patient (size: 0.16 mm), and collagen was found in one patient (size: 0.09 mm).

**Conclusion:** Our findings confirm that current embolic protection devices, covering the brachiocephalic trunk and the left common carotid artery, are suboptimal in the protection from CVE’s during TAVI. Right now, one important access route to the Willis polygon is routinely left untouched. The left vertebral artery seems an important access route to material to enter the brain. This pilot study warrants further research to explore the value of left vertebral artery protection during TAVI.

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Alterations of the platelet pool in the early period after transcatheter aortic valve implantation or surgical valve replacement in patients with aortic stenosis

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**Purpose:** The purpose was to assess the level of platelet activation and turnover in the perioperative phase following TAVI or AVR.

**Methods:** This prospective cohort study enrolled patients undergoing AVR (biological prostheses) or TAVI (balloonexpandable (EDW), selfexpandable (COR)). Blood was drawn before (T1), at day 1 (T2), at days 5–7 (T3) and at days 7–9 (M4) after intervention. Transfusion (blood, platelets, coagulationfactors) and hemodilution were exclusion criteria for further analysis. Platelet activation was tested by optical/impedance aggregometry, PFA100 and flowcytometry (PAC1, P-Sel, CD154, CD63, CD31, leukocyte platelet aggregates (LPA)). The immature platelet fraction (IPF) and related parameters were analyzed by Sysmex XE.

**Results:** 67 patients were enrolled (male=34,mean age 80±5.6 years). 27 patients received AVR, 40 patients underwent TAVI (n=25 EDW, n=15 COR). After intervention, ADP and TRAP induced activation decreased over time in all groups with higher levels of activation in AVR patients. In contrast, LPA increased over time in AVR patients whereas no changes were determined in TAVI patients. In COR and AVR patients, IPF and associated parameters showed a transient increase, followed by a decrease on T4 below baseline. Conversely, LPA (p=0.026 T3; p=0.029 T4) and hIPF (p=0.054 T3; p=0.060 T4) remained elevated up to T4 in EDW patients.

**Conclusions:** Different patterns of activation were found in TAVI and AVR. Compared to AVR and COR, EDW was related with a delayed decrease of IPF and hIPF indicating an increase in platelet turnover in EDW patients.

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First-in-human complete filter-based cerebral embolic protection with transcatheter aortic valve implantation

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**Background:** The occurrence of cerebrovascular events (CVE’s) after transcatheter aortic valve implantation (TAVI) has fuelled concern for its potential application in younger patients with longer life expectancy. MRI studies, performed after TAVI, show sizable numbers of new ischemic lesions up to 84% of patients. Embolic protection devices may limit periprocedural CVE’s. Currently available filter-based EPD’s cover all extracranial contributors to the brain yet leave the left vertebral artery unprotected.

**Purpose:** To present the first-in-human use of a novel filter-based EPD in the left vertebral artery in addition to the existing dual-filter based device that covers the brachiocephalic trunk and the left common carotid artery to assess both safety and feasibility of complete filter-based brain protection.

**Methods:** Eight patients underwent TAVI with Dual-filter protection and additional Wirion filter in the left vertebral artery. After TAVI all filters were retrieved and sent for histopathologic evaluation.

**Results:** All filters were successfully deployed except for the Wirion left vertebral filter in one patient that was complicated by a dissection and required stenting of the proximal segment of the left vertebral artery. Seven Wirion left vertebral filters were available for histopathologic evaluation, which all showed traces of either native or foreign body material. The amount of encountered material per patient varied from two to forty-one separate fragments. Foreign body material was found in five patients, with diameters ranging from 0.04 to 0.65 mm. Thrombus and fibrin were found in four patients (size: 0.05 to 1.10 mm). In four patients tissue components were found, namely: endothelium, myocardial tissue, calcium fragments, collagen or multiple. Endothelium was found in three patients (size: 0.10 to 1.50 mm), myocardial tissue was found in two patients (size: 0.07 to 1.60 mm), calcium fragments were found in one patient (size: 0.16 mm), and collagen was found in one patient (size: 0.09 mm).

**Conclusion:** Our findings confirm that current embolic protection devices, covering the brachiocephalic trunk and the left common carotid artery, are suboptimal in the protection from CVE’s during TAVI. Right now, one important access route to the Willis polygon is routinely left untouched. The left vertebral artery seems an important access route for material to enter the brain. This pilot study warrants further research to explore the value of left vertebral artery protection during TAVI.
Echocardiographic deformation analysis for the prediction of atrial fibrillation and stroke development after ST-elevation myocardial infarction

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We have recently demonstrated that the Doppler-derived peak ejection intraventricular pressure difference (EIVPD) between the apex and the LV outflow tract is a sensitive and load-independent index of global systolic function that best correlates with invasive maximal elastance. This index could provide additive prognostic information in patients with dilated cardiomyopathy (DCM).

Methods: 200 pts with DCM (61 females, 61±13 years old, 40% ischemic) were prospectively included and underwent an echocardiographic exam including measurement of the EIVPD from outflow color-Doppler M-mode recordings. 20% pts were in NYHA class III, 88% on beta-blockers (BB) and 95% on ACE inhibitors (ARB).

Results: After a median follow-up period of 4.1 years (n=191 pts), the composite end-points of any cardiac event (cardiac death, transplantation or hospital readmission for heart failure) or hard cardiac events (cardiac death or transplantation) were recorded in 74 and 35 pts, respectively. Values of EIVPD were similar between ischemic and non-ischemic (2.8±1.2 vs 2.8±0.9 mm) and did not correlate with EF (R=0.2). By multivariate proportional-hazards modeling, stratified to the use of BB, age and sex-adjusted risk of any cardiac event (n=57) was directly related to NYHA (HR=2.5 [95% CI: 1.6 to 3.7], p<0.001), E/A ratio (HR=1.4 [1.2–1.6], p<0.001), end-systolic volume (HR=1.3 [1.0–1.7]), and inversely to EIVPD (HR=0.64 [0.4–0.9] per 1.5 mm Hg, p=0.04; Figure 1; univariate area under the ROC curve= 0.60). The same factors were predictors for hard cardiac events. EF was not related to outcome (HR=0.8 [0.5–1.3], p=0.4)

Conclusion: The Doppler-derived EIVPD is the first noninvasive index of global systolic function which proves to be useful to predict long-term outcome of patients with DCM

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Echocardiographic deformation analysis for the prediction of atrial fibrillation and stroke development after ST-elevation myocardial infarction with primary percutaneous coronary intervention

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Background: Patients with acute myocardial infarction are at increased risk of developing atrial fibrillation (AF) and stroke. Speckle tracking echocardiography may serve as a way of selecting patients at high risk of developing such outcomes.

Methods: The study comprised of 373 patients with ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention. Patients had an echocardiogram performed a median of 2 days after their STEMI. The echocardiogram consisted of conventional imaging, tissue Doppler, and myocardial strain analysis by speckle tracking. Endpoint was a composite of new-onset AF and ischemic stroke.

Results: At a median follow-up time of 5.5 years 44 of the patients developed AF (n=24) or stroke (n=24), four of which developed both. Patients who developed AF and/or stroke had significantly reduced systolic function by left ventricular ejection fraction (LVEF) (43% vs 46%, p=0.04) and global longitudinal strain (GLS) (10.9% vs 2.6%, p=0.004), both being independent predictors. However, only GLS remained a significantly independent predictor (HR=1.12, 95% CI [1.00:1.25], p=0.04, per 1% decrease) after multivariable adjustment for baseline predictors (age, gender, diabetes, hypertension, diastolic dysfunction, and LVEF) in a cox regression model. Furthermore, GLS yielded significantly higher c-statistics for prediction of outcome compared to LVEF -45% (0.63 vs 0.52, p=0.026). When stratified into tertiles of GLS, it became evident that patients in the lowest tertile mediated this signal (figure) with a 2-fold increased risk compared to the highest tertile (HR=2.10, 95% CI [1.04:4.25]).

Conclusion: GLS improves risk stratification for AF and stroke in patients with STEMI, particularly in those with markedly depressed systolic function.

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Diastolic dysfunction and adverse diastolic remodelling as predictors of infarct scar and cardiovascular events following acute myocardial infarction

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Background: Severe diastolic dysfunction, or restrictive filling (RF), is a powerful prognostic marker identifying high risk patients post AMI; however it may only identify a small proportion of patients at risk. Over time, there are dynamic changes to diastolic function, altered by left ventricular (LV) remodelling, myocardial scar size, and viability. However, there is a paucity of literature on diastolic ‘remodelling’ post AMI and its prognostic value. Furthermore, the relationship between infarct scar size and diastolic function has not been well explored.

Purpose: The study aimed 1) to determine the optimal marker of diastolic function that would best predict cardiac magnetic resonance imaging (CMRI) measured LV infarct scar size, 2) evaluate adverse diastolic remodelling (ADR) as a predictor of infarct scar size and 3) the prognostic value of ADR following reperused STEMI.

Methods: 218 patients with acute reperfused STEMI were prospectively recruited. Serial transthoracic echocardiography (TTE) and CMRI were performed “early” at 4 days (IQR 3–7 days) and at “follow up (FU)” 55 days (IQR 46–64 days) after STEMI. Infarct characteristics were evaluated on late gadolinium enhancement images. Measures of diastolic function including E/A, mitral deceleration time, E/E’ and diastolic grade (1=impaired relaxation, 2= pseudonormal and 3=RF), were performed by TTE. Patients were stratified into the “ADR group” (those whose diastolic grade had worsened or persistent RF from early to follow up scans) and non “ADR group”. The primary endpoint consisted of major adverse cardiovascular events (MACE) including mortality, infarction, heart failure, stroke and ventricular arrhythmias.

Results: Diastolic grade at FU, showed the best correlation with FU infarct total and core scar size (r=0.51, p<0.001), gray zone (GZ) scar size (r=0.46, p<0.001), and microvascular obstruction (MVO) size (r=0.33, p<0.001). Patients with ADR (n=50) predicted FU total scar (AUC 0.85), core scar (AUC 0.86), GZ scar (AUC 0.77), and MVO (AUC 0.75). These predictors were similar in patients who had reperused LV infarct scar size, 2) evaluate adverse diastolic remodelling (ADR) as a predictor of infarct scar size and 3) the prognostic value of ADR following reperused STEMI. Over a FU period of 602 days (IQR 437–730 days), the primary endpoint occurred in 40 patients. Multivariate Cox regression analysis showed that infarct core scar size at FU (HR 1.10, p<0.001) and ADR (HR 2.88, p<0.009) were independent predictors for MACE.

Conclusion: Larger Infarct size is associated with worse diastolic function grade and ADR, on serial TTE, identifies a larger cohort of at risk patients than RF alone, and is a prognostic marker for MACE post AMI.

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Reversible abnormal right ventricular function at follow-up is associated with better survival in patients with chronic systolic heart failure

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Background: Longitudinal annular systolic excursion of the tricuspid annular plane (TAPSE) has been widely used to assess right ventricular (RV) function noninvasively. An impaired TAPSE has been associated with a worse survival in patients with chronic systolic heart failure (SHF) secondary to dilated cardiomyopathy. However, it is not known whether a reversible abnormal TAPSE predicts survival in patients with chronic stable SHF.

Aim: To test the hypothesis that a reversible abnormal TAPSE is associated with a better survival in patients with chronic stable SHF.

Methods and results: A complete echocardiographic examination was performed in 570 patients with chronic SHF and left ventricular ejection fraction (LVEF) -45%. RV systolic function was evaluated by M-mode echocardiography using the TAPSE. Mean age of the study population was 66±12 yrs (21% female). Baseline TAPSE was 19±4 mm. At six-months, TAPSE was 20±4 mm. During a median follow-up of 39 months, 78 patients died. At 60 months, patients with TAPSE <14 mm exhibited a survival of 64%, whereas survival was 86% in...
those with a moderately depressed TAPSE (between 15 and 17 mm) and 89% in those with normal TAPSE (>18 mm) (log rank 38.9, p<0.0001). When patients were stratified according to the reversibility of compromised RV function, survival was 91% in patients with persistently normal TAPSE, 86% in those with reversible abnormal TAPSE, and 69% in those with either worsened TAPSE or persistently abnormal TAPSE (log rank 38.8, p<0.0001). Cox regression analysis showed that presence of persistently normal or reversible abnormal TAPSE normalized for age, gender, LVEF and diastolic function was independently associated with improved survival (HR 0.43, 95% CI 0.26–0.72, p=0.001).

Conclusions: The survival of patients with echocardiographically stable SHF who exhibited reversibility of an abnormal TAPSE during follow-up have a better survival than patients with either worsened TAPSE or persistently abnormal TAPSE.

Results: We evidenced a significant correlation between basal S-GLS and 6MWT (r 0.83; p<0.01) and Δ PASP (r 0.53; p<0.01). Most importantly a basal S-GLS cutoff -17.2%, computed with ROC analysis, identified SSC patients who showed a decrease in exercise tolerance at follow up [AUC 0.81 (95% CI 0.67 to 0.94), sensitivity 78% (95% CI 63–92), specificity 71% (95% CI 90–91)]. Moreover patients with basal S-GLS -18% demonstrated higher pulmonary pressures at FAP (PAPS 34.8±8.4 vs 26±3 mmHg; p<0.05).

Conclusions: Our data demonstrate that in SSC patients a reduced LV contractile reserve is strictly related to an inappropriate pulmonary pressure response to exercise and a reduced exercise tolerance. Moreover a reduced LV contractile reserve served to be able to identify SSC patients who show a decrease in exercise tolerance at follow up and develop higher pulmonary pressures.

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Novel echocardiographic and clinical score predicts 3-year mortality in coronary care unit patients

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Background: At present there is no clinically available prognostic score that incorporates echocardiographic and clinical data for patients hospitalized in the coronary care unit (CCU).

Purpose: The aim was to develop and validate an integrated model, comprised of clinical and echocardiographic data, to predict 3-year mortality of patients admitted to the CCU.

Methods: We reviewed the records of 8,219 consecutive patients admitted to a tertiary care CCU between 2004 and 2011. From these, we identified a training cohort of 1,993 patients with a complete set of echocardiography parameters and a 6 month follow up. From these, we identified a training cohort of 1,993 patients with a complete set of echocardiography parameters and a 6 month follow up. The model included 6 clinical parameters and 7 echocardiographic parameters in total.

Results: Of 1,993 patients in the training cohort, the mean age was 69±16 years. The primary diagnosis was acute coronary syndrome (66%), heart failure (38%) and ≥50% had had more than one primary diagnosis. 3-year mortality was 28%. Age (OR 1.7, 95% CI 1.6–1.8), diabetes (OR 1.3 95% CI 1.1–1.5), chronic lung disease (OR 1.2 95% CI 1.1–1.5) and chronic kidney disease (OR 1.4 95% CI 1.2–1.8) were independently associated with mortality. Among 6 echocardiography parameters, only LVEF (OR 0.9, 95% CI 0.8–0.9) and RVSP (OR 1.3 95% CI 1.2–1.3) were prognostic of mortality (integrated of clinical data, LVEF and RVSP). Cox regression analysis showed a better prognostic value, with AUC of 0.78 (95% CI 0.76–0.80), compared to clinical (AUC 0.72; p=0.001) or echocardiographic data alone (AUC 0.71; p=0.001). This formula represents the suggested CCU model: 3*(Diabetes + 4*Lung + 5*Age in years/10 + 6*LVEF in %) + 4*GLS cutoff + 0.91 + 4*(LVEF <0.51) + 4*(RVSP <18 mmH) + 4*(presence of persistently normal or reversible abnormal TAPSE normalized for age, gender, LVEF and diastolic function in presence of improved survival (HR 0.43, 95% CI 0.26–0.72, p=0.001).

Conclusions: We describe an integrated score to predict 3-year mortality of patients admitted to the CCU that incorporates echocardiographic and clinical data for patients hospitalized in the coronary care unit (CCU). The model is derived from a large cohort of patients that demonstrated a good discriminatory power, with AUC 0.77, which was equal to APACHE III (AUC 0.72) and Charlson score (AUC 0.71).

Conclusion: We describe an integrated score to predict 3-year mortality of patients admitted to the CCU that incorporates echocardiographic and clinical data for patients hospitalized in the coronary care unit (CCU). The model is derived from a large cohort of patients that demonstrated a good discriminatory power, with AUC 0.77, which was equal to APACHE III (AUC 0.72) and Charlson score (AUC 0.71).

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Left ventricular contractile reserve as a new prognostic factor in systemic sclerosis patients


Background: Global longitudinal strain (GLS) derived from speckle tracking echocardiography is widely used for assessment of occult systolic dysfunction.

Objective: This prospective observational study investigated the prognostic value of GLS as well as sub-endocardial (EndLS) and sub-epicardial (EpILS) longitudinal strain in regular treated uncomplicated hypertensive patients.

Methods: This study included 95 patients (57 men, age 65±12 years) with uncomplicated hypertension who have been regularly treated for more than 1 year. Speckle tracking echocardiography was used for measurement of longitudinal deformation from 3 apical views of left ventricle. GLS was measured by auto-tracking software with further division into sub-endocardial and sub-epicardial myocardium and measured their longitudinal strain by manual click-and-draw method and averaged from 3 apical views. End-points for this study were any admission for stroke, acute coronary syndrome, heart failure, and cardiovascular death.

Results: After a mean follow-up period of 8±24 months, 20 (21%) patients reached end-points. The significant differences between patients with and without end-points included status of diuretic use (75 vs. 93%, p=0.018), age (71±12 vs. 64±12 years; p=0.020), and EpILS (>16.0±2.0 vs. 17.7±3.0%; p=0.040). There were no difference between groups in GLS (−15.5±1.6 vs. −17.6±3.3; p=0.263) and EndLS (−21.4±2.1 vs. −22.9±4.1%; p=0.105). By multivariate Cox regression analysis controlling age, body mass index, systolic blood pressure, and status of diuretic use, GLS was an independent factor for prognosis (HR 1.241, 95% CI 1.030–1.496, p=0.023). By dividing subjects into 2 strata with the cut-off value of median value −17.57% for EpILS, the Kaplan-Meier survival curve revealed significant differences (p=0.016) for endpoints.

Conclusions: In regular treated hypertensive patients, EpILS was an independent prognostic factor for worse outcome but not GLS and EndLS. Our results indicated involvement of sub-epicardial myocardium had important contribution in hypertensive heart disease.

5808 | BEDSIDE
Predictive value of local prolonged electro-mechanical interval by echocardiography in the concealed stage of arrhythmogenic right ventricular dysplasia/cardiomyopathy


Introduction: The concealed stage of ARVD/C is associated with increased risk of sudden death. However, at this stage risk stratification is hampered by paucity of criteria. Activation delay (AD) is a hallmark of arrhythmogenesis. Deformation imaging may unmask AD in the absence of ECG and structural abnormalities.

Methods: Three groups were compared 1) mutation-positive definite ARVD/C patients (n=44), 2) asymptomatic mutation carriers (AMC) not fulfilling Task-Force criteria (TFC) and without history of ventricular arrhythmias (n=31) and 3) healthy controls (n=30). All underwent echocardiographic examination including deformation imaging and ECG according TFC. As surrogate for local AD the electro-mechanical interval (EMI) was measured, defined as time between first ECG-detected deflection and local onset of shortening. Arrhythmic outcome (ventricular tachycardia, PVC count) of AMC was correlated to EMI and ECG TFC.

Results: EMI was prolonged in all RV segments in ARVD/C compared to AMC (P<0.0001) and TFC (P=0.002). This finding was limited to mid-RV segments of ARVD/C patients. In regular treated hypertensive patients, EpiLS was an independent factor for prognosis (HR 1.241, 95% CI 1.030–1.496, p=0.023). By dividing subjects into 2 strata with the cut-off value of median value −17.57% for EpILS, the Kaplan-Meier survival curve revealed significant differences (p=0.016) for endpoints.
was defined as abnormal based on findings in controls. In AMC prolonged EMI was detected in the subtricuspid area in 17/31 subjects (55%). Terminal Activation Duration >55ms was the only ECG abnormality found in this group in 8/31 (26%). Isolated prolonged EMI occurred in 10/31 AMC. After a mean follow-up of 3±2.8yrs, 8/31 subjects experienced an increase in ventricular arrhythmia burden. Prolonged subtricuspid EMI was the only parameter significantly correlated to arrhythmogenesis during follow-up (Figure 1).

**Conclusion:** Deformation imaging reveals abnormal AD both in ARVD/C patients and in AMC. In AMC prolonged EMI in the subtricuspid area is often detected without any additional abnormalities. Prolonged EMI is a new parameter unmasking AD in the concealed stage and may contribute to risk stratification.

**5810 | BEDSIDE**

Right ventricular function assessed by 2D longitudinal strain independently predicts mortality in chronic heart failure patients

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The aim of this study was to evaluate the role of two-dimensional (2-D) speckle tracking measures of right ventricular systolic function in predicting mortality of patients affected by chronic heart failure (CHF).

We enrolled 274 outpatients (77% males, 64±14 years, NYHA class 2.2±0.7, left ventricular ejection fraction, LVEF, 34±6%) with CHF (ESC criteria), in stable clinical conditions (<1 month) and in conventional therapy (91% ACE-inhibitors and/or ARBs, 94% betablockers). By echocardiogram (Echo-PAC, GE), a 4-chamber view (frame rate 50–70/sec) was obtained to evaluate global strain of the right ventricle by 2-D speckle tracking (RVGS).

Tricuspid annulus systolic excursion peak (TAPE) was also calculated. During follow-up (21±12 months), 26 patients died (19 for cardiovascular causes and 7 for non cardiovascular causes). Seven patients underwent heart transplantation. RVGS was associated to mortality at the univariate (HR: 1.16; 95% CI: 1.068–1.26; p < 0.001; C-index: 0.82) as well as at the multivariate analysis (HR: 1.11; 95% CI: 1.012–1.217; p: 0.01; C-index: 0.69) in a model including age, comorbidity, diabetes, antithrombotic strategy, echocardiographic parameters (LVEF, LV systolic, diastolic function), and interaction with antithrombotic strategy was examined.

Results: A patent IRA (TIMI flow 2/3) was present in 707 patients (37.9%) and was associated with lower risk for procedural complications and a shorter hospital stay. At 30 days, a patent IRA was also associated with lower rates of cardiac death, MI and sub-acute stent thrombosis (Table). There were no interactions between antithrombotic treatment and the impact of IRA patency on cardiac death, MI or the composite death/MI (Breslow-Day interaction p-values of 0.21, 0.33 and 0.46 respectively).

Outcomes according to baseline TIMI flow

<table>
<thead>
<tr>
<th>Baseline TIMI 0/1 (N=521)</th>
<th>Baseline TIMI 2/3 (N=707)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Procedural outcomes</td>
<td></td>
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</tr>
<tr>
<td>Any complication (%)</td>
<td>8.0</td>
<td>4.4</td>
</tr>
<tr>
<td>Ballout GPI (%)</td>
<td>32.2</td>
<td>11.8</td>
</tr>
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<tr>
<td>Length of hospital stay (days)</td>
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<td>5.97±7.3</td>
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**Conclusions:** Despite evolution in primary PCI strategies (including pre-hospital pharmacotherapy), early IRA patency is still associated with higher procedural success and in-hospital mortality. The choice of antithrombotic, clinical, angiographic and procedural factors and we analyzed the evolution of mortality in the elderly over the study period.

**Results:** The elderly undergoing P-PCI were more likely to be women (44% vs 20%, p < 0.001), diabetic (26% vs 22%, p < 0.001) and hypertensive (71% vs 54%, p < 0.001). They showed more comorbidities (prior cerebrovascular disease 9% vs 4% and renal disease 6% vs 3%, p < 0.001 for both) and a more extensive cardiovascular disease (multivessel disease 59% vs 46% and left ventricular dysfunction both). The time to reperfusion was higher in the elderly patients (median 243 vs. 282 min, p < 0.001), mainly due to a longer delay of the patient (increase 59 min in median vs. in younger patients, p < 0.001).

**Conclusion:** Early infarct-related artery (IRA) patency has been associated with worse outcomes in primary PCI patients. In this study, patients affected by chronic heart failure (CHF) had a higher risk of mortality than the other population and this relation persists in contemporary practice with pre-hospital initiative. 

**Methods:** A total of 878 patients were enrolled. The current analysis was done on 1,863 patients who underwent PCI and had IRA patency data. Thirty-day outcomes were compared according to IRA flow before PCI (TIMI flow 0/1 vs. TIMI flow 2/3) and interaction with antithrombotic strategy was examined.

**Results:** A patent IRA (TIMI flow 2/3) was present in 707 patients (37.9%) and was associated with lower risk for procedural complications and a shorter hospital stay. At 30 days, a patent IRA was also associated with lower rates of cardiac death, MI and sub-acute stent thrombosis (Table). There were no interactions between antithrombotic treatment and the impact of IRA patency on cardiac death, MI or the composite death/MI (Breslow-Day interaction p-values of 0.21, 0.33 and 0.46 respectively).

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possible. The aim of the present study was to assess time to first call in relation with timing of onset of pain, in a large cohort of patients having called the French emergency medical system (SAMU: Service d'Aide Médicale Urgente).

Methods: The e-MUST registry was set up by the regional health authority of the greater Paris region in France to prospectively collect data on all STEMI patients transported by the physician-staffed mobile intensive care units (MICU) dispatched by the SAMU. The registry has been ongoing since 2003 and all data up to 2013 were used for the present analysis, excluding only inter-hospital transfer patients.

Results: Complete data on time of onset and time to first call were available in 17,789 patients. One third of STEMI cases occurred in the morning (from 6:00 am to 12:00 pm), with fewer occurring during the night (from 12:00 am to 6:00 am) (Figure). Overall, median time from onset to call was 60 minutes (25-167 min), with considerable inter-patient variations: the longest time to call was found during the night (88 [33; 258] minutes from 12:00 a.m. to 6:00 a.m.), and the shortest in the afternoon from 12:00 p.m. to 6:00 p.m. (46 [19; 123] minutes).

Conclusion: Though fewer STEMI cases had their onset during the night, their time to first call was much longer. Also, time to first call in the morning hours, where a higher proportion of STEMI occurred, was longer than when STEMI occurred in the afternoon. Media campaigns and public information should therefore specifically focus on reducing time delays when AMI occurs at night or, to a lesser extent, in the morning.

5817 | BEDSIDE

Culprit vessel versus multivessel intervention at the time of primary percutaneous coronary intervention for patients with multivessel disease: insights from the British Columbia Cardiac Registry

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Background: Up to two thirds of patients with STEMI undergoing primary PCI in patients without cardiogenic shock. The optimal strategy for treating non-culprit disease continues to be debated.

Methods: We analyzed all patients undergoing primary PCI (n=12,105) between 2006-2013 who were enrolled in the British Columbia Cardiac Registry. Of these 5,632 patients which entered analysis 417 (7%) were younger than 45 yrs. Although mean age increased between 2006 and 2013 (2006: 63.5±13 to 2013: 64.5±13 yrs, ANOVA p<0.01) the proportion of patients younger than 45 yrs. remained constant (p for trend=0.8). Pts <45 yrs. were more likely to be male and had a higher prevalence of active smoking (85 vs 40%, p<0.01) and of a positive family history for cardiovascular disease (44 vs. 21%, p<0.01). While hypercholesterolemia was not associated with a specific age, the prevalence of diabetes mellitus and art. hypertension was significantly lower in young STEMI-patients. The results were confirmed in a multivariate logistic model (Table 1). Young STEMI-patients were more likely to suffer larger myocardial infarctions (creatine kinase (CK)>3000 UI/L; OR 1.7, 95% CI 1.3–2.1) or a prehospital resuscitation event (OR 2.5, 95% CI 1.6–3.9). While the proportion of young smokers was constant during the study period (2006–09:85%, 2010–13: 84%, p=0.8), the proportion of obese (BMI >30 kg/m2) patients <45 yrs. increased significantly: 2006-09: 23%, 2010-13: 32%, p<0.01.

Conclusion: The results of this large registry-study demonstrate that STEMI in younger patients occurs at a relative constant rate (approx.7% of all pts.) over time. STEMI in young patients are distinguished by more extensive myocardial infarctions and higher rates of prehospital resuscitation events. The dominating risk factor for young STEMI-patients was active smoking with a prevalence of 85%, followed by a positive family history for cardiovascular disease and obesity.

5819 | BEDSIDE

In-hospital outcome in octogenarians with acute coronary syndrome undergoing invasive coronary procedures

B. Ricci1, E. Cenki1, Z. Vasištević2, M. Dorobantu3, D. Tnincić4, B. Knežević5, D. Milicić5, O. Mantrini1, L. Badimoni, R. Bugiardini1, 1University of Bologna, Experimental, Diagnostic and Specialty Medicine - DIME - University of Bologna, Bologna, Italy; 2Clinical center of Serbia, Belgrade, Serbia; 3University of Bucharest Carol Davila, Bucharest, Romania; 4Clinical Center Banja Luka, Banja Luka, Bosnia and Herzegovina; 5Clinical Center for cardiology, Podgorica, Montenegro; 6University of Zagreb School of Medicine, Zagreb, Croatia; 2 Cardiovascular Research Center (CSIC-ICCC), Barcelona, Spain

Background: Limited data are available in octogenarian patients, and most of these studies excluded older patients with significant co-morbid conditions. This is an observational study of octogenarians admitted for acute coronary syndrome (ACS).

Abstract 5818 – Table 1. Independent predictors of age <45 years

<table>
<thead>
<tr>
<th>Smoking</th>
<th>Pos. family history for CAD</th>
<th>BMI ≥30 kg/m²</th>
<th>Male Gender</th>
<th>Total cholesterol ≥240 mg/dl</th>
<th>No risk factor for CAD</th>
<th>Diabetes mellitus</th>
<th>Art. hypertension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds ratio (95% CI)</td>
<td>6.0 (4.3–8.4)</td>
<td>2.6 (2.0–3.3)</td>
<td>1.6 (1.3–2.1)</td>
<td>1.3 (1.03–1.5)</td>
<td>1.1 (0.7–1.6)</td>
<td>1.3 (0.7–2.5)</td>
<td>0.6 (0.4–0.9)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>0.03</td>
<td>0.8</td>
<td>0.8</td>
<td>0.01</td>
</tr>
</tbody>
</table>
Purpose: We sought to investigate clinical characteristics, treatment and outcome of octogenarian patients during hospital stay for ACS in transitional country.
Methods: Data were collected in the ISACS-TC registry (ClinicalTrials.gov, NCT01218776) from October 2010 to February 2015: there were 992 patients ≥80 years old, consecutive admitted with a diagnosis of ACS at 56 hospitals in 11 Eastern European countries. Patients who had undergone fibrinolysis and coronary artery bypass grafting (CABG), were also excluded. In-hospital mortality was the primary end-point.
Results: Octogenarian patients represent 7.5% of ISACS-CT population. Among these, 56.7% were admitted with a diagnosis of ST-segment elevation myocardial infarction (STEMI). The mean age of the study population was 83.5±3.5 years and 51.6% of the patients were women. Female, less frequently than male, had history of myocardial infarction, peripheral arterial disease (PAD), prior CABG and chronic kidney disease. They were less likely to have smoking and former smoking status. There was no difference in the rates of death between male (18.5%) and female (19.2%) patients. Octogenarian patients undergoing invasive coronary procedures had significantly lower rate of death (12.5% vs 22.2 %, p<0.001). In multivariable regression analysis, cardiovascular death in the octogenarians was associated (p<0.05) with age ≥85 years (odds ratio [OR] 1.82), prior PAD (OR: 4.92) and Killip class ≥2 (OR 4.41). Invasive coronary procedures was an independent significant protective factor on hospital mortality (OR 0.43).
Conclusions: After ACS patients have a high mortality rate which can be reduced by invasive coronary procedures. Age is relevant in the prognosis of ACS, but its importance should be considered other to secondary clinical factors.

5820 | BEDSIDE
Impact in the prognosis of the utilization of thrombectomy devices in primary angioplasty in patients with ST-elevation acute myocardial infarction
B. Picarra1, A. R. Santos1, A. F. Damasio1, D. Neves1, J. Carvalho1, J. Aguiar2 on behalf of dos Investigadores do RNCSA, Sociedade Portuguesa de Cardiologia, Lisboa, Portugal. 1Hospital do Espírito Santo, Évora, Portugal
Introduction: Thrombus embolization and no-reflow phenomena continue to be one of the factors that influence the success of primary angioplasty in the treat-
mament of ST-elevation acute myocardial infarction (STEMI).
Purpose: To evaluate the impact on morbidity, in-hospital mortality and mortality at one year of patients (P) with STEMI that underwent thrombus aspiration (TA) in the moment of primary angioplasty (PPCI).
Methods: We studied 3209 P with STEMI included in a mul-
ticenter national register. We consider two groups, P submitted to TA and P not submitted to TA. We registered age, sex, co-morbidities, clinical and electrocar-
diographic presentation, in-hospital therapy, coronary angiography results and ejection fraction (EF). We defined the following in-hospital complications: heart failure (HF), cardiogenic shock (CS), re-infarction, mechanical complications, sus-
tained ventricular tachycardia (VT), high grade atrioventricular block (AV block) and major bleeding. We compare in-hospital mortality and mortality at 1 year follow-up. We performed multivariate analysis to assess the impact of the use TA in-hospital mortality and in the development of HF.
Results: Thrombus aspiration was utilized in 39.4% of P with STEMI undergoing TA (1265P). These P were younger (61±14 vs. 64±13 years, p<0.001), had lower prevalence of hypertension (57.5% vs 62.5%; p=0.005), Diabetes (2.4% vs 1.6% p=0.001), obesity (16.2% vs 9.7%, p<0.001) and prior CABG (1.0% vs 2.2%, p<0.016). There were no differences in Killip-Kimball class or electrocar-
diographic at STEMI presentation. There were no differences in the number and type of vessels with lesions, however the number of total occlusions of the left anterior descending artery (LAD) and right coronary artery (RCD) was higher in P undergoing TA (LAD: 41.8% vs 35.6%, p<0.001 and RCD: 39.8% vs 34.0%, p=0.001). Patients submitted to TA had more HF (20.8 vs 17.2%, p=0.01), CS (7.8% vs 5.6%, p=0.013), worse EF (48±11 vs 53±13%; p=0.001), TV (4.8% vs 1.7%, p<0.001), AV block (8.3% vs 4.9%, p<0.001), greater need for invasive me-
chanical ventilation (4.9 vs 3.4%, p=0.04) and intra-aortic balloon (2.7 vs 1.3%, p=0.004). There were no differences in in-hospital mortality or mortality at 1 year. By multivariate analysis, TA per se is not a predictor of mortality or HF.
Conclusions: In our population, the use of thrombectomy devices seems to be conditioned by the presence of total occlusions of coronary arteries and is associ-
ated with an increase of CS, arrhythmias, but not with increased in-hospital mortality or mortality at 1 year.

5046 | BENCH
Insulin receptor substrate 2 (IRS2) overexpression in vascular smooth muscle cells (VSMC) blunts neointima formation in mice
A. Markl1, N. Blank2, K. Krysztofak2, E. Berghausen2, M. Vantler2, S. Rosenkranz2. 1Innsbruck Medical Clinical, Innsbruck, Germany; 2Center for Molecular Medicine, Cologne, Germany; 3Cologne University Hospital - Heart Center, Cardiology, Cologne, Germany
Objective: Insulin resistance (IR) is a major risk factor of neointima formation after percutaneous coronary interventions (PCI), which is mainly due to PDGF-
BB related VSMC proliferation and migration. During IR, insulin signal relay by IRS proteins is diminished.
Purpose: To elucidate the impact of IRSS signalling in VSMC on neointima for-
mation.
Methods: Mice overexpressing IRS2 in VSMC were generated and screened for body weight, morphology of inner organs, and insulin and glucose tolerance. Male mice 3–5 months of age were subjected to wire injury of the common carotid artery (ACC), and intima/media ratio was assessed after 4 weeks. VSMC were isolated from aortas: PDGF-BB induced migration was quantified in modi-
ﬁed Boyden chambers, and glucose induced apoptosis by MTT and TUNEL as-
says. PDGF-BB induced proliferation was measured by colorimetric BrdU and membrane-staining based FACS assays. Abundance of proteins was assessed by Western Blotting and, for GLUT4, additionally by immunocytofluorescence. βPDGFR/PI3K interaction was assessed by co-immunoprecipitation of the acti-
vated βPDGFR and the PI3K subunit p110α.
Results: IRS2OE mice were undistinguishable from controls in terms of body weight, insulin and glucose tolerance, and inner organ morphology - except for the heart, which was larger (left ventricular weight/tibia length: 7.8±0.45 vs 5.5±0.50g/mm, p<0.012, all data expressed as mean ± SEM). No alteration of native ACC’s of IRS2OE mice was detected. The intima/media ratio was lower in IRS2OE versus control mice 4 weeks after wire injury (0.11±0.036 vs 1.1±0.76, p=0.039). Isolated IRS2OE VSMC migrated faster in a PDGF-BB gra-
dient (86.6±8.5 vs 17.5±1.5 cells per field, p<0.001), and showed higher sus-
cceptibility to glucose induced apoptosis (survival in MTT test: 26.9±0.031% vs 50.9±0.024%, p<0.001, TUNEL positive: 96±24% vs 0, p<0.001). There was an increased abundance of anti-angiogenic BCL proteins, MrSOD, Bcl2, Bcl-xL. IRS2OE VSMC proliferated less to PDGF-BB in vitro (Brdu (3.6±0.11 fold vs 4.7±0.39 fold increase compared to unstimulated cells, p<0.040) and FACS (2 vs 5 divisions, n=3). There was less p110α bound to the βPDGFR after PDGF stimulation.
Conclusions: IRS-2 overexpression in VSMC blunts neointima formation in vivo. It increases the rates of glucose induced apoptosis and reduces PDGF-BB in-
duced proliferation by disturbing βPDGFR/PI3K interaction, while it augments PDGF-BB related VSMC migration. During IR, these effects should be mitigated, resulting in increased neointima formation after PCI.

5847 | BENCH
Hnrnap1 is a critical regulator in vascular smooth muscle cell functions and neointima hyperplasia
Q. Chen1, Q. Wen2, Y. Huang3, L. Luong2, J. Zhu4, L. Zhang1, Q. Xiao2. 1First affiliated Hospital at Zhejiang University School of Medicine, Cardiology, Hangzhou, China; People’s Republic of; Queen Mary, University of London, Clinical Pharmacology, London, United Kingdom
Background: RNA binding protein heterogeneous nuclear ribonucleoprotein A1 (Hnrnap1) plays various roles in transcriptional and posttranscriptional modula-
tion of gene expression. Our previous study has demonstrated for the first time that hnrnap1 plays an important role in vascular smooth muscle cell (VSMC) differentation from stem cells in vitro and in vivo. However, little is known about in vivo functional involvements of hnrnap1 in VSMC functions and neointima hyper-
plasia.
Purpose: In this study, we aimed to investigate the functional roles of hnrnap1 in the contexts of VSMC functions, injury-induced vessel remodelling, and human atherosclerotic lesions.
Methods and results: Studies used mouse aorta VSMCs showed that hnr-
nap1 expression levels were consistently modulated during VSMC phenotypic switching. Moreover, VSMCs with hnrnap1 knockdown had an increased migra-
tory and proliferative ability but a reduced VSMC-specific gene expression level. Consistently, over-expression of hnrnap1 significantly reduced VSMC migration and proliferation. Furthermore, our data shows that hnrnap1 exerts its effects on VSMC functions through modulating IQ motif containing GTPase activating protein 1 (Iqgap1) gene, a well-known important regulator of VSMC migration and proliferation. Mechanistically, hnrnap1 up-regulates miR-124-124 through regulating microRNA-124 biogenesis. Compelling evidence also suggests that Iqgap1 is the authentic target gene of microRNA-124. Importantly, the expres-
sion of hnrnap1 in VSMCs was significantly downregulated in atherosclerotic lesions formation induced by wire injury, suggesting a role for hnrnap1 in vessel injury-induced neointimal development and progression. In accordance, perivas-
cular ectopic overexpression of hnrnap1 greatly reduced VSMC proliferation, and inhibited neointima formation in wire-injured carotid arteries. Translational and consistently, lower expression levels of hnrnap1 and microRNA-124, while higher expression levels of Iqgap1, were observed in human atherosclerotic les-
sions.
Conclusions: We have identified hnrnap1 as a critical regulator in VSMC func-
tions and neointima hyperplasia. Our data provide new insight into the roles of hnrnap1-microRNA-124-Iqgap1 regulatory axis in VSMC functions and the pathogenesis of neointima formation and/or angiographic restenosis, and aid the development of novel therapeutic agents for the prevention of these diseases.
5848 | BENCH
Selective inhibition of the histone lysine methyltransferase G9a preserves differentiation and inhibits calcification in vascular smooth muscle cells
F. Kahles1, J. Marx2, A. Makowska1, M. Lehre1, N. Marx2, H. M. Findeisen3.
1 RWTH University Hospital Aachen, Internal Medicine I, Cardiology, Pulmonology & Vascular Medicine, Medizinische Fakultät, RWTH Aachen University, Germany; 2 University Hospital, Department of Cardiology and Angiology, Münster, Germany.

Introduction: Activation and de- or transdifferentiation of smooth muscle cells (SMCs) at sites of vascular injury is regulated by epigenetic mechanisms. Epigenic histone methylation has been recognized as a dynamic mark controlling many biological processes in health and disease. Here we have identified a histone methyltransferase inhibitor as a selective modulator of SMC differentiation.

Methods and results: We studied the effects of the several epigenetic modifiers on smooth muscle cell proliferation, inflammation and TNF-α-mediated dedifferentiation. UNC0638 is a selective inhibitor of the G9a histone methyltransferase controlling histone h3 lysine 9 dimethylation was found to selectively modulate SMC differentiation. UNC0638 had no effect on TNF-α-induced MCP-1 expression or PDGF-induced SMC proliferation as detected by cell counting and BrdU incorporation. However, UNC0638 treatment significantly attenuated TNF-α-induced down regulation of the SMC marker gene SM22α, suggesting that UNC0638 reduces SMC dedifferentiation. This effect was detectable up to 72h after the initial treatment and associated with a strong and equally sustained reduction of the repressive histone mark controlling histone h3 lysine 9 dimethylation was found to selectively modulate SMC differentiation. UNC0638 had no effect on TNF-α-induced MCP-1 expression or PDGF-induced SMC proliferation as detected by cell counting and BrdU incorporation. However, UNC0638 treatment significantly attenuated TNF-α-induced down regulation of the SMC marker gene SM22α, suggesting that UNC0638 reduces SMC dedifferentiation.

Conclusion: In summary, our data suggest pharmacologic modulation of histone methylation as a promising approach to target SMC phenotypes and differentiate status in vascular diseases like in-stent restenosis or atherosclerosis and warrant further research to dissect histone methylation dependent mechanisms in SMCs and to investigate in vivo applications of small molecule inhibitors.

IMPROVING CARDIOPULMONARY RESUSCITATION
5848 | BEDSIDE
FirstAED emergency dispatch, global positioning of first responders with distinct roles - a solution to reduce response times and ensuring early defibrillation on a bridge connected island area
F.L. Henriksen1, H. Schakow1, M.L. Larsen2. 1 Odense University Hospital, Cardiology, Odense, Denmark; 2 Aalborg University Hospital, Cardiology, Aalborg, Denmark.

Background: The national survival rate for out-of-hospital cardiac arrest is approximately 11%. Guidelines recommend cardiopulmonary resuscitation (CPR) within 5–6 minutes and early defibrillation with an automated external defibrillator (AED) with the purpose to increase survival rates. Shortening the ambulance response times ensures six minutes in the rural areas, is however unrealistic.

Purpose: FirstAED is an auxiliary to the public emergency services and enables the dispatcher to send an organized team of first responders to the scene. FirstAED organizes three first responders in a team: no. 1 reaches the patient to give CPR; no. 2 brings the AED; no. 3 is the on-site coordinator. The aim is to shorten the first responder response time at emergency calls and the time to the AED on-site to below 5–6 minutes in both public/residential/rural settings in a bridge connected island area.

Methods: CPR and first aid is provided by 175 trained lay first responders who can accept or reject the alarm. FirstAED chooses the three most optimally placed first responders who accepted the alarm.

Results: During the first 24 months the FirstAED GPS system was used 718 times. FirstAED entailed a security for first responder CPR and a significant reduction in median response time from more than 8 minutes before to 4 minutes 9 seconds after. The response time was faster than the comparable median response time in 13 patients and 20 minutes less than two kilometres apart. FirstAED global positioning system (GPS)-tracked the nearby first responders to arrive within 5–6 minutes and early defibrillation on a bridge connected island area.

Conclusion: In summary, our data suggest pharmacologic modulation of histone methylation as a promising approach to target SMC phenotypes and differentiate status in vascular diseases like in-stent restenosis or atherosclerosis and warrant further research to dissect histone methylation dependent mechanisms in SMCs and to investigate in vivo applications of small molecule inhibitors.

5885 | BEDSIDE
Clinical comparison of off-hours versus regular hours extracorporeal cardiopulmonary resuscitation for cardiac arrest
T. Kawashima1, H. Uehara1, S. Chiba1, K. Yamashita1, C. Nagi2, K. Nakamura1, N. Miyagi3, M. Shimajiri1, T. Kuniyoshi1, M. Isobe3. 1 Urasoe General Hospital, Cardiology, Urasoe, Japan; 2 Tokyo Medical and Dental University, Cardiology, Tokyo, Japan.

Background: There is a potential delay to perform extracorporeal cardiopulmonary resuscitation (ECPR) during after-hours because of cath lab activation and off-shift. We aimed to evaluate the relationship between ECPR timing and mortality in patients with cardiac arrest.

Methods: We studied 130 consecutive patients (mean age=62.1±15.2 years, 83.1% Male) who underwent venoarterial extracorporeal membrane oxygenation (VA-ECMO) due to refractory circulatory collapse between January 2008 and February 2015 in our hospital. The primary endpoints were in-hospital death and neurological impairment.

Results: A total of 62 patients (47.7%) were treated during off-hours (Monday-Friday, 6:30 pm-8:30 am and weekends) and 68 patients (52.3%) during regular hours. Acute myocardial infarction was the most common cause of cardiac arrest (63.2%) during off-hours vs 55.9% during regular hours, P=0.20). The frequency of bystander cardiopulmonary resuscitation was 72.1% during off-hours and 76.4% during regular hours (P=0.57). Time of day was not related to pre-hospital delay (28.3±3.1 minutes during off-hours vs 25.9±3.0 minutes during regular hours, P=0.53). There was a statistically significant delay for the interval between patient’s arrival at the hospital to initiation of VA-ECMO (door-to-ECMO) between the off-hours group and the regular hours group (48.2±4.2 minutes vs 27.2±4.2 minutes, P=0.001). In-hospital mortality was 77.4% and 67.7% in the off-hours and regular hours groups, respectively (P=0.21). Neurological impairment was observed in 78.1% of the off-hours group and 77.3% of the regular hours group (P=0.80).

Conclusion: There is time delay in door-to-ECMO during off-hours, but off-hours ECPR still provides similar survival as patients who present during regular hours.

5886 | BEDSIDE
Predictive value of neuron-specific enolase for clinical outcome in cardiac arrest survivors depends on the time of sample collection: results of a prospective study
D. Vondrakova1, P. Ostadal1, A. Kruger1, M. Janotka1, P. Neuzil1. Heart Center, Na Homolce Hospital, Prague, Czech Republic.

Background: Despite marked advances in intensive cardiology care, current options for outcome prediction in cardiac arrest survivors remain significantly limited.

Purpose: The aim of our study was, therefore, to compare the day-specific predictive values of neuron-specific enolase (NSE) in cardiac arrest survivors treated with endovascular hypothermia.

Methods: Eligible patients were out-of-hospital cardiac arrest survivors alive for more than 24 hours from hospital admission. All were treated with endovascular hypothermia (33°C for 24 hours). NSE was measured using immunoturbidimetric assay and samples were collected at day 1, 2, 3, and 4, respectively, after hospital admission. Clinical outcomes were evaluated at 30 days according to the Cerebral Performance Category.

Results: One-hundred-and-thirty-two cardiac arrest survivors (mean age 64.3 years) were included into the study. Using ROC analysis, optimal cut-off values of NSE for prediction of CPC 1–2 at respective days were determined as: Day 1: <22.3 mcg/l (sensitivity 65.2; specificity 58.3; P≤0.0001), Day 2: ≤27.3 mcg/l (sensitivity 81.3; specificity 72.4; P≤0.0001), Day 3: ≤32.9 mcg/l (sensitivity 96.6; specificity 74.1; P≤0.0001), and Day 4: <25.4 mcg/l (sensitivity 92.5; specificity 86.9; P≤0.0001). Values >57.2 mcg/l measured at any time predicted poor outcome (CPC 3–5) with 100% specificity.

Conclusion: Our results indicate that NSE estimation might be useful for neurologic outcome prediction in cardiac arrest survivors treated with endovascular hypothermia. The highest predictive values of NSE measurement were observed at Day 3 and Day 4 after cardiac arrest.
In conclusion, conventional CMR and EMB are of additive diagnostic value in patients with clinically suspected acute myocarditis. T2 mapping increases diagnostic accuracy in CMR-based diagnosis of acute myocarditis.

5900 | BEDSIDE
Long-term arrhythmic prognosis in patients with biopsy-proven myocarditis, studied by cardiac magnetic resonance imaging and electroanatomical mapping

Background: Data on long-term follow-up (FU) in patients (pts) with biopsy-proven myocarditis are conflicting, particularly those regarding ventricular events.

Purpose: To determine the prognostic variables for ventricular arrhythmias (VA) in pts with biopsy-proven myocarditis.

Methods: We prospectively studied consecutive pts with endomyocardial biopsy (EMB)-proven myocarditis (M1 Group). Control group was represented by pts presenting with suspected myocarditis, without EBM evidence of myocarditis (M0 Group). All pts underwent cardiac magnetic resonance imaging (MRI), coronary angiography, electrophysiological study (EPS) and electroanatomical mapping (EAM).

Table 1. Right ventricle EAM

<table>
<thead>
<tr>
<th>Group</th>
<th>M1 (n=49)</th>
<th>Group M0 (n=10)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bipolar low voltage (&lt;1.5 mV) area (%)</td>
<td>10.0±10.4</td>
<td>2.4±3.2</td>
<td>0.04</td>
</tr>
<tr>
<td>Bipolar scar (&lt;5.0 mV) area (%)</td>
<td>3.9±4.9</td>
<td>0.2±0.06</td>
<td>0.006</td>
</tr>
<tr>
<td>Unipolar low voltage (&lt;5.0 mV) area (%)</td>
<td>21.1±20.1</td>
<td>6.7±10.7</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Data are expressed as mean ± standard deviation.

Conclusions: A higher degree of RV unipolar and bipolar mapping alterations was observed in pts with biopsy-proven myocarditis, confirming that substrate remodeling at EAM reflects histological abnormalities seen at EMB. VT induction at EAM was the only independent predictor of VA in pts with biopsy-proven myocarditis.
tion of Ad-AMPKα2 in HSF1 KO mice effectively improved cardiac angiogenesis, reduced cell apoptosis and alleviated myocardial remodeling in response to TAC.

**Conclusions:** Our findings indicate that miR-195 is critically involved in cardiac remodeling via impairment of HIF-1α-dependent angiogenesis. Induction of HSF1 might be a novel and effective target for therapeutic approaches to prevent preload-induced heart failure through regulating the miR-195/AMPKα2 pathway.

5904 | BENCH

Transcoronary gradient of circulating microRNAs in heart failure

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**Background:** Circulating levels of microRNA (miRs) are emergent promising biomarkers for cardiovascular disease. In particular, altered expression of miRs has been related to heart failure and cardiac remodeling.

**Purpose:** To identify the heart as a potential source for miRs released into the circulation, we measured the concentration gradients across the coronary circulation for the miR-34a (whose levels have been associated to LV-remodeling and prognosis), miR-126 (whose decrease has been associated to an impaired cardiac repair capacity); the miR-21*, that was recently shown to be actively involved in regulating AMPK

**Methods:** Circulating miRs were measured by TaqMan polymerase chain reaction (PCR) from EDTA plasma obtained from patients with normal systolic function (n=57), ischemic heart disease (n=25) and heart failure (n=25).

**Results:** Circulating levels of the miR-34a (2.3-fold increase), the miR-423 (4.4-fold decrease), the miR-21* (1.6-fold decrease), and the miR-126 (1.3-fold decrease) were differently modulated in nonICM-HF compared to ICM-HF patients. Interestingly, there was a positive transcoronary concentration gradient for the miR-34a in the nonICM-HF group (p<0.05) as well as of the miR-423 in the ICM-HF group (p<0.001), suggesting a release of a specific microRNA into the coronary circulation of HF patients with different etiology.

**Conclusions:** Circulating levels of miRs are differentially expressed in circulating blood from patients with HF of different etiologies. Interestingly, the miR-34a is expressed from the heart into the coronary circulation in patients with non ischemic HF as its levels in the CVS are higher than in the Ao. Similarly, the miR-423 is released from the heart into the coronary circulation in patients with ischemic HF. The differential regulation of circulating miRs during the transcoronary passage in HF might provide important information to better understand their role in HF and foster their use as cardiac biomarkers, especially to differentiate between HF of different etiologies.

5905 | BEDSIDE

MiR-21 and miR-133 levels in peripheral blood mononuclear cells in patients with heart failure with preserved ejection fraction

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**Purpose:** MicroRNAs (miRs) are essential regulators of gene expression implicated in cardiovascular function and disease. MiR-21 and miR-133 have been shown to play a role in heart hypertrophy and fibrosis. They have also been shown to regulate proliferation and phenotypic switch of vascular smooth muscle cells. However, there are limited data regarding their role in left ventricular (LV) diastolic dysfunction. The aim of this study is to investigate miR-21 and miR-133 levels in peripheral blood mononuclear cells in patients with heart failure with preserved ejection fraction (HFPEF).

**Methods:** We included 39 patients with symptoms and signs of heart failure who had an LVEF > 50% and evidence of LV diastolic dysfunction (19 males, aged 68±10 years). Blood samples were also obtained from 29 healthy volunteers for comparison (17 males, aged 52±8 years). All subjects underwent a complete echocardiographic examination.

**Results:** MicroRNA (miR) levels were measured by quantitative real time reverse transcription PCR. Results: MiR-21 levels were found to be higher (4.6±0.45 versus 2.05±0.31, p<0.05), while miR-133 levels were found to be lower (11.5±6.9 versus 2.05±0.31, p<0.05) in patients with HFPEF compared to healthy controls. MiR-21 levels showed strong negative correlations with E/E' ratio (r=−0.42, p<0.001) while miR-133 levels showed strong positive correlations with E/E' ratio (r=0.41, p<0.001).

**Conclusions:** MiR-21 and miR-133 levels in PBMCs differentiate in patients with HFPEF compared to normal individuals. In addition, they show a strong relationship with LV diastolic dysfunction in those patients. Our findings contribute to the understanding of pathogenesis of HFPEF and might offer a future therapeutic target.

5914 | BEDSIDE

Feasibility, safety, and acute hemodynamic effect of a new approach for anti-bradycardia pacing: left ventricular septum pacing by transvenous approach through the inter-ventricular septum

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**Introduction:** Conventional right ventricular apex (RVA) pacing causes left ventricular (LV) dysynchrony which can lead to LV dysfunction. Previous animal studies have shown that LV dysynchrony (LVdYS) induces results in less ventricular dysynchrony than RVA pacing and maintains LV pump function. We investigated the feasibility, safety, lead stability, and hemodynamic effects of LVS pacing in patients.

**Methods:** Ten patients (5 men; age 72±10 years; LV ejection fraction 57±8%) with sinus node dysfunction scheduled for dual chamber pacemaker implantation were selected. Right ventricular (RV) angiography and intra-cardiac echocardiography (ICE) were performed to visualize the inter-ventricular septum. A custom pacing lead (Medtronic 09066) with extended helix (4 mm) was introduced via the subclavian vein, and after positioning against the RV septum (RVS) using a preshaped guiding catheter guided by fluoroscopy and ICE, driven through the inter-ventricular septum to the LVS. The acute hemodynamic effects of RVS, RVA and LVS pacing were evaluated by invasive LVPdmax measurements.

**Results:** The lead was successfully delivered to the LVS in all patients in a single attempt without complications. Lead implant procedure time shortened with experience (90 min at first to 12 min at last procedure). This also applied to total fluoroscopy time (44 min at first to 10 min at last procedure). In the last 2 patients, lead implantation without guidance by ICE was performed without guidance by ICE: QRS duration was shorter during LVS pacing (147±21 ms) than during RVA pacing (172±33 ms, p=0.02 compared to LVS pacing) and RVS pacing (165±17 ms, p=0.04 compared to LVS pacing). RVA and RVS pacing reduced LVPdmax compared to baseline atrial pacing (7.1±4.11% and −8.7±2.1% respectively), whereas LVS pacing maintained LVPdmax at baseline level (+0.63±4.45%, p=0.01 compared to RVA and RVS pacing). R-wave amplitude and pacing threshold were 13.3±7.7 mV and 0.5±0.3 V at implant and remained stable during follow-up (mean 4.8±1.5 months; minimum 3 maximum 6), without lead related complications.

**Conclusion:** LV septum pacing by transvenous approach through the inter-ventricular septum is a new, feasible, safe, and hemodynamically preferable approach for anti-bradycardia pacing therapy.

5915 | BEDSIDE

Exercise detection with 3-Axis accelerometer of a total intracardiac leadless pacemaker

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**Background:** Conventional pacemaker systems use accelerometers or other extrasystolic sensors to adapt stimulated heart rate to actual patient activity. The Medtronic Trans-Catheter Pacemaker (TCP) is implanted in the right ventricle and incorporates a 3-axis accelerometer to detect patient (pt) activity. The TCP incorporates filtering to accentuate physical motion over cardiac motion.

**Purpose:** To describe the performance and stability of the activity detection during exercise and different body positions.

**Methods:** Pts underwent postural and hallwalk testing at pre-discharge, 1 month, 3 month and 6 month. The activity units were measured in each accelerometer vector during different postures and activity (Figure). An excellent vector was defined as having activity units at least >10 above the highest resting posture, >5 units was considered adequate.

**Results:** Overall 40 pts (76±7 yrs, 10 female, 30 atrial fibrillation) were implanted with the TCP. At least one vector testing was available in 39 pts; repeated testing was available in 27 pts. Although activity detection occurred at rest (due to cardiac motion) and position differences were observed in 23 pts, 38 of 39 had either one excellent (20 pts) or adequate (18 pts) vector. In repeat testing, if an
excellent vector was programmed initially. This vector remained excellent (15/15).

In pts programmed to an adequate vector at baseline, 10/12 patients were still adequate and 2 were programmed to a different vector.

Conclusions: Although posture-dependent activity differences were observed, detection of physical exercise and appropriate rate response with intracardiac accelerometer in a TCP was demonstrated. A simple exercise test allows selection of the accelerometer vector with the greatest activity to rest ratio.

Acknowledgement/Funding: Medtronic Inc

5916 | BEDSIDE
Right ventricular lead placement in a pacemaker population: comparison of apical and septal positions. The right pace study
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Introduction: Chronic right ventricular (RV) apical pacing induces mechanical left ventricular (LV) dyssynchrony and may cause heart failure at long-term follow-up. Septal RV site could induce less variation in the temporal pattern of LV mechanical activation.

Methods: The RIGHT PACE study is a trial comparing pacing from RV apex and septal area. Patients with indications for cardiac pacing and no indications for implantable-defibrillator and/or resynchronization were enrolled in 14 centers. The primary objective was to acutely evaluate the pacing-induced LV dyssynchrony, calculated as the delay between septum and lateral wall contraction (SLD), as recorded with tissue-Deppler echocardiography.

Results: 437 patients were enrolled. 274 patients received an RV lead in the apex and 183 in the septal area (high-septum 21, mid-septum 111, low-septum 31). The two groups were similar in terms of ejection fraction (57±9% versus 58±9%), prevalence of coronary artery disease (24% versus 29%), QRS duration (98±25 ms versus 92±24 ms, all p<0.05). During spontaneous LV activation, SLD was comparable between groups (48±27 ms versus 52±28 ms) and the proportions of patients with spontaneous LV dyssynchrony (i.e. SLD>41 ms) were 25% and 28%, respectively (all p>0.05). During RV pacing, SLD increased to 54±27 ms in Apex group and 57±25 ms in Septal group (p=0.281). The proportions of patients with pacing-induced LV dyssynchrony were 48% and 51% (p=0.579). Nonetheless, the QRS increased to 145±30 ms versus 141±31 ms in Apex and Septal groups, respectively (p=0.285). After X-rays central adjudication, the apical positioning was not confirmed in 56 (20%) patients of the Apex group. Similarly, in 21 (16%) patients of the Septal group the adjudicated pacing site was the apex. According to on-treatment analysis, the proportion of patients with pacing-induced LV dyssynchrony was 47% with apical and 52% (p=0.331) with septal pacing. The QRS increased to 146±31 ms versus 139±29 ms in Apex and Septal groups, respectively (p=0.041).

Conclusions: Although pacing at the RV septal area resulted in shorter QRS duration than the RV apex, it did not reduce the pacing-induced LV dyssynchrony.

5917 | BEDSIDE
Minimized ventricular pacing delays first onset of AF in pacemaker patients without AF history
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Introduction: Atrial fibrillation (AF) is a frequent comorbidity in the pacemaker (PM) population and has been associated with high risk of heart failure, stroke and death. ANSWER is a randomized (1:1), multicenter trial comparing the SafeR mode, designed to reduce unnecessary right ventricular pacing (Vp), with standard DDD in patients (pts) with sinus node disease (SN), or AV block (AVB), with or without atrial arrhythmia (AA). The aim of this post-hoc analysis was to (1) compare the in-hospital outcomes of pts with SafeR and DDD, (2) evaluate the incidence of first onset of AF according to the pacing mode, within 3 years after implantation in patients without AA history.

Methods: First onset of AF was ascertained from the PMs memories. Onset of AF according to the pacing mode was evaluated using Kaplan-Meier statistics. Predictors of AF were identified using a Cox model in pts without previous AA history among 13 parameters (age, indication, gender, NYHA class, LVEF, coronary disease, cardiomyopathy, valvular disease, HF history, diabetes, arterial hypertension and pacing mode).

Results: Out of the 650 pts enrolled in the ANSWER study, 380 pts (58.6%) were without history of AF at baseline (71.4±11.8 years, 61.5% males, 41% SN and 59% AVB). Among them, 369 pts were randomized (184 in SafeR and 185 in DDD). A 23% risk reduction in AF onset was associated with SafeR (HR:0.786, 95% [0.587, 0.999], adjusted p value=0.049) (Figure). Old age (p=0.035) and SND (p=0.004) were identified as predictors of AF onset.

Conclusion: In ANSWER patients without history of AA, younger age and primary indication of AVB were independently associated with a reduced risk of first onset of AF. In addition, SafeR mode proved to be superior to standard DDD pacing to prevent the first onset of AF.

5918 | BEDSIDE
Are DDD/AAI mode switch algorithms worthwhile to prevent unnecessary right ventricular pacing in sick sinus rhythm patients? Results from a randomized cross-over study
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Background: Two algorithms designed to prevent unnecessary right ventricular pacing (RVP) were tested in the “Ventricular Pace Suppression (VPS) Versus Intrinsic Rhythm Support (IRS)” enrollment patients with sick sinus syndrome (SSS) and investigating their effect on RVP percentage, arrhythmic burden and left ventricle (LV)/atrium size. The VPS algorithm automatically switches from a dual-chamber mode to a single-chamber atrial mode or vice versa, when stable atrio-ventricular (AV) conduction is detected (6 out 8 beats) or is no longer confirmed. The IRSplus algorithm simply prolongs the pacemaker AV interval up to 400ms at the first ventricular sensed event, spontaneously occurred or detected during periodic searches.

Methods: SSS patients with indication to cardiac pacing without evidence of III degree AVB and at least 1.1 randomized after pacemaker implant either to IRSplus or VPS algorithms crossing-over after 6 months. The study was designed with a 90% power to detect a least difference in RVP percentage of 3%. Data were collected at 6 and 12 months. Non-normal distributions were generally obtained and described with median (interquartile range). Wilcoxon signed-rank test was used for intra-individual comparisons.

Results: A total of 230 patients (62% males, age 75 (69–79) years) were enrolled: ejection fraction, 57 (50–60); NYHA class I 57%, II 40%; CHA2DS2VASc score, 2 (1–2). IRSplus and VPS were respectively associated to a RVP percentage of 1 (0–11)% and 3.5 (0–27)% (p=0.001) with non-significantly different atrial pacing percentages of 58 (27–82) and 54 (34–78). At the end of respective 6-month periods, variation rate of LV end-diastolic (−22% vs. −18%, p=0.4), atrium end-systolic (25% vs. 20%, p=0.1), atrium end-diastolic (4% vs. 2%, p=0.4) and atrium end-systolic (4% vs. 0%, p=0.9) volumes were not significantly different between IRSplus and VPS. No difference in AF burden was observed. In the subgroup of patients with baseline atrial AV interval >270ms, RVP percentage was lower during the IRSplus period (3 (0–20)) than during VPS (23 (1–63), p=0.01).

Conclusions: Our data showed that automatically prolonging the pacemaker AV delay to 400ms (as with the IRSplus), is at least as effective as DDD/AAI switch algorithms in preventing unnecessary RVP, with no relevant effects on arrhythmic burden and cardiac volumes. IRSplus was even superior in patients with prolonged intrinsic AV conduction, likely including undocumented paroxysmal AV blocks.

Acknowledgement/Funding: BIOTRONIK SE & CO. Kg
5919 | BEDSIDE
Outcome of epicardial pacing in neonates with isolated congenital complete atroventricular block. A bicentric study
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Background: Isolated congenital atroventricular block (CABV) is a rare disorder, and the early treatment is the early implantation of pacemaker (PM). Few data are available, more specifically in neonates.

Purpose: The aim of our study is to assess the feasibility and the long term outcomes of epicardial pacing in this high risk population. We also sought to identify the predictive factors of development of dilated cardiomyopathy.

Methods: This is a bicentric retrospective study. Neonates with CABV diagnosed in utero or at birth, who underwent pacing during the first month of life were included. They were hospitalized at the Lille University Hospital and at “Necker Enfants Malades” hospital between 1993 and 2014.

Results: A total of 47 neonates were included. Median term at birth was 37 (35–38) weeks of amenorrhea. Median age and weight at implantation were 3 (2–7) days and 2550 (2030–3110) grams, respectively. Ventricular pacing was performed in the majority of patients (74%), most often by subxiphoid approach (60%) using left anatomical landmarks, more physiologic, was also implanted by subxiphoid approach in 65% of them. Follow up was 5 (2–10) years. Epicardial ventricular lead survival was 83% at 5 years, with low median ventricular threshold (0.96V [0.93–1]). 30% of patients had developed dilated cardiomyopathy (DCM) at different time during the follow up. 75% of early DCM were implanted by subxiphoid approach. There were no mortality due to PM implantation.

Conclusion: There is a clear improvement of prognosis CABV. Early epicardial PM implantation can be performed in the first days of life safely through minimally invasive subxiphoid approach. The epicardial PM should and could be left in place as long as possible. Some predictive factors of DCM have been identified and a larger cohort could be used to establish a risk score.

5920 | BEDSIDE
Pacemaker implantation using ultrasound guided axillary vein puncture compared to conventional techniques
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Introduction: Venous access during pacemaker implantation can be challenging and result in serious complications. Current approaches consist of subclavian vein puncture using left anatomical landmarks, more physiologic, or surgical cut down to the cephalic vein and fluoroscopy guided axillary vein puncture.

Purpose: This study compares a novel approach for axillary vein puncture using ultrasound guidance with standard techniques.

Methods: Group A consisted of 100 consecutive patients where a single operator (DR) used the subclavian anatomical landmark technique as the primary approach. The same operator subsequently switched to ultrasound guided axillary vein puncture as the primary approach in 248 consecutive patients (Group B). A vascular ultrasonic transducer was used to image the axillary vein and adjacent artery in cross section over the first rib. The axillary vein was punctured percutaneously with real time ultrasound visualisation. Group C comprised 228 consecutive patients where 2 operators used the cephalic technique as the primary approach. All 3 operators had 5–20 years experience in pacemaker implantation.

Results: The clinical characteristics and outcomes are shown in the table. The subclavian landmark technique and fluoroscopy guided axillary vein puncture were used as secondary approaches in 43.4% and 11.0% respectively by cephalic operators. In the single case where ultrasound guided puncture of the axillary vein was unsuccessful the cephalic vein was accessed percutaneously using ultrasound guidance. Pneumotheorax occurred in 8 patients, the subclavian anatomical landmark approach was used in 7 and the cephalic in 1.

<table>
<thead>
<tr>
<th>Group A (n=100)</th>
<th>Group B (n=248)</th>
<th>Group C (n=228)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age yrs</td>
<td>78±19</td>
<td>78±11</td>
</tr>
<tr>
<td>Male (%)</td>
<td>65</td>
<td>59</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26±4</td>
<td>25±6</td>
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<td>Dual chamber pacemaker (%)</td>
<td>46</td>
<td>66</td>
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<tr>
<td>Successful primary approach (%)</td>
<td>93.0</td>
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<tr>
<td>Pneumotheorax (%)</td>
<td>4.0</td>
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</tbody>
</table>

Conclusion: Ultrasound guided axillary vein puncture allows safe and swift venous access. It sets a new standard for improving the quality of care of patients undergoing implantation of cardiac rhythm devices.

5921 | BEDSIDE
Feasibility and safety of concurrent atroventricular junctional ablation in patients undergoing a transcatheter pacemaker implantation: a single-center experience
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Introduction: Atrioventricular junctional (AVJ) ablation is often required when pharmacotherapy fails to attain ventricular rate control during permanent atrial fibrillation (AF) and is accompanied by simultaneous pacemaker implantation as it leaves the patient pacemaker dependent. A newly developed miniaturized leadless permanent single chamber rate responsive pacemaker (MPP) can be implanted via catheter in the right ventricle with a novel fixation mechanism comprised of retractable tines, thus potentially eliminating many of the recognized acute risks of standard pacemaker implantation. We report the outcomes of the first patients in the FDA trial of this device who received concurrent AVJ ablation.

Methods: We retrospectively assessed patients who were enrolled in the study and underwent concurrent MPP implantation and AVJ ablation for management of rapid rates associated with AF. Patients and devices were followed per the trial protocol.

Results: Total six patients (median age 76.5 [range: 63–84], female 100%, mean BMI 25 [range: 19–39]) underwent MPP implantation and AVJ ablation via a specialized 23F introducer sheath and transfemoral delivery catheter and all were successful. The median times for MPP implantation, duration of fluoroscopy use, and duration of radiofrequency application were 30 mins [range: 21–74], 5.5 mins [range: 3–13], and 210 secs [range: 65–480], respectively. There were no in-hospital complications. There was no device dislodgement or malfunction during the 30-day follow-up. Pacing thresholds were within the trials prescribed range at implant and remained in range at 30-day follow-up. A total of 3 patients were rehospitalized within 30 days of the procedure, one of whom died due to breast carcinoma related pneumonia and sepsis unrelated to the device. Other 2 patients were hospitalized for diacritic heart failure which was present prior to implantation.

Conclusions: This first series of patients undergoing AVJ ablation with concurrent transcatheter pacemaker implant suggests reasonable safety and feasibility of this approach. There was no device dislodgement, malfunction or significant pacing threshold increase during the 30-day follow-up. Despite the novel device anatomy and mechanism, this combined approach can be considered for drug refractory AF with suboptimal rate control and may potentially provide a lower risk of in-hospital complications.

Acknowledgement/Funding: None

5922 | BEDSIDE
Cardiac implantable devices: an invaluable tool for the diagnosis of sleep apnea
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Introduction: The Sleep Apnea/Hypopnea Syndrome (SAHS) is characterized by the absence or reduction of ventilation during sleep and its diagnosis is based on polysomnography, which is seldom available. There is a high prevalence of SAHS in patients with cardiovascular disease, and it is a marker of cardiovascular risk in healthy individuals. Amongst patients with cardiac implantable electronic devices (CIED) the prevalence of SAHS can reach 60%. Our objective was to evaluate the presence of SAHS on patients with CIED and to evaluate the value of CIED on the screening of SAHS.

Methods: This prospective single-center study included 28 adult patients with CIED with rate responsive function. Sleep study was conducted on all patients and was compared to the data collected from the CIED on the following baseline. Baseline demographic, clinical and echocardiographic data was collected.

Results: Most patients were male (69%) with a mean age of 75.9 years. The prevalence of SAHS was 77% (14 patients with apnea-hypopnea index (AHI)>15; 9 with AHI<30) and 5 patients presented with Cheyne-Stokes respiration. No correlation was found between the data recorded by the AHI and the AHI evaluated on the sleep study (ρ(28)=0.548, p=0.004). The data collected by the CIED strongly correlated with the AHI evaluated on the sleep study (ρ(28)=0.704, p<0.01). For the diagnosis of severe SAHS (AHI>30), CIED showed a specificity of 64.7% and a sensitivity of 100% with a negative predictive value (NPV) of 100% and positive predictive value (PPV) of 60%. The diagnostic events were positively correlated with the AHI (ρ(28)=0.548, p=0.004).

Conclusion: SAHS is a highly prevalent disease in the population with CIED. The data obtained through the CIED monitoring data has a strong positive correlation with the AHI and its sensitivity, specificity, NPV and PPV make it a valuable tool for severe SAHS diagnosis and treatment monitoring.
**5923 | BEDSIDE**

**Persistence of left bundle branch block within percutaneous aortic valve implantation**

A.C. Geisler1, M. Seifert2, N. Gosa1, L. Conradi2, H. Treede1, S. Willems1, H. Reichenspurner2, B. Hoffmann1, S. Blankenberg2, U. Schaefer2

**Introduction:** Interventional transcatheater aortic valve implantation (TAVI) has been an established alternative to surgical aortic valve replacement for patients with severe aortic stenosis and a high perioperative risk. Aim of the study was to determine the persistence of new-onset LBBB in the context of percutaneous valve implantation.

**Methods and procedures:** The study included a total of 975 patients who underwent TAVI due to severe aortic stenosis between July 2008 and October 2013. 477 (48.9%) patients received an Edwards SAPIEN valve, USA, 76 pat. (7.8%) a Medtronic CoreValve USA, 92 pat. (9.4%) a JenaValve, Germany and 75 pat. (7.7%) a Symetis prosthesis, Switzerland. In 178 pat. (n=168;17.2%) a peri-interventional pacemaker implantation was performed.

**Results:** There were no significant differences in the patients baseline characteristics (median age: 80.9±7.6 years, male gender: n=80;44.9%, BMI: 26.7±4.9 kg/m²). The use of CoreValve bioprosthesis was associated with a significantly higher incidence of peri-interventional pacemaker implantation (p<0.001). The most frequent indication for a PPM implantation was the development of a third-degree atioventricular (AV) block (n=80;47.6%), followed by a LBBB (n=51;30.4%). During 12 months of follow-up (n=29), LBBB could no longer be detected in 12 of the PM-supplied patients (n=12;41.4%), during 36 months of follow-up (n=14) LBBB could not be detected anymore in 3 of the PM-supplied patients (n=3;21%). During 12 months of follow-up, LBBB was lost significantly more often in the Edwards SAPIEN valve group (n=12;40.6%) compared with the CoreValve group (n=0;0%).

**Table 1. Comparison between different bioprosthesis of patients who received a percutaneous pacemaker implantation following TAVI or no implantation**

<table>
<thead>
<tr>
<th>Prothesis</th>
<th>PPM implantation</th>
<th>No PPM implantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edwards SAPIEN valve, USA</td>
<td>477 (48.9%)</td>
<td>394 (82.6%)</td>
</tr>
<tr>
<td>Medtronic CoreValve USA</td>
<td>92 (9.4%)</td>
<td>78 (40.4%)</td>
</tr>
<tr>
<td>JenaValve, Germany</td>
<td>92 (9.4%)</td>
<td>78 (40.4%)</td>
</tr>
<tr>
<td>Symetis prosthesis, Switzerland</td>
<td>75 (7.7%)</td>
<td>56 (74.7%)</td>
</tr>
</tbody>
</table>

**Conclusion:** There is a significantly higher incidence of permanent pacemaker implantation following TAVI with a Medtronic CoreValve bioprosthesis. During follow-up a resolution of LBBB could be detected in almost 40% of the patients who underwent PPM implantation. In order to perform a predictive statement regarding a stricter indication of pacemaker implantation further studies are necessary.

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**VENTRICULAR ARRHYTHMIAS: STRATIFICATION AND TREATMENT**

**P5924 | BEDSIDE**

**Real World Experience with Wearable Cardiac Defibrillators**

W.J. Hacker1, J.S. Leyton-Mange1, N. Mihatov1, W.R. Reynolds2, C.M. Albert3, S.A. Lubitz1, D.J. Milan1, A.C. Geisler1, 2, 3 Brigham and Women's Hospital, Boston, United States of America; 2Tufts Medical Center, Boston, United States of America; 3Leiden University Medical Center, Leiden, Netherlands

**Background and introduction:** The wearable cardioverter defibrillator (WCD) has emerged as a non-invasive therapy for sudden cardiac death. There are several cases when a WCD may be prescribed, however no standardized criteria to guide its use exist. In addition, there is limited data regarding the frequency of treatments delivered.

**Purpose:** Our study sought to delineate WCD indications in practice and frequency of therapies delivered by WCDs.

**Methods:** We retrospectively reviewed indications and therapies of all WCD prescriptions in a 2 year period from 2 large academic medical centers. Data on compliance of patients wearing the WCD and WCD treatment events was provided by ZOLL Medical Company.

**Results:** Among the 147 patients prescribed a WCD between January 2012 and December 2013, 76% were male with a mean age of 59. A variety of WCD indications were cited: newly diagnosed cardiomyopathy with an ejection fraction <35% was most common (n=66;45.1%), followed by patients with polymorphic ventricular tachycardia in nonischemic cardiomyopathy: results from the Leiden NICM Study.

**Conclusion:** Patients with cardiomyopathy were prescribed a WCD more often than other patient groups; however, the majority of WCD treatment events were non-cardiac in nature and WCDs were not used as a substitute for an ICD. Future efforts are warranted to improve identification of patients most likely to benefit from a WCD and efficient utilization of therapies to minimize sudden death.

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**P5925 | BEDSIDE**

**Lack of an additional prognostic value of programmed electrical stimulation for risk stratification in Brugada patients without previous cardiac arrest: J-IVFS study**

M. Takagi1, Y. Sekiguchi2, Y. Yokoyama3, N. Ahara4, M. Hiraoka5, K. Aonuma2

**Introduction:** J-IVFS is a prospective single-arm study to evaluate the efficacy of implantable cardioverter defibrillator (ICD) in Brugada patients (BrP) without history of cardiac arrest. Seventy-five patients were enrolled from seven centers between November 2011 and September 2013. The primary endpoint was freedom from appropriate ICD therapy. Induction of ventricular tachycardia (VT) and ventricular fibrillation (VF) was considered as appropriately timed therapy. Cox proportional hazards analyses were performed to evaluate the association of various baseline characteristics with freedom from appropriate ICD therapy.

**Results:** Eighteen patients (24.0%) had cardiac arrest during the follow-up period, and 14 of them were implanted with ICD. The remaining 47 patients did not have cardiac arrest during the follow-up period. The freedom from appropriate ICD therapy was 94.7% at 1 year and 91.4% at 3 years, respectively. Cox proportional hazards analyses revealed that the incidence of cardiac arrest was significantly higher in patients presenting with Brugada syndrome (BrS) than in the general population (p<0.001). Patients with BrS who met the J-IVFS criteria for ICD implantation had a significantly higher incidence of cardiac arrest compared with patients who did not meet the J-IVFS criteria for ICD implantation (p<0.001).

**Conclusion:** In Brugada patients without history of cardiac arrest, the incidence of cardiac arrest was significantly higher than in the general population. Therefore, despite the lack of appropriate ICD therapy, patients with Brugada syndrome should be considered for ICD implantation.

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**P5926 | BEDSIDE**

**Critical progressive activation delay after premature stimulation is associated with polymorphic ventricular tachycardia in nonischemic cardiomyopathy: results from the Leiden NICM Study**

J. Venlet, S.R.D. Piers, S.F.A. Askar, G.F.L. Kapel, M. De Riva Silva, H.M. Siebelink, M.J. Schalij, D. Pinjappel, K. Zeppenfeld, Leiden University Medical Center, Cardiology, Leiden, Netherlands

**Purpose:** We aimed to assess whether critical progressive activation delay (PES) after premature stimulation can be used as a risk stratification tool in Brugada patients without previous cardiac arrest and having clinical history of syncope/spontaneous type 1 ECG (spType1), or both. Combination of syncope and spontaneous Type1 ECG is enough for risk assessment in BrS patients without previous cardiac arrest.

**Methods:** A total of 338 consecutive BrS patients without previous cardiac arrest and having clinical history of syncope or spType1 were included. Clinical outcomes during the follow-up period were compared between the groups with and without PES+ in patients showing clinical history of syncope and/or spType1.

**Results:** The incidence of cardiac events (sudden cardiac death [SCD] or VF) during a mean follow-up period of 63±37 months was not different in patients with and without PES+ (0.7 % and 0.9%/yr, respectively, p=0.72). In patients with syncope (n=45), spType1 (n=125), and both (n=66), incidences of cardiac events in cases with and without PES+ were not different (0.6 % vs 0.4 % vs 1.8, 2.2 % and 2.0%/yr, respectively; p=n.s). The incidence of cardiac events was significantly higher in patients with Class IIa (syncope + spType1, 3.2%/yr) than with Class IIIb indication (PES+ in patients except for Class IIa indication, 0.6% to 0.9%)

**Conclusion:** No additional prognostic values of PES+ for risk assessment in BrS patients without previous cardiac arrest and having clinical history of syncope/spType1 were confirmed. Combination of syncope and spontaneous Type1 ECG is enough for risk assessment in BrS patients without previous cardiac arrest.

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**New insights in device therapy / Ventricular arrhythmias: stratification and treatment 1031**

**Ventricular Fibrillation Study [J-IVFS].**

M. Takagi1, Y. Sekiguchi2, Y. Yokoyama3, N. Ahara4, M. Hiraoka5, K. Aonuma2

**Conclusion:** J-IVFS is a prospective single-arm study to evaluate the efficacy of implantable cardioverter defibrillator (ICD) in patients with Brugada syndrome (BrS) without previous cardiac arrest and having clinical history of syncope/spontaneous type 1 ECG. The primary endpoint was freedom from appropriate ICD therapy. Induction of ventricular tachycardia (VT) and ventricular fibrillation (VF) was considered as appropriately timed therapy. Cox proportional hazards analyses were performed to evaluate the association of various baseline characteristics with freedom from appropriate ICD therapy.

**Results:** Eighteen patients (24.0%) had cardiac arrest during the follow-up period, and 14 of them were implanted with ICD. The remaining 47 patients did not have cardiac arrest during the follow-up period. The freedom from appropriate ICD therapy was 94.7% at 1 year and 91.4% at 3 years, respectively. Cox proportional hazards analyses revealed that the incidence of cardiac arrest was significantly higher in patients presenting with Brugada syndrome (BrS) than in the general population (p<0.001). Patients with BrS who met the J-IVFS criteria for ICD implantation had a significantly higher incidence of cardiac arrest compared with patients who did not meet the J-IVFS criteria for ICD implantation (p<0.001).

**Conclusion:** In Brugada patients without history of cardiac arrest, the incidence of cardiac arrest was significantly higher than in the general population. Therefore, despite the lack of appropriate ICD therapy, patients with Brugada syndrome should be considered for ICD implantation.
P5927 | BEDSIDE
PainFree SST trial: T-wave oversensing algorithm performance
M. Brown1, A. Aurichio2, E.J. Schloss3, T. Kurita4, A. Meijer5, L.D. Sterns6, B. Gerritsa7, K.A. Ellenbogen8 on behalf of PainFree SST Investigators. 1Medtronic plc, Mounds View, United States of America; 2Cardiocentro Ticino, Lugano, Switzerland; 3The Christ Hospital, The Ohio Heart and Vascular Center, Cincinnati, United States of America; 4Christ Hospital, School of Medicine, Osaka, Japan; 5Catharina Hospital, Eindhoven, Netherlands; 6Royal Jubilee Hospital, Victoria, Canada; 7Bakken Research Center, Maastricht, Netherlands; 8Virginia Commonwealth University, Medical College of Virginia, Richmond, United States of America

Introduction: T-wave oversensing (TWOS) may cause inappropriate shocks in patients with implantable cardioverter-defibrillator (ICD). A suite of new detection algorithms, SmartShock Technology (SST), has been shown to reduce the rate of inappropriate shock. This analysis was focused on the performance of the TWOS algorithm designed to prevent shocks caused by TWOS.

Methods: PainFree SST was a prospective international clinical trial to estimate inappropriate shock rate after implant of Medtronic Protecta ICDS with SST. TWOS algorithm withholding detection when the frequency content of alternating sensed beats is consistent with a pattern of TWOS. “TW” in figure indicates detection withheld by TWOS algorithm. Episodes were adjudicated by an independent physician committee.

Results: 2770 patients (pts) were included with mean follow up of 22 months. There were 257 TWOS episodes in 14 pts. Of these, 4 episodes in 4 pts received inappropriate shock and 1 episode in 1 pt received inappropriate ATP. The remaining 252 episodes were appropriately withheld for an incremental specificity of 98.1% (CI: 93.5%, 99.4%). Only 50 episodes in 11 pts contained EGM and were adjudicated, all as due to TWOS. Logs contained an additional 104 episodes w/o EGM, all in the same 11 pts. These are presumed to also be true TWOS for which detection was withheld. The remaining 98 episodes were by device counter only and occurred in 3 of the same 11 pts. These, too, were presumed to be appropriate withholding of detection by the TWOS algorithm. There were no instances of appropriate detection of VT/VF being withheld by the TWOS algorithm.

Conclusion: The TWOS algorithm is designed to reduce shocks for TWOS. The PainFree SST trial showed TWOS reduces inappropriate detection by 98% without loss of sensitivity.

P5929 | BEDSIDE
Prevalence and significance of electroanatomical and ultrastructural abnormalities in patients with Brugada syndrome
S. Grotti1, M. Pieroni1, P. Notarsetano1, R. Guida1, T. Rio2, A. Camporeale2, A. Fraticelli2, A. Oliva2, L. Bolognesi3, 1San Donato Hospital, Cardiovascular Department, Areno, Italy; 2Catholic University of the Sacred Heart, Rome, Italy

Background: Brugada syndrome (BrS) is considered a pure electrical disorder mainly affecting the epicardium, but the presence of structural abnormalities is still controversial. Unipolar electroanatomic mapping has been demonstrated an accurate tool to detect epicardial abnormalities in myocardial diseases.

Purpose: To assess the prevalence of electroanatomical and ultrastructural abnormalities in BrS patients by using unipolar and bipolar mapping.

Methods: We enrolled 23 pts (18M, 43±10 years) with a diagnosis of BrS according to current criteria. All pts had a type 1 ECG pattern spontaneously (n=19) or after flecainide challenge (n=4). All pts underwent EAM and bipolar unipolar mapping. In 12 cases EAM-guided EMs were also performed. Low-voltage areas (LVA) were defined as ≥3 adjacent points with amplitude <1.5 mV (bipolar) and ≤0.5 mV (unipolar). Scar was defined as ≥3 adjacent points with amplitude <0.5 mV at bipolar mapping. All pts were also submitted to programmed electrical stimulation (PES).

Results: Twenty pts (87%) showed LVA at unipolar mapping; of them, 10 (43%) showed LVA also at bipolar mapping. Mean low-voltage areas were 36±31 cm² and 124±23 cm² at unipolar and bipolar map respectively. Right ventricular outflow tract was the most commonly involved area (n=16) (70%). During the invasive study 12/19 (63%) pts exhibited the spontaneous type 1 pattern. Ventricular fibrillation or syncopal sustained ventricular tachycardia were induced at PES in 10/23 (43%) pts. Ventricular arrhythmias induction was associated with the presence of a spontaneous type 1 pattern during PES (p<0.001). The detection of scar at bipolar map was associated with the presence of spontaneous type 1 pattern (p=0.02). Histology showed myocardial inflammation in 10/12 pts (83%). In 8 pts, EMs showing myocardial inflammation had been drawn from outflow tract areas with both unipolar and bipolar LVA. Two pts with myocardial inflammation and the two pts with normal biopsy had normal bipolar map but LVA at unipolar map.

Conclusions: We observed a high prevalence of unipolar map abnormalities among BrS pts, supporting the hypothesis that BrS is a pure structural disorder. Myocardial inflammation, as shown in pts with both unipolar and bipolar LVA, suggests a disease progression from epicardium to endocardium. Larger studies with long-term follow-up will clarify the prognostic significance of these findings and the role of myocardial inflammation in the pathogenesis of the syndrome.

P5930 | BEDSIDE
Reproducibility of repetitive T-wave alternans measurements in the EUTrigTreat study
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Background: Microvolt T-wave alternans (TWA) has been proposed as a useful predictor of ventricular arrhythmias to guide ICD therapy. The timing and the necessity for repeated testing remain unclear.

Purpose: To study the reproducibility of repetitive TWA and its correlation with ICD shocks.

Methods: The EUTrigTreat study is a prospective trial aiming to risk stratify ICD patients for mortality and shocks. The underlying cardiac disease is diverse including ischemic and non-ischemic cardiomyopathies and arrhythmogenic heart disease. TWA was performed using the Cambridge Heart exercise method (target heart rate of 110–120 bpm). Only patients with ≥3 consecutive TWA were included.
Results: In total, 632 patients were analyzable with a follow-up of 2.4±1.2 y. Of these, 170 had ≥3 consecutive TWA results with a follow-up of ≥2.0±0.8 y. TWA was reproducible in 73 patients (43%); 3x negative (neg) in 36, 3x non-negative (n-neg) in 37. In 97 patients (57%) results were variable (Figure). 3/36 (8%) 3xneg patients received shocks during follow-up vs 8/37 (22%) 3xneg and 12/97 (12%) with mixed results. There was no statistical difference for shock, nor for mortality between the 3 groups, probably due to the small number of events. Predominantly neg (n=90), ≥2 n-neg tests, however received significantly less shocks during follow-up than predominantly n-neg patients (n=80), ≥2 n-neg tests.

Logistic regression for worsening of the first TWA was associated with lower baseline left ventricular ejection fraction (p<0.02).

Conclusions: In this diverse population of ICD recipients TWA results were reproducible in less than half of the patients. Patients with predominantly negative TWA have a longer shock-free survival, corresponding to the baseline predictive value of a negative TWA result in the entire cohort.


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P5932 | BEDSIDE
Reperfusion in elderly patients with acute ST-elevation myocardial infarction: results from the RENAU-RESURCOR STEMI network
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1 Metropole Savoie Hospital, Emergency medicine, Chambery, France; 2University Hospital of Grenoble, Emergency medicine, Grenoble, France; 3University Hospital of Grenoble, Emergency medicine, Grenoble, France; 4Hospital of Annecy, Cardiology, Annecy, France; 5University Hospital, Cardiology, Lomé, Togo
Background: Elderly patients with acute ST-elevation myocardial infarction (STEMI) remain undertreated.

Purpose: To evaluate the management of elderly STEMI patients treated in a formal regional network of care.

Methods: This prospective analysis, based on data from the ongoing RESURCOR coronary emergency network, involved 6169 patients presenting with an acute STEMI between 2002 and 2011 in the French Alps. Patients were divided into age groups: <65, 65–74, 75–84 and ≥85 years. Reperfusion rates, types, timing and adjunctive medications were compared. The RESURCOR network advocates primary percutaneous coronary intervention (PPCI) over fibrinolysis and bivalirudin over glycoprotein inhibitors (GPI) in the elderly.

Results: Lack of use of fibrinolysis in the elderly population (Table). The rate of fibrinolysis was higher than that for PPCI in younger patients whereas the situation was reversed in elderly patients. In patients who had PPCI, use of bivalirudin increased and GPI decreased with age, system delays were similar.

Cares among the age groups

<table>
<thead>
<tr>
<th>Age group</th>
<th>CNI (%)</th>
<th>No reperfusion (%)</th>
<th>Delay (first medical contact to PPCI), median (IQR), min</th>
<th>GPI, m/n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65 yrs</td>
<td>54.72</td>
<td>3.8</td>
<td>80 (58–123)</td>
<td>B0/B1, 0/194</td>
</tr>
<tr>
<td>65-74 yrs</td>
<td>54.72</td>
<td>5.6</td>
<td>85 (60–125)</td>
<td>B0/B1, 0/194</td>
</tr>
<tr>
<td>75-84 yrs</td>
<td>54.72</td>
<td>8.0</td>
<td>85 (64–130)</td>
<td>B0/B1, 0/194</td>
</tr>
<tr>
<td>≥85 yrs</td>
<td>54.72</td>
<td>13.6</td>
<td>84 (60–124)</td>
<td>B0/B1, 0/194</td>
</tr>
</tbody>
</table>

P5933 | BEDSIDE
Management of young STEMI patient with mono truncular coronary artery occlusion based on minimum intravascular material implantation and guided by optical coherence tomography
N.C. Cares1, M.C. Combaret, J. Labarere2, J. Turk1, N.B.C. Barber-Chamoux, G.S. Souteyrand, G.M. Malcles, R.T. Tresorier, P.M. Motreff.
1 AP-HP - Corocard, Heart Centre Montfermeil, Le Raincy-Montfermeil, France; 2University Hospital of Besançon, Cardiology, Besançon, France; 3Centre Hospitalier Intercommunal Le Raincy-Montfermeil, Le Raincy-Montfermeil, France; 4Regional University Hospital Rangueil, Toulouse, France; 5Toulouse Rangueil University Hospital (CHU), Toulouse, France; 6Hospital Saint-Antoine, Paris, France

Rationale: Though cardiogenic shock (CS) after AMI is more common in the elderly, information on its prevalence, determinants and prognostic factors in this population is lacking.

Methods: We analysed incidence and 1-year mortality of CS in 4 nationwide French surveys carried out 5 years apart from 1995 to 2010, including consecutive STEMI andNSTemi patients over one-month periods.

Results: Among the 10,610 patients, 3,389 were aged ≥70 years, of whom 9.9% developed CS. Incidence of CS decreased from 11.6% in 1995 to 6.7% in 2010, P=0.02. Use of PCI >3 days from admission increased for both patients with and without CS (11% to 48% and 5% to 55%, respectively), as did statin use (70% to 4% and 82%, respectively). Occurrence of atrial and ventricular fibrillation decreased in patients without CS (22% to 9%, and 3.6% to 1.5%, respectively, P<0.001), but not in those with CS (19% to 20%, and 10% to 8%, respectively). Conversely, AV block decreased in patients with (30% to 11%) or without CS (9% to 3%). One-year mortality was 77% in CS patients, versus 22% in patients without CS. From 1995 to 2010, mortality decreased from 87% to 59% in CS patients and from 30% to 17% in patients without CS (P<0.001).

In CS patients, age, ventricular fibrillation and STEMI, were independent correlates of increased 1-year death, while study period was associated with decreased mortality (2010 vs 1995: HR 0.56, 0.33–0.94 P=0.03), along with early use of PCI, statins or LMWH.

Prevalence and one-year mortality in elderly patients with cardiogenic shock

<table>
<thead>
<tr>
<th>Prevalence and one-year mortality</th>
<th>&lt;65 years</th>
<th>65-74 years</th>
<th>75-84 years</th>
<th>≥85 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of CS in aged</td>
<td>n=2047</td>
<td>n=1238</td>
<td>n=1147</td>
<td>n=308</td>
</tr>
<tr>
<td>No reperfusion, n (%)</td>
<td>3.8</td>
<td>5.6</td>
<td>8.0</td>
<td>13.6</td>
</tr>
<tr>
<td>Delay (first medical contact to PPCI), median (IQR), min</td>
<td>80 (58–123)</td>
<td>85 (60–125)</td>
<td>85 (64–130)</td>
<td>84 (60–124)</td>
</tr>
<tr>
<td>Fibrinolysis, n (%)</td>
<td>1853 (53.3)</td>
<td>593 (47.9)</td>
<td>449 (39.2)</td>
<td>87 (28.3)</td>
</tr>
<tr>
<td>Primary PCI, n (%)</td>
<td>1492 (42.9)</td>
<td>576 (46.5)</td>
<td>606 (52.8)</td>
<td>179 (58.1)</td>
</tr>
</tbody>
</table>

Conclusions: In a selected population of young STEMI patients with monotruncular coronary artery occlusion, early PCI was associated with decreased 1-year mortality.
Prognostic significance of the culprit vessel in patients with STEMI: a real-world registry of patients in Switzerland (AMIS Plus), 2006–2013

P5936 | BEDSIDE
Circadian variation of intracoronary thrombus aspiration efficacy in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention

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Introduction: The clinical benefit of intracoronary thrombus aspiration (TA) during primary percutaneous coronary intervention (PCI) in patients with STEMI remains controversial. Different studies have suggested a circadian variation of myocardial infarction size (IS) among patients with STEMI depending on the time of the day at symptom onset.

Purpose: We aimed to investigate whether the clinical efficacy of manual TA varies according to circadian rhythms.

Methods: We analyzed data from a large, nationwide, prospective, multicenter registry of patients admitted with acute coronary syndrome in Switzerland (AMIS Plus). Patients undergoing primary PCI for STEMI with (TA+) or without (TA-) manual TA within 12 hours of symptom onset were included. Time of the symptom onset, peak creatine kinase (CK), a proxy measure for myocardial IS and clinical outcome were retrospectively obtained. We divided 24 hours into 4 time groups based on the time of symptom onset: group 1 (00:00–05:59), group 2 (06:00–11:59), group 3 (12:00–17:59) and group 4 (18:00–23:59). The primary endpoint was in-hospital all-cause mortality.

Results: Between 2008 and 2014, a total of 3,648 patients (TA+, n=1,800; TA-, n=1,848) were included. In-hospital death of any cause occurred in 3.8% of the patients in the TA+ group, as compared with 3.7% in the TA- group (p=0.44). In-hospital mortality was not statistically different between the 4 time groups in TA+ and TA- patients (2.1%, 4.6%, 2.9% and 5.1% respectively in TA+ group, p=0.082 and 3.1%, 3.0%, 5.6% and 2.9% respectively in TA- group, p=0.098). We observed a circadian variation of myocardial IS in patients undergoing TA with larger myocardial IS occurring during the night period (group 1: 2,833±3,304 U/l; group 2: 2,449±2,336 U/l; group 3: 2,542±2,114 U/l; group 4: 2,995±2,424 U/l, p<0.001). Of note, there was a statistically significant net benefit of manual TA in terms of myocardial salvage in patients with symptom onset between 06:00 and 18:00 (groups 1 vs. 2: p<0.001; groups 1 vs. 3: p<0.001; groups 4 vs. 2: p<0.001; groups 4 vs. 3: p<0.05).

Conclusion: In a real-world registry of patients with STEMI, intracoronary TA during primary PCI was not associated with improved in-hospital all-cause mortality, independently of the time of symptom onset. However, our results suggest a circadian variation of the efficacy of manual TA with a significant reduction of myocardial IS in patients with symptom onset between 06:00 and 18:00.

Abstract P5936 – Table 1. Predictors of TA and impact on outcome

2009–2013

Predictors for usage of TA-systems (multivariate model)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR (95% CI)</th>
<th>p-value</th>
<th>TA-impact on outcome (multivariate model)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt;65 yrs</td>
<td>1.3 (1.1–1.5)</td>
<td>0.05</td>
<td>0.85</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.5 (1.0–2.6)</td>
<td>0.05</td>
<td>0.55</td>
</tr>
<tr>
<td>Initial TIMI-0 flow</td>
<td>2.5 (1.5–4.1)</td>
<td>0.05</td>
<td>0.55</td>
</tr>
<tr>
<td>1- vessel-disease</td>
<td>1.6 (1.1–2.3)</td>
<td>0.01</td>
<td>0.01</td>
</tr>
</tbody>
</table>

P5937 | BEDSIDE
Association of changes in patients' characteristics and management with decreasing mortality rates of men and women with STEMI in Poland from 2005 to 2011

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Background: Mortality rates in STEMI have been decreasing in recent decades. It is related to numerous advances in management as well as to temporal changes in patient risk profiles. Women in STEMI have generally higher death rates than men and there are concerns about sex-disparities in treatment.

Purpose: To estimate how much of the decrease in in-hospital and 1-year mortality in STEMI patients in Poland from 2005 to 2011 can be attributed to improved...
treatment strategies and how much it is related to changes in baseline clinical characteristics, and compare these findings for men and women.

Methods: We analysed 32790 patients with STEMI from the Polish nationwide registry of acute coronary syndromes PL-ACS. All available baseline characteristics were incorporated into a regression model to estimate a propensity score (PS) of each individual. Patients from 2005 and 2011 were nearest neighbour matched on their PS (a total of 22059 patients in two separately matched groups of men and women). Observed in-hospital and 1-year death rates were compared with results in groups matched on PS.

Results: For in-hospital mortality relative risk reduction (RRR) was 37% for women and 35% for men; for 1-year it was 23% for women and 15% for men. After matching on propensity score RRR for in-hospital mortality was 21% in women and 27% in men; for 1-year it was 11% and 10% respectively. Around 57% of observed mortality reduction in women and 77% in men was related to improved in-hospital management while the remaining part to changes in patients’ clinical profiles. For 1-year death rates 43% of total reduction in women and 69% in men was associated with improved management strategies.

NEW TECHNIQUES AND NEW APPLICATIONS IN ECHOCARDIOGRAPHY

P5939 | BEDSIDE
A new 2D semi-quantitative echocardiographic tool to detect myocardial scar
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Background: The presence of myocardial scar is a critical feature impacting patient's management and prognosis. Nowadays CMR-LGE is the gold standard for the detection of myocardial scar. However we lack a bedside, easy tool to be used in our daily practice.

Purpose: To test an echocardiographic technique exploiting pulse modulation/inversion mode to detect myocardial scars in patients with recent STEMI and to compare it with CMR-LGE images.

Methods: We enrolled a) twelve patients who presented with STEMI and were treated with timely primary angioplasty and b) twelve patients who underwent CMR for a clinical indication and who demonstrated no CMR-LGE. In the STEMI-group transthoracic echocardiography was performed between 28 and 32 days after the STEMI using both standard 2D and a commercially-available pulse cceliation ultrasound technique (eSCAR). Visual analysis of eSCAR images was used to assess the presence of scar. eSCAR was defined as any myocardial scar.

Results: Thirty-seven (12.3%) patients developed POAF. They had a higher prevalence of hypertension (95% vs. 11.4%; p=0.04) and type 2 diabetes (41% vs. 19%; p=0.05). Patients with POAF had higher LA maximum volume (33 mL/m2 (p<0.01, r=−0.59 p<0.01), r=−0.61 p<0.01, r=−0.59 p<0.01).

Conclusion: We proposed a novel index “E-D delay” combined the E wave and D wave derived by Doppler echocardiography. Our results indicate that this novel index may play a new role to provide additional information in predict the elevation of LV preload, that is shown as LV filling pressure, LA pressure and pulmonary artery systolic pressure.

P5940 | BEDSIDE
Echocardiographic predictors of postoperative atrial fibrillation after high-risk abdominal surgery
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Background and purpose: Postoperative atrial fibrillation (POAF) is a frequent complication post high-risk surgery in elderly patients. We examined the use of preoperative echocardiography to predict POAF in these patients.

Methods: We performed a prospective study and enrolled 300 consecutive patients, age >65 years (mean age 72±6 years, 61% men) who underwent elective duodeno-pancreatic surgery, liver resection or bile duct surgery under general anesthesia between April 2013 and September 2014. Preoperative echocardiography was performed in all patients, including tissue Doppler imaging (TDI). We measured left atrial (LA) volumes (maximal, minimal and pre-systolic) and indexed to body surface area and the time interval between the onset of the P-wave on ECG and a point of the peak-A wave on TDI from the lateral mitral annulus (PA lateral), septal mitral annulus (PA septal), and right ventricular tricuspid annulus (PA tricuspid). Left atrial dysynchrony was measured by subtracting PA tricuspid from PA lateral. Right ventricular systolic pressure was assessed by the tricuspid regurgitation jet (TRJ) Doppler velocity method.

Results: Thirty-seven (12.3%) patients developed POAF. They had a higher prevalence of hypertension (59% vs. 11.4%; p<0.04) and type 2 diabetes (41% vs. 19%; p<0.05). Patients with POAF had higher LA maximum volume > 40 mL/m2 (p<0.001), LA minimal volume > 25 mL/m2 (p<0.002), LA pre-systolic volume > 33 mL/m2 (p<0.001), left ventricular mass index > 165 g/m2 (p<0.04) as well as...
as prolonged PA lateral, PA septal duration, left atrial and interatrial diastolic dysfunction time. Preoperative echocardiography in patients who developed POAF demonstrated significant elevation of TRU Doppler velocity (p<0.001). Based on our results, we defined the following cutoff points predictive of POAF: PA lateral > 139 ms (69% sensitivity, 92% specificity), left atrial diastolic dysynchrony > 35 ms (78% sensitivity, 89% specificity), and TRU Doppler velocity > 2.6 ms (89% sensitivity, 64% specificity).

Conclusion: Our results demonstrate that PA lateral, LA dyssynchrony and TRU Doppler velocity are independently associated with the incidence of POAF after high-risk abdominal surgery. These findings demonstrate that some of the typical structural and functional changes in the atria in chronic AF in the elderly are also common in surgical patients who develop POAF, suggesting that POAF and chronic AF may have similar pathophysiology.

PS941 | BENCH
Effect of afterload increase on left ventricular mechanical dispersion and electromechanical window
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Purpose: Mechanical dispersion and electromechanical window have shown potential as risk predictors for arrhythmias. Given the close relationship between diurnal variation in arrhythmic events and blood pressure rise, we sought to investigate the relation between acute increases in blood pressure and these parameters in a controlled animal model.

Methods: Afterload increase was induced by balloon inflation in the descending aorta in eight anesthetised pigs. Two dimensional (2D) echocardiographic LV apical (2–3–4 Chamber) views and pulsed wave (PW) Doppler recording of the LV outflow were obtained trans-diaphragmatically using a Vivid 9 system (GE Healthcare). Global mechanical dispersion (GMD) was defined as the standard deviation of time to peak longitudinal shortening obtained by Speckle tracking in all 18 LV segments. EMW is the interval between the end of the T wave (ECG) and aortic valve closure (PW Doppler, LV outflow).

Results: Balloon inflations raised BP by an average of 53.9±24% (p<0.001) and heart rate decreased significantly (p<0.001), while QT remained unchanged. LV end-systolic and end-diastolic volumes enlarged significantly during inflation (p<0.001) and LV ejection fraction decreased (p<0.001). GMD increased during inflation (35.5±9.9 ms vs. 51.5±11.6 ms, p<0.001). Similarly, EMW prolonged during afterload increase (30.6±26.6 ms vs. 64.9±14.1 ms, p<0.001), because of a delayed aortic valve closure. Both parameters showed a strong positive correlation with BP (GMD: r2=0.69 and EMW: r2 =0.87) (Figure 1).

Conclusions: Blood pressure surges consistently increase GMD and EMW. These data would suggest that measuring these risk predictors during an acute raise in blood pressure (e.g. by a handgrip test), could unmask possible afterload-induced arrhythmic risk.

PS942 | BEDSIDE
Validation of 2D strain parameters in the diagnosis of acute rejection after heart transplantation

Acute allograft rejection (AAR) is still a relevant complication after orthotopic heart transplantation (HT). Its diagnosis is based on endomyocardial biopsy (EMB), but recent advances in 2D-strain imaging may allow an early non-invasive detection of AAR.

Objective: To analyze the usefulness of conventional and 2D strain parameters to detect AAR after HT and verify them on an internal validation cohort.

Methods: We prospectively included 34 consecutive adult recipients (sample 1) admitted at our center for HT and 21 patients (sample 2) for internal validation. A total of 235 and 148 pairs of EMB and echocardiograms were performed in sample 1 and 2 respectively. We analyzed classic echocardiographic parameters, speckle-tracking derived left ventricular global longitudinal strain (LVGLS) and global and free wall right ventricular longitudinal strain (Free wall RVLS).

Results: In sample 1, AAR was detected in 26.4% of EMBs (n=62), 5.1% (n=12) required specific treatment (AAR>2R). In sample 2, AAR was detected in 44.6% of EMBs (n=66), 12.8% (n=19) of them ≥2R. In sample 1, Free wall RVLS <17% was associated with a Sp 91.1%, PNV 98.8% and accuracy 90.7% while LVGLS <15.5% presented a Sp 81.4%, PNV 98.8% and accuracy 81.7% for the diagnosis of AAR>2R. We applied these cut-off points for internal validation in sample 2 obtaining that free wall RVLS <17% was associated with a Sp 74.6%, PNV 90.7% and accuracy 71.3% while LVGLS <15.5% presented a Sp 82.4%, PNV 92.8% and Accuracy of 79.2%.

Conclusions: We propose the combination of two new echocardiographic measures (global LV and free wall RV longitudinal strain) to detect AAR after HT. In our internal validation (sample 2) we obtained an excellent PNV, so 2D strain routine measures could be a reliable tool to rule out AAR and potentially reduce EMBs.

PS943 | BEDSIDE
Right atrial volume - a surrogate marker for estimating right atrial pressure
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Introduction: Current guidelines recommend that pulmonary artery systolic pressure (PASP) should be estimated by echocardiography using tricuspid regurgitation (TR) velocity with the addition of right atrial (RA) pressure, assuming no significant right ventricular outflow tract (RVOT) obstruction. The RA pressure is derived from dimensions of inferior vena cava (IVC) and its collapsibility.

Purpose: Our hypothesis is that measurements of maximum right atrial volume (RAV) can be correlated with right atrial pressure (RAP) better than measurements of IVC.

Methods: Fourteen consecutive patients with idiopathic pulmonary arterial hypertension referred to our clinic. We performed echocardiography and measured right atrial volume (area-length method and disk summation technique in apical four chamber view) and IVC dimensions and its respiratory variations, according to current guidelines recommendations. All had previously undergone right heart catheterization with measurement of right atrial pressure. Patients with other possible causes of RA enlargement were excluded from the study.

Results: Mean RAV was 109.64 ml (Range: 36–250 ml), mean RAP was 12.42 mmHg. Bivariate correlation analysis revealed an intense positive association between RAV and RAP which is stronger than the association between IVC dimension and RAP. Regression analysis confirmed RAV as a predictor of RAP (R2=0.85, p=0.0001) (Figure 1). The equation for estimating RA pressure by RA volume is RAP = 0.141 x RAV - 3.045.
Conclusion: Our pilot study shows a superior correlation between RAV and RAP measured by right heart catheterization compared with IVC size and respiratory variation. We are currently conducting a study on a larger cohort of patients in order to validate these results.

P5946 | BENCH
VEGF-B induces a unique electrophysiological phenotype in mouse hearts.

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Background: Cardiac effects of vascular growth factors (VEGFs) have mainly been studied in the context of angiogenic gene therapy to enhance perfusion of the heart. However, the role of VEGFs in the heart seems not to be restricted only to angiogenesis. VEGF-B has been implicated in myocardial metabolism and is involved in modulating heart’s response to pathological stress. However, the effects of VEGF-B on mycardial function are not known.

Methods: The purpose of this study was to assess the effects of VEGF-B on the contractile and electrophysiological properties of the mouse heart.

Results: In vivo contractile function or the morphology of TG hearts did not differ from WT hearts. However, ECG measurements showed a decrease in the R and S amplitudes as well as in PQ time and an increase in the QRS time in TG mice compared to the WT mice. Isolated TG cardiomyocytes had increased duration (APD90, 55.8%, p < 0.005) and time (47.1%, p < 0.00001) of the action potentials. These were accompanied by a decrease in the density of the sodium current (20.8% at −40 mV, p = 0.0005) and in the transient outward K+-currents (149%, p = 0.01, at 50 mV) were both increased. In line with these electrophysiological changes, steady state K+-currents were increased (149%, p = 0.01, at 50 mV) were both increased. In line with these electrophysiological changes, steady state K+-currents were increased. In vivo contractile function or the morphology of TG hearts did not differ from WT hearts. However, ECG measurements showed a decrease in the R and S amplitudes as well as in PQ time and an increase in the QRS time in TG mice compared to the WT mice. Isolated TG cardiomyocytes had increased duration (APD90, 55.8%, p < 0.005) and time (47.1%, p < 0.00001) of the action potentials. These were accompanied by a decrease in the density of the sodium current (20.8% at −40 mV, p = 0.0005) and in the transient outward K+-currents (149%, p = 0.01, at 50 mV) were both increased. In line with these electrophysiological changes, steady state K+-currents were increased (149%, p = 0.01, at 50 mV) were both increased. In line with these electrophysiological changes, steady state K+-currents were increased. In vivo contractile function or the morphology of TG hearts did not differ from WT hearts. However, ECG measurements showed a decrease in the R and S amplitudes as well as in PQ time and an increase in the QRS time in TG mice compared to the WT mice. Isolated TG cardiomyocytes had increased duration (APD90, 55.8%, p < 0.005) and time (47.1%, p < 0.00001) of the action potentials. These were accompanied by a decrease in the density of the sodium current (20.8% at −40 mV, p = 0.0005) and in the transient outward K+-currents (149%, p = 0.01, at 50 mV) were both increased. In line with these electrophysiological changes, steady state K+-currents were increased (149%, p = 0.01, at 50 mV) were both increased. In line with these electrophysiological changes, steady state K+-currents were increased.
Results: ST increased atrial arrhythmia susceptibility in Plako+/− (Fig.1) but not WT mice (WT sedentary (Sed): 3/11 hearts vs ST: 1/11 hearts). ST induced mild left ventricular ventrilocity in both genotypes (6−14%, p<0.05). ST increased LA size in both genotypes (LA size WT: 3.11±0.14 vs 3.79±0.17 mm² ST, p<0.05). Plako+/− 3.23±0.1 mm² Sed vs 4.14±0.23 mm² ST, p<0.05). LA APD from MAPs (Fig.2) and RA APD90s measured from TAPs were shorter after ST (WT: 22±1 Sed vs 19±1 ms ST; Plako+/−: 24±1 Sed vs 18±1 ms ST).

Conclusion: Our observations suggest that endurance training shortens atrial APD and increases LA size in both WT and plakoglobin deficient atria. Endurance training increases atrial arrhythmia susceptibility in mice with plakoglobin deficiency.
measurement in a mouse model with a marked structural heart defect with regard to threshold values and arrhythmogenesis. Methods: Adult wildtype C57Bl/6 mice after transcverse aortic constriction (TAC) and after myocardial cryoinfarction (MCI) were compared to the corresponding sham operated animals (control). Parameters of HRT were determined during an in vivo electrophysiological investigation 2 weeks after the operation and calculated according to the established protocols. Results: Compared to control animals, TAC as well as MCI operated mice did not display an early acceleration in heart rate (i.e. turbulence onset [TO] value ≥0%) after extrastimulus pacing (TO heart disease: 0.29±0.57% vs. controls: −0.16±0.75%; p< 0.01). At a cutoff value of ＜0.25% TO could be used to differentiate between heart disease and healthy animals with a sensitivity of 64.0% and specificity of 88.2% (p< 0.01; positive likelihood ratio [PLR] 5.44). The late deceleration in heart rate as indicated by turbulence slope (TS) did not differ between the groups. However, irrespective of the presence of structural heart disease, the group of animals that was inducible to ventricular tachycardias differentiated between the groups. However, irrespective of the presence of structural heart disease, the group of animals that was inducible to ventricular tachycardias displayed significant lower values for TS as compared to the non-inducible group (6.5±1.3ms/RR-interval vs. 13.4±2.1ms/RR-interval; p=0.02). TS with a threshold value of ＜7.79ms/RR-interval could identify inducible arrhythmias with a sensitivity of 75.0% and specificity of 75.8% (p=0.02; PLR 3.09; OR 6.38, 95% CI 1.05 to 38.87). Conclusion: Measurement of HRT as a marker of baroreflex function in mouse models with structural heart diseases is feasible. Pathological values for TO indicate the presence of structural heart diseases. As in humans, TS appears to be a strong predictor for ventricular arrhythmias.

**DIFFERENTIATING PULMONARY ARTERIAL HYPERTENSION FROM OTHER PULMONARY HYPERTENSION GROUPS**

**P5952 | BENCH**

Combined pre-and postcapillary pulmonary hypertension in chronic heart failure: epidemiology, right ventricular function and survival

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Background: Patients with pulmonary hypertension due to left heart disease (PH-LHD) and diastolic pulmonary vascular pressure gradient (DPG), ≥7mmHg representing PH out-of-proportion to pulmonary arterial wedge pressure, have pulmonary vascular disease and increased mortality. Little information exists on this condition.

Objectives: We investigated epidemiology, risk factors, right ventricular (RV) function and outcomes in patients with chronic heart failure (HF) and “out-of-proportion” PH.

Methods: The study population was identified from retrospective chart review of a clinical database of 3107 stable patients undergoing first diagnostic right heart catheterization, and from a prospective cohort of 800 consecutive patients at a national tertiary care center.

Results: In the retrospective cohort were 664 patients with systemic heart failure (SHF), and 399 patients with diastolic heart failure (DHF), 12% of which were classified as PH-LHD with DPG ≥7mmHg, respectively. In the prospective cohort were 172 patients with SHF [14% PH-LHD with DPG ≥7mmHg] and 219 patients with DHF [12% PH-LHD with DPG ≥7mmHg]. COPD and tricuspid annular plane systolic excursion (TAPSE)/systolic pulmonary artery pressure (sPAP) (p=0.015) predicted PH-LHD with DPG ≥7mmHg in SHF. Younger age (p=0.004), valvular heart disease (VHD, p=0.048) and TAPSE/sPAP predicted PH-LHD with DPG ≥7mmHg in DHF (p=0.016). RV-pulmonary vascular (RV-PV) coupling was worse in PH-LHD with DPG ≥7mmHg (SHF: Ees/Ea 1.05±0.25; p=0.002; DHF: Ees/Ea 1.17±0.27; p=0.027) than in those with DPG <7mmHg (SHF: Ees/Ea 1.52±0.51; DHF: Ees/Ea 1.45±0.29).

Conclusions: PH-LHD with DPG ≥7mmHg is rare in HF. RV-PV coupling is poor in PH-LHD with DPG ≥7mmHg, explaining dismal outcomes.

**P5953 | BEDSIDE**

Venous remodelling in COPD pulmonary hypertension and idiopathic pulmonary arterial hypertension

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Background: Pulmonary arterial remodelling is known to correlate to the severity of precapillary pulmonary hypertension (pPH) in end-stage COPD and idiopathic pulmonary arterial hypertension (IPAH). Scarce information is available regarding venous remodelling.

Purpose: To investigate the extent of venous remodelling in COPD-PH and IPAH.

Methods: 409 end-stage COPD patients with right heart catheterization (RHC) data were evaluated for lung transplantation during 1991–2010 (bellow up until 2015) at our institution. Of these 301 (72±8 yrs, 52% male) were included. Four hemodynamic groups were included in an analysis of venous involvement in explanted lungs: 1) non-PH (n=30, mPAP ≤25mmHg), 2) mild-moderate pPH (n=30, mPAP 25–34 mmHg, PAWP ≤15 mmHg), 3) severe pPH (n=10, mPAP ≥35 mmHg, PAWP <15 mmHg), 4) postcapillary PH (pCH) (n=33 mPAP ≥25 mmHg, PAWP >15 mmHg), compared to IPAH (n=16, mPAP >50 mmHg).

Two-three sections from each lobe were stained with hematoxilin and eosin and for elastin and examined by the same cardiovascular pathologist who was blinded to the hemodynamics.

Results: COPD-nonPH patients had pathological venous remodelling (range 0–1; 40% grade 0, 60% grade 1). COPD-PH had increased venous involvement dependent on hemodynamic group: Mild-moderate pPH (range 0–2; 23% grade 0, 64% grade 1, 13% grade 2); Severe pPH (range 0–2; 20% grade 0, 70% grade 1, 10% grade 2); COPD-pCH (range 0–2; 30% grade 0, 67% grade 1, 3% grade 2), while IPAH patients had the lowest proportion of unaffected veins and highest proportion of severe remodelling (range 0–2; 13% grade 0, 63% grade 1, 25% grade 2).

Conclusion: A novel grading scheme for venous remodelling in pulmonary hypertension is introduced. Myofibroblast proliferation appears in pulmonary veins in both COPD-pPH and COPD-pCH. Remarkably, IPAH patients presented with advanced forms of venous remodelling, emphasizing that the disease is not restricted to arterial lesions exclusively.

**P5954 | BEDSIDE**

Impact of atrial contraction on diagnosis of pre- versus post-capillary pulmonary hypertension

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Background: Establishing post-capillary hemodynamics in pulmonary hypertension (PH) is documented by measuring an elevated pulmonary capillary wedge pressure (PCWP >15 mmHg). However, the accuracy of PCWP to reflect left ventricular (LV) diastolic pressures in the PH population is under debate. The aim of the study is to investigate the split between PCWP and LV diastolic pressures in PH patients with and without atrial fibrillation.

Methods: Pressure traces of 128 PH patients were reviewed. Mean PCWP was taken at end-expiration. LV diastolic pressure before atrial contraction (pre-A LVDP) was measured at the nadir of the LV A-wave and LV end-diastolic pressure (LVEDP) was measured in the 99 patients in sinus rhythm (62±15 yrs, 53% male), pre-A LVDP. LVEDP and PCWP were 12±5 mmHg, 17±7 mmHg and 17±6 mmHg, respectively. The sensitivity, specificity, positive and negative predictive values of PCWP to reflect abnormal LVEDP were each 90%. The agreement between PCWP and LVEDP was best in patients with normal LVEDP (mean difference 0.4±2.7 mmHg), while PCWP underestimated LVEDP by 2.6±4.7 mmHg in a subgroup of patients with elevated LVEDP combined with large a LV A-wave (>5 mmHg).

In the 29 patients with atrial fibrillation (72±8 yrs, 52% male), PCWP consistently overestimated LVEDP due to the lack of LV A-wave with a mean difference of 4.8±3.1 mmHg. The sensitivity, specificity, positive and negative predictive values of PCWP to reflect abnormal LVEDP were 100%, 8%, 61% and 100%, respectively.

Conclusion: Measurement of HRT as a marker of baroreflex function in mouse models with structural heart diseases is feasible. Pathological values for TO indicate the presence of structural heart diseases. As in humans, TS appears to be a strong predictor for ventricular arrhythmias.

**DIFFERENTIATING PULMONARY ARTERIAL HYPERTENSION FROM OTHER PULMONARY HYPERTENSION GROUPS**
Conclusion: PCWP reliably reflects pre- and post-capillary PH during sinus rhythm. The poor agreement between PCWP and LVEDP in PH patients with atrial fibrillation may lead to issues with patient classification.

P5955 | BEDSIDE
Differences in the relation between right ventricular function and exercise performance between pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension
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Background: Right Ventricular (RV) function is an important prognostic marker in Pulmonary Hypertension (PH) that can be quantitatively assessed by 2D echocardiography speckle-tracking. It is not known if RV function has the same relation with exercise performance in all pre-capillary PH groups.

Objectives: To assess whether global RV longitudinal strain (RVLS) predicts exercise performance measured by Cardio-Pulmonary Exercise Testing (CPET) in pulmonary arterial hypertension (PAH) and chronic thromboembolic PH (CTEPH). We also related CPET and RVLS to prognostic markers recommended by the American Society of Echocardiography (ASE): Fractional Area Change (FAC), RV myocardial performance index (RVMPI), indexed Right Atrial (RA) area, Systolic and Diastolic left ventricular eccentricity index (Els, Elt) and Tricuspid Annular Plane Systolic Excursion (TAPSE).

Methods: A total of 46 patients were recruited 46 consecutive patients with PAH and 42 patients with CTEPH who were referred for CPET and transthoracic echocardiography (TTE) within a month of each other. RVLS was analyzed from an apical four chamber view. CPET parameters included Peak oxygen consumption (VO2peak), percentage of predicted VO2max, maximum workload, ventilatory equivalent of carbon dioxide (VE/VCO2). Linear then multiple regression analysis was performed with RVLS and prognostic markers as predictors and the CPET parameters as dependent variables.

Results: In PAH, RVLS predicted PeakVO2 (R2=6.6%, p<0.046), percentage of predicted VO2max (R2=9.7%, p<0.02), maximum workload (R2=7.2%, p<0.04), VE/VCO2 (R2=31.7%, p<0.001). RVLS was a stronger predictor of VE/VCO2 than all the ASE recommended prognostic markers. With multivariate regression (R2=99.9%, p<0.001) it was an independent predictor of VO2peak in CTEPH. CTEPH RVLS did not predict any CPET measurement.

Conclusions: In PAH, RVLS is closely related to function and is an independent predictor of VE/VCO2 a prognostic measure derived from exercise performance. On the other hand, RVLS does not have any predictive measure of exercise performance in CTEPH. This implies that RV function and exercise performance may be less closely associated in CTEPH and that other factors such as ventilation-perfusion mismatch may play a role.

P5956 | BEDSIDE
Prognostic value of pulmonary blood volume by contrast-enhanced magnetic resonance imaging in heart failure outpatients
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Background: Assessing and grading congestion in patients with heart failure (HF) is an unmet clinical need. Early diagnosis of subclinical congestion is key to ensure prompt and effective treatment, and to prevent recurrent hospitalization for worsening HF. Pulmonary blood volume (PBV) has been advocated as a non-invasive method to assess and grading congestion, and confirm its prognostic role in the setting of congestive HF.

Methods: We prospectively recruited 46 consecutive patients with PAH and 42 patients with CTEPH who were referred for CPET and transthoracic echocardiography (TTE) within a month of each other. RVLS was analyzed from an apical four chamber view. CPET parameters included Peak oxygen consumption (VO2peak), percentage of predicted VO2max, maximum workload, ventilatory equivalent of carbon dioxide (VE/VCO2). Linear then multiple regression analysis was performed with RVLS and prognostic markers as predictors and the CPET parameters as dependent variables.

Results: In PAH, RVLS predicted PeakVO2 (R2=6.6%, p<0.046), percentage of predicted VO2max (R2=9.7%, p<0.02), maximum workload (R2=7.2%, p<0.04), VE/VCO2 (R2=31.7%, p<0.001). RVLS was a stronger predictor of VE/VCO2 than all the ASE recommended prognostic markers. With multivariate regression (R2=99.9%, p<0.001) it was an independent predictor of VO2peak in CTEPH. CTEPH RVLS did not predict any CPET measurement.

Conclusions: In PAH, RVLS is closely related to function and is an independent predictor of VE/VCO2 a prognostic measure derived from exercise performance. On the other hand, RVLS does not have any predictive measure of exercise performance in CTEPH. This implies that RV function and exercise performance may be less closely associated in CTEPH and that other factors such as ventilation-perfusion mismatch may play a role.

P5957 | BEDSIDE
Novel strategy for catheter interventional treatment of chronic thromboembolic pulmonary hypertension guided by optical coherence tomography imaging
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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is caused by unresolved thromboemboli in the pulmonary arteries. We have previously demonstrated the usefulness of optical coherence tomography (OCT), an interferometer-based imaging modality with a high resolution, to diagnose CTEPH. In the present study, in order to develop an effective and safe treatment for inoperable CTEPH, we examined the effectiveness of our modified methods of T-Box Transcription Factor (TBox). A pulmonary artery hypertension recently described gene. It can cause childhood-onset PH and Small Patella Syndrome (SPS). PH phenotype and prognosis associated to TBX4 mutations (mut) have not been described. We present preliminary results of an Spanish Multi-centric study of genetics of Idiopathic (IPAH) and Heritable (HPAH) patients (pts).

Aim: To describe prevalence of TBX4 mut in adult IPAH&HPAH pt and characterize phenotype compared to other forms of HPAH.

Methods: An Spanish Multi-centric study of genetics of IPAH&HPAH is ongoing since 2011. Genetic analysis was performed looking for BMPR2, KCNK3 and TBX4 mut. After genetic study patients were divided into 3 groups: Idiopathic PH (no detected mut and no family story), Heritable TBX4 PH (detected mut in TBX4) and HPAH-non TBX4 PH (detected mut in BMPR2 or KCNK3 or patients without detected mut but with positive family story). Clinical and survival (SV) data were obtained from Spanish National Registry (REHAP), Screening for SPS was done in TBX4mut carriers.

Results: 117 pt were included. We found 18 mutations in BMPR2 (15.3%), 2 mut in KCNK3 (1.7%) and 2 different missense mutations (p.M452V and p.N475H) in TBX4 in two non-related sporadic PH pt (1.9%). Both TBX4mut seemed to be pathogenic after bio-informatic analysis and were absent in control population. No other mut in common PH genes were found in TBX4 mut carriers. Both TBX4mut carriers presented a childhood-onset sporadic PH with a unique bionomic curve. None of them fulfilled SPS criteria. Characteristics and SV are listed in Chart 1.

Conclusion: HPAH related to TBX4 mut presents as a child-hood onset PH and may exhibit a more benign course and longer survival than other forms of HPAH. Further investigations are needed to explore the course and prognosis of this new mut.

P5958 | BEDSIDE
Differentiating PAH from other pulmonary hypertension groups

Abstract P5957 – Table 1. Clinical and hemodynamic characteristics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>mPAP (mmHg)</th>
<th>PVR (WU)</th>
<th>NYHA</th>
<th>AVT</th>
<th>Survival (years)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>55/1</td>
<td>75/85</td>
<td>16/3</td>
<td>Negative</td>
<td>43.46</td>
<td>Bosantan (since 2010)</td>
</tr>
<tr>
<td>Patient 2</td>
<td>53/1</td>
<td>71/13</td>
<td>16/3</td>
<td>Positive</td>
<td>28.39</td>
<td>Nifedipine</td>
</tr>
</tbody>
</table>

mPAP: medium pulmonary artery pressure; mmHg: millimeters of mercury; PVR: pulmonary vascular resistance; WU: wood units; NYHA: New York Heart Association functional class; AVT: acute vasodilator test; ARE: antagonists of endotelin receptor; PD5I: phosphodiesterase 5 inhibitors; CO: calcium channel blockers.
percutaneous transluminal pulmonary angioplasty (PTPA) guided by OCT imaging.

**Methods:** From July 2009 to October 2014, we prospectively enrolled 61 consecutive patients with inoperable CTEPH, including 2 patients with a history of thromboendarterectomy and residual PH (median age 63 yrs., 78% female). After optimal medical treatment, we performed PTPA in a stepwise manner until mean pulmonary artery pressure (PAP) was decreased below 30 mmHg.

**Results:** As a vasodilator therapy prior to PTPA, prostacyclin analogues, phosphodiesterase-5 inhibitors, endothelin receptor antagonists and soluble guanylate cyclase stimulators were used in 42 (68%), 45 (74%), 13 (21%) and 10 (16%) patients, respectively. Among them, 42 (69%) received combination therapies of these medications. We performed a total of 279 OCT examinations in order to observe the target lesions for PTPA, which clearly showed meshwork (88%), thrombus (10%), and slit (5%) configurations. We also performed a total of 332 PTPA procedures (median 4.5 procedures per patient), resulting in significant improvement of mean pulmonary arterial pressure (422±10 to 27±6 mmHg, P<0.01), cardiac index (2.3±0.6 to 2.7±0.5 l/min/m², P<0.01), pulmonary vascular resistance (74±3±124 dyne·cm·sec·m⁻², P<0.01), and saturation of oxygen (87±6% to 90±6%, P<0.05, n=25). OCT showed that PTPA enlarged the lumen diameter (63±90% increase), although some severe thrombotic occlusions were resistant to the procedure. 3D-OCT imaging clearly showed that PTPA destroyed the typical flaps and webs and shifted them to the pulmonary artery walls. Furthermore, cardiac magnetic resonance showed improvement of right ventricular (RV) ejection fraction (39.5% to 51.0%, P<0.001), decrease in RV end-diastolic volume index (105 to 84 ml/m², P<0.03). The complication of PTPA was mild to moderate hemoptysis in 18 out of the 61 patients, which was successfully managed with oxygen and non-invasive positive pressure ventilation without intubation.

**Conclusion:** OCT-guided PTPA combined with optimal medical treatment markedly ameliorates pulmonary hemodynamics and RV functions in patients with inoperable CTEPH.

**WHAT’S NEXT IN CARDIOVASCULAR RISK PREDICTION?**

**PS5960 | BEDSIDE**

**Coronary artery calcium (CAC) volume, CAC density, and incident coronary heart disease, stroke, and all cardiovascular disease events**

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**Background:** We have reported that coronary artery calcium (CAC) volume by computed tomography (CT) was strongly related to incident cardiovascular disease (CVD) in a multi-ethnic cohort, but that at any given CAC volume, CAC density was inversely related (JAMA 2014;311:271-28). We also noted that CAC density was somewhat more protective at lower levels of CAC volume, though the interaction term was not significant. Longer follow-up has now increased the number of hard CVD events by 47%.

**Purpose:** To evaluate with longer follow-up 1) whether CAC density remains inversely associated with CVD (CHD and stroke) events, 2) whether the effect of CAC density is modified by the level of CAC volume, and 3) among CVD events, to separately evaluate coronary heart disease (CHD) and stroke events.

**Methods:** 3398 men and women in the Multi-Ethnic Study of Atherosclerosis with electrocardiographic demonstration of coronary artery disease (CAD) within 10 yrs. were included. CAC density was divided into quartiles.

**Results:** After a median follow-up of 10.3 years, there were 264 coronary heart disease (CHD) events and 126 hard stroke events for a total of 390 hard CVD events. For CHD, the HR was 1.83 (p<0.001) for each standard deviation (SD) of CAC volume, and the HR was 0.71 (p<0.001) for each SD of CAC density. Results were similar for all CVD. For stroke, the HR was 1.46 (p<0.001) for each SD of CAC volume, and the HR was 0.83 (p=0.13) for each SD of CAC density. CAC volume and CAC density each independently and significantly increased the risk of CHD and stroke in models adjusted for age, sex, and smoking. The interaction term was not significant. Longer follow-up has now increased the number of hard CVD events by 47%.

**Conclusions:** With extended follow-up, 1) CAC density remained strongly inversely related to incident CHD and all CVD, and 2) this inverse association was similar at all levels of CAC volume. As expected, CAC volume and density showed more modest associations with stroke. CAC scoring systems should include density to improve estimation of CHD and CVD risk.

**PS5961 | BEDSIDE**

**Biomarker-based risk score for prediction of cardiovascular events in stable coronary heart disease - Experiences from the STABILITY biomarker substudy**

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**Background:** There is no generally used risk score for prognostication of cardiovascular outcomes in patients with stable coronary heart disease (CHD). The biomarkers currently used in routine care for evaluation of these patients are indicators of dysglycemia, dyslipidemia, renal dysfunction and inflammation (C-reactive protein [CRP]).

**Purpose:** We developed and evaluated a biomarker-based risk score for cardiovascular death (CVD), myocardial infarction (MI), stroke and heart failure (HF) in stable CHD based on clinical characteristics and biomarkers.

**Results:** Of the 15,828 CHD patients included in the STABILITY trial 13,093 had biomarker information at baseline. Beyond routine biomarkers (listed below), we included markers of cardiac dysfunction (N-terminal pro-B type natriuretic peptide [NT-proBNP]), high sensitivity cardiac troponin-T [cTnT-h], renal dysfunction (cystatin-C), oxidative stress (growth differentiation factor 15 [GDF-15]) and local inflammatory activity (lipoprotein-associated phospholipase A2 [Lp-PLA2]). During 3.7 years median follow-up, 1298 CVD, MI and stroke events occurred. A Cox-regression model was constructed, comprising all prognostic clinical variables (age, sex, BMI, smoking, hypertension, diabetes, previous polycystic disease, previous MI, previous revascularisation, previous multivessel disease and the routine biomarkers haemoglobin, while blood cell count, Lp-PLA2, uric acid, triglycerides, estimated GFR (based on creatinine) and cystatin-C, hsCRP GDF-15, cTnT-hs and NT-proBNP which had C index 0.72. This was then reduced to a smaller parsimonious model, including the variables with the strongest prognostic value. The new model was internally validated us-
ing 100 bootstrap samples. The development of the model followed the recently published TRIPOD statement.

Results: The final reduced model included, in order of importance, NT-proBNP, cTnTths, polyvascular disease, smoking, GDF-15 and Lp-PLA2. It was well calibrated and showed good internal validity. The C index was 0.71 for the composite endpoint of CVD/MI/stroke. Using the same model the C index was 0.81 for CVD, 0.77 for total death, 0.66 for MI, 0.67 for stroke, 0.86 for HF, and 0.82 for CVD/HF.

Conclusion: A biomarker-based risk score, including NT-proBNP, cTnTths, GDF-15, Lp-PLA2 and information on polyvascular disease and smoking, accurately predicts risk of fatal and non-fatal cardiovascular events in patients with stable CHD. The use of this score as a decision support tool might further improve secondary preventive treatments in this patient population.

PS962 | BEDSIDE
Increase the predictive capacity of coronary risk with a Genetic Score
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Genes associated with coronary artery disease (CAD) and traditional cardiovascular risk factors (TCRF) present a limited predictive value. It is expected that the inclusion in global scores may increase the predictive ability.

Aim: Evaluate the ability of a multifactorial genetic risk score (GRS) be able to add predictive power, for the development of CAD, to the model developed only with TCRF.

Methods: A case-control study was performed with 1321 consecutive coronary patients and 1148 controls selected to be similar to cases in terms of gender and age. Traditional risk factors were evaluated according to the international criteria. The genetic variants were analyzed with specific primers and the GRS was determined in the population, based on 29 genetic variants previously associated with atherosclerotic disease in general and, in particular, with CAD. A multiplicative model was then used based on risk multiplication (OR) of each genotype of the 29 studied variants. Subsequently, a multivariate analysis was done only with the TCRF or with the TCRF plus GRS. A ROC curve was constructed for both settings.

Results: After multivariate analysis, the GRS was found to be an independent predictor for CAD (OR=1.5). The AUC increased from 0.71 to 0.74 after the inclusion of GRS to the TCRF in the multivariate analysis (Figure).

Conclusions: In our population, the multiplicative GRS was an independent predictor for CAD. When analyzed together with traditional risk factors, it adds little predictive value. Its usefulness, in clinical practice, may be directed to the intermediate risk group, in which a possible risk reclassification can have different therapeutic measures.

PS963 | BEDSIDE
Changes in the Framingham 10-year risk of cardiovascular disease and the European 10-year risk of fatal cardiovascular disease in a large untreated urban population
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Background: Screening of cardiovascular risk factors (CVRFs) is of importance and may lead to detect them and improve patients’ life expectancy and functional status. However, surveys measuring effectiveness in reducing CVD incidence have yielded equivocal findings. The aim of this study was to assess the changes in the Framingham 10-year risk of cardiovascular disease and the European 10-year risk of fatal cardiovascular disease in a large untreated urban population.

Methods: Between 2007 and 2012, we conducted a screening campaign for CVRFs in men aged 40 to 65 yrs and women aged 50 to 70 yrs in the west suburb of Paris. Data were complete for 20,324 participants of which 14,709 were untreated. We systematically calculated the Framingham 10-year risk of cardiovascular disease and the 10-year risk of fatal cardiovascular disease based on the European Systematic COronary Risk Evaluation (SCORE).

Results: The prevalence trend over six years significantly decreased for hyper- tension (p<0.002 in men and p<0.001 in women) and for tobacco smoking in men (p<0.0001). We observed a significant decrease in the mean Framingham 10-year risk from 13.3±6.2 in 2007 to 11.7±9.0 in 2012 in men and from 8.0±4.1 in 2007 to 5.9±3.4 in women (both p<0.0001). The 10-year risk of fatal CVD (SCORE) showed a significant decrease in men and in women (1.2±1.1 in 2007 and 0.6±0.7 in 2012, p<0.0001).

Conclusions: Our screening campaign found a significant decrease of the 10-year risk of cardiovascular disease, measured by Framingham or SCORE methods. These results suggest that community prevention programs may improve the control of CVRFs with a potential impact of prognosis in a general population.

P9564 | BEDSIDE
Additional value of a combined genetic score to Framingham risk score
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Cardiovascular risk stratification has included traditional risk factors as smoking, cholesterol and blood pressure adjusted to age and gender. The utility of genetic risk scores as independent risk predictors remains inconclusive.

Aim: Evaluate the ability of a multiloci genetic score (GS) to provide additive value to Framingham 10 years risk score (FS) to predict coronary arterial disease (CAD).

Methods: Case-control study of 2555 individuals: 1321 (51.7%) coronary patients and 1234 (48.3%) controls matched for age and gender divided in three groups according to FS (FS<5%, FS 5%-20% and FS>20%). The multiloci GS was determined with specific primers of 29 different genetic variants associated with atherosclerotic disease. ROC curves and area under curve (AUC) were performed using the traditional risk factors (TRF) and repeated adding GS.

Results: By multivariate analysis GS was an independent predictor for CAD (OR=2.05, 1.66–2.45, p<0.0001) Diabetes, arterial hypertension, dyslipidemia and smoking (OR=3.07, 2.47–3.80; OR=2.07, 1.73–2.49; OR=3.1, 2.37–4.07; OR=3.11, 2.58–3.74); all p<0.0001) were also independent CAD predictors. GS also added predictive value to TRF across all risk subgroups. In individuals within low risk (FS<5) the AUC increased from 0.76 to 0.77, in intermediate risk (FS 5–20) increased from 0.70 to 0.73 and in the high risk (FS>20) subgroup the TRF prediction was lower (AUC=0.68) increasing to 0.72 after the inclusion of the GS.

Conclusions: In our population, GS increased the predictive value of traditional risk factors across all FS risk subgroups. GS proved a better incremental value in intermediate and high risk subgroups. In these subgroups of patients, the inclusion of genotyping may be considered to better stratify cardiovascular risk.

P9565 | BEDSIDE
Clinical Impact of Ankle Brachial Index in patients undergoing successful PCI
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Purpose: To examine the utility of Ankle-Brachial Index (ABI) on major adverse cardiovascular events (MACE) in patients undergoing percutaneous coronary intervention (PCI).

Methods: The subjects were 2052 patients who underwent successful PCI at our institution from July 2007 to May 2010 and simultaneously performed ABI. Of them, we excluded 39 patients due to lack of ABI, 121 patients who underwent previous endovascular therapy for peripheral artery disease or previous surgery for abdominal aortic aneurysm, and 1 patient who did not have sufficient data. Finally, we analyzed 1891 patients and investigated the relationship between ABI and MACE (all-cause death, myocardial infarction, or stroke) in patients who underwent successful PCI.

Results: The mean follow interval was 42.4±13.7 months. MACE occurred in 250 patients (13.2%). At 4 years, compared with normal ABI group, low ABI (<0.90) and high ABI (≥1.40) group had significant worse MACE rates (normal 11.4%, low 32.0%, high 28.8%, log-rank p<0.0001). After adjustment, low ABI was still significant predictor for MACE (Hazard ratio (HR) 2.23 [1.66–2.98], p<0.0001).

Conclusion: High ABI also had a tendency to be a risk factor of MACE, however it was not
significant (HR 2.07 [0.91–4.09], p=0.08). The HRs for MACE for different levels of ABI compared with a reference ABI of 1.21–1.30 formed a U-shaped curve.

**ANTI-TROMBOTICS IN CLINICAL PRACTICE**

**PS966 | BEDSIDE**

Treatment with clopidogrel reduces major amputation after endovascular therapy in hemodialysis patients with critical limb ischemia

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**Background:** Clopidogrel, a selective inhibitor of phosphodiesterase 3, has been reported to have beneficial effects on preventing limb events in peripheral artery disease (PAD) patients. However, for PAD patients undergoing endovascular therapy (EVT), the role of clopidogrel is not well understood.

**Methods:** This study compared clopidogrel with ticagrelor in patients undergoing EVT. The primary endpoint was major amputation at 1 year post-EVT. Adjustments were made for baseline differences.

**Results:** The study included 193 patients randomized to clopidogrel and 189 patients to ticagrelor. The primary endpoint, major amputation, was significantly lower in the ticagrelor group (HR 0.48 [0.28–0.82], p=0.004). Other endpoints also favored ticagrelor, with a reduction in the risk of stroke and death.

**Conclusions:** Ticagrelor is a more effective antiplatelet agent compared to clopidogrel in patients undergoing EVT for critical limb ischemia.

**PS968 | BEDSIDE**

Long-term safety and efficacy of evolocumab in patients with statin intolerance

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**Purpose:** To assess the long-term safety and efficacy of evolocumab in patients who discontinued statins due to intolerance.

**Methods:** This was a long-term follow-up study of patients who discontinued statins due to intolerance. Patients were randomized to either evolocumab or placebo in a blinded manner.

**Results:** A total of 492 patients were enrolled. At 1 year, the reduction in low-density lipoprotein cholesterol (LDL-C) was maintained, with a mean reduction of 56% compared to baseline. The most common adverse events were muscle aches and tenderness.

**Conclusions:** Evolocumab is safe and effective in patients who discontinued statins due to intolerance, maintaining the benefits observed in short-term studies.

**Table 1. Safety and efficacy summary**

<table>
<thead>
<tr>
<th>Safety outcome</th>
<th>Open-label extension randomised group</th>
<th>Evolocumab + SoC (n=251)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C (mg/dL)</td>
<td>110 (9.0, 12.9)</td>
<td>110 (9.0, 12.9)</td>
</tr>
<tr>
<td>Patients who discontinued the study, n (%)</td>
<td>8 (3.2)</td>
<td>16 (4.2)</td>
</tr>
<tr>
<td>Any AE</td>
<td>99 (75.6)</td>
<td>191 (76.1)</td>
</tr>
<tr>
<td>AE leading to drug discontinuation</td>
<td>5 (3.8)</td>
<td>9 (3.6)</td>
</tr>
<tr>
<td>Muscle-related events, n (%)</td>
<td>40 (15.3)</td>
<td>35 (13.9)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>11 (8.4)</td>
<td>21 (8.4)</td>
</tr>
<tr>
<td>Muscular weakness</td>
<td>1 (0.8)</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>7 (5.3)</td>
<td>4 (1.6)</td>
</tr>
</tbody>
</table>

**LDL-C (calculated)**

| Phase 2 study baseline, mg/dL | 115 ± 30 (n=38) | 115 ± 30 (n=38) |
| LDL-C change from baseline, % | -42 ± 15 (n=38) | -42 ± 15 (n=38) |

**Conclusions:** Evolocumab maintains its safety and efficacy over long-term use in patients with statin intolerance, with a reduction in LDL-C of 56% at 1 year.

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*OSLER-2 values are from week 48.

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P5969 | BEDSIDE
The effects of optimal medical therapy on coronary plaque
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Background: The results of the COURAGE trial which is a well-known study had a considerable impact on us as interventionists in the circulatory organ area.

Purpose: We evaluated the effects of optimal medical therapy (OMT) on coronary plaque using intravascular ultrasound (IVUS).

Methods: We simultaneously performed IVUS and VH-IVUS on 82 coronary plaque lesions, which were mild stenotic lesions not requiring PCI, in 65 stable angina patients who required PCI and performed qualitative and quantitative assessments. Ten months later, we divided the patients into an OMT group (30 cases, 33 lesions) and a standard treatment group (non-OMT group; 35 cases, 49 lesions) to re-evaluate the therapies using IVUS and VH-IVUS of the target lesions for each of the groups. Plaque regression and compositional change rates were compared between the groups. The OMT group was defined as follows: 1) smoking was allowed (including non-smokers); 2) systolic pressure of 140 or below and diastolic pressure of 90 or below measured both at home and physician’s office were met at least 80% of the time; 3) HbA1c levels were consistently below 7 during follow-up; and (4) LDL cholesterol levels were consistently below 50 mg/dl for at least 300 minimum doses of antiplatelet agents (aspirin or thienopyridine), statins, β-blockers and ACE-inhibitors. Optimal medical treatment was defined if patients used all of these medications. Their primary endpoint was to compare plaque volume regression of the index lesion from baseline to 10 months.

Results: No significant differences were observed between the two groups at baseline. The rates of CHF, MI, stroke, PCI and PRU, and prevalence of bleeding events at 1-month were not significantly different. During follow-up, ischemic events rarely occurred (n=1), but BARC bleeding events were frequently observed (n=69; 24.4%, 7.2% and 0.4% of type 1, 2 and 3 events). In 1-month FU, PRU and Phenotype showed the higher level of platelet reactivity compared with PR10 (p < 0.001). Prevalence to match “therapeutic window” was greater in PRAS and Phenotype than in PRAS (p < 0.001). Compared with PRA10, bleeding risk was reduced in PR5 (HR, 0.75; 95% CI, 0.51 to 1.09) and Phenotype (HR, 0.73; 95% CI, 0.49 to 1.07). In ROC curve analysis, optimal cutoffs for BARC type 1 and BARC type ≥ 2 events were <145 PRU (AUC, 0.638; 95% CI, 0.533 to 0.863; p = 0.011) and ≤ 88 PRU (AUC, 0.645; 95% CI, 0.510 to 0.780; p < 0.001) (Figure: right).

Conclusions: Among ACS patients, compared with prasugrel 10 mg/d, prasugrel 5 mg/d and VerifyNow-based dosing were associated with increase in matching therapeutic window and decrease in bleeding risk. Proposed LPR criteria should be taken into consideration to develop tailored antiplatelet strategy for patients.

P5970 | BEDSIDE
Medical compliance after acute myocardial infarction in the Netherlands
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Purpose: Optimal medical treatment is associated with increased survival and lower rate of new cardiovascular incidents. Current study assess medical compliance one year after acute myocardial infarction between 89 Dutch hospitals.

Methods: In 2008 and 2009, national diagnose-codings of 89 Dutch hospitals were included into the non-OMT group.

Results:

**Compliance:**

- Cardiac care was met at least 80% of the time: 3) HbA1c levels were consistently below 7 during follow-up; and (4) LDL cholesterol levels were consistently below 50 mg/dl for at least 300 minimum doses of antiplatelet agents (aspirin or thienopyridine), statins, β-blockers and ACE-inhibitors. Optimal medical treatment was defined if patients used all of these medications. Their primary endpoint was to compare plaque volume regression of the index lesion from baseline to 10 months.

Conclusions: Among ACS patients, compared with prasugrel 10 mg/d, prasugrel 5 mg/d and VerifyNow-based dosing were associated with increase in matching therapeutic window and decrease in bleeding risk. Proposed LPR criteria should be taken into consideration to develop tailored antiplatelet strategy for patients.

P5971 | BEDSIDE
Fixed-dose (10 mg and 5 mg) versus phenotype-based prasugrel dose to match therapeutic zone with acute coronary syndrome: the A-MATCH trial


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The results of the COURAGE trial which is a well-known study had a considerable impact on us as interventionists in the circulatory organ area.

Purpose: To determine proper dose strategy of P2Y12 inhibitor and develop “therapeutic window” in patients.

Methods: After standard prasugrel therapy, PCI-treated ACS patients were randomized to prasugrel 10mg/d (PRA10), prasugrel 5mg/d (PRAS) or LPR-based dosing (Phenotype) (Figure: left). Pharmacodynamic effects were assessed with VerifyNow (PRU), and prevalence of bleeding events at 1-month was measured using BARC questionnaires. Primary endpoint was percentage to match “therapeutic window in population” (95%-P[RU]<208).

Results: During follow-up, ischemic events rarely occurred (n=1), but BARC bleeding events were frequently observed (n=69; 24.4%, 7.2% and 0.4% of type 1, 2 and 3 events). In 1-month FU, PRU and Phenotype showed the higher level of platelet reactivity compared with PR10 (p < 0.001). Prevalence to match “therapeutic window” was greater in PRAS and Phenotype than in PRA10 (p < 0.001). Compared with PRA10, bleeding risk was reduced in PRA5 (HR, 0.75; 95% CI, 0.51 to 1.09) and Phenotype (HR, 0.73; 95% CI, 0.49 to 1.07). In ROC curve analysis, optimal cutoffs for BARC type 1 and BARC type ≥ 2 events were <145 PRU (AUC, 0.638; 95% CI, 0.533 to 0.863; p = 0.011) and ≤ 88 PRU (AUC, 0.645; 95% CI, 0.510 to 0.780; p < 0.001) (Figure: right).

Conclusions: Among ACS patients, compared with prasugrel 10 mg/d, prasugrel 5 mg/d and VerifyNow-based dosing were associated with increase in matching therapeutic window and decrease in bleeding risk. Proposed LPR criteria should be taken into consideration to develop tailored antiplatelet strategy for patients.
95% CI 1.2–8.0; p=0.02); all other factors (DOAC pretreatment, HASBLED, anti-platelet therapy, procedural details) were not associated with the occurrence of bleeding events (p<0.05).

Conclusions: Peri-procedural complications are rare and bridging therapy is uncommon in patients with direct acting oral anticoagulants undergoing cardiac catheterisation. Independent risk factors for bleedings are the use of heparins during OAC interruption, a history of bleeding and procedural details.

**MANAGEMENT IN HEART FAILURE: NEW PERSPECTIVES**

**P5974 | BEDSIDE**

Influence of angina and revascularization in patients with left ventricular systolic dysfunction and coronary artery disease: insights from the STICH trial

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Introduction: The effect of angina on disease outcome is still a matter of debate. We aimed to determine whether angina is associated with a worse prognosis in patients with left ventricular systolic dysfunction.

Methods: A total of 3063 patients (1531 with angina) were enrolled in the STICH trial. Patients were categorized according to presence or absence of angina using the Canadian Cardiovascular Society (CCS) Grading Scale at baseline and each follow-up visit. Patients were categorized according to presence or absence of angina if CCS ≥1. We used multivariable Cox models to assess the association between CABG vs. MED and outcomes in patients with and without angina. To ascertain relation between CABG vs. MED and presence of angina at follow-up, we modeled a multivariable logistic regression model associating ≥1 CCS grade improvement as dependent variable.

Results: At baseline, 770 patients (64%) reported angina and 442 patients (36%) reported no angina. Among patients assigned to MED, mortality rates were similar in patients with and without angina (HR=1.05; 95% CI [0.79–1.38]). All-cause mortality was similar in patients assigned to CABG compared to MED whether they had angina (HR=0.89; 95% CI [0.71–1.13]) or not (HR=0.68; 95% CI [0.50–0.94]] (p interaction=0.14). When cross-overs were considered, CABG reduced mortality in patients with and without angina (HR=0.67; 95% CI [0.53–0.83] and HR=0.54; 95% CI [0.43–0.71], respectively). Composite of all-cause death or rehospitalisation was lowered in patients assigned to CABG whether they had angina (HR=0.78; 95% CI [0.66–0.93]) or not (HR=0.80; 95% CI [0.64–1.00]). Patients who reported angina before CABG were more likely to improve their symptoms with CABG (odds ratio, 1.43; 95% CI, 1.11 to 1.83; p<0.01).

Conclusions: Angina does not predict death in medically treated patients, nor does it identify patients with LV dysfunction and CAD that are more or less likely to benefit from CABG. However, CABG improves anginal symptoms to a greater extent than MED alone. These findings may influence clinical practice by diminishing the relevance of angina for treatment decisions and prognostication in patients with ischemic cardiomyopathy.

**P5975 | BEDSIDE**

Adherence to treatment guidelines and its association with clinical outcomes in chronic heart failure patients

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Background: Heart failure is a common disease characterized by high mortality and frequent exacerbation resulting in repetitive re-hospitalization. Pharmacological treatments—indicated in the chronic heart failure (CHF) treatment guidelines published by Japan Circulation Society—are reported to be effective. However, no large-scale study has evaluated adherence to the guidelines and its effects on outcomes.

Purpose: We aimed to investigate adherence to the CHF guidelines for drug therapy and the association between adherence and re-hospitalization in Japanese CHF patients.

Methods: We included CHF patients with records of New York Heart Association (NYHA) class at the first hospitalization in a prescription database of Japanese acute hospitals. Adherence was evaluated using class adherence indicator (CAI)—defined as the proportion of patients prescribed at least 1 drug from each class recommended in the guidelines—and global adherence indicator (GAI). For each patient, we calculated the GAI-5 value, which is the proportion of indicated care (across all five therapeutic classes) that was prescribed. Patients were categorized into 3 groups based on the GAI-5 values (good, 100%; intermediate, 50–80%; poor, <40%). We performed a Cox proportional hazard analysis to identify risk factors associated with poor prognosis.

Results: In total, 533 CHF patients (mean age, 74.4 years; 54.6% men; NYHA class I, 9.6%; II, 30.7%; III, 31.5%; IV, 28.2%) were eligible for analysis. CAI for angiotensin-converting enzyme inhibitors or angiotensin receptor blocker was 63.6% (such patients were termed ‘adherers’). Of the patients, 89.7%, 61.0%, 58.2%, and 22.0% showed adherence to diuretics, beta-blockers, mineralocorticoid receptor blockers, and digitalis, respectively. Furthermore, 20.0%, 58.4% and 21.5% showed good, intermediate, and poor adherence, respectively. Kaplan-Meier curves with the log-rank test revealed that risks for re-hospitalization due to CHF worsening or due to any other cause within 360 days of discharge were higher in those with lower GAI-5 values.

Conclusions: To our knowledge, this is the first large-scale study on adherence to the Japanese CHF guidelines for treatment and its effects on outcomes. Similar to the reports of previous studies, CHF treatment in Japanese patients remained suboptimal. Our results suggest that poorer adherence to the guidelines may result in higher re-hospitalization rates. Thus, optimal pharmacological therapies that are in accordance with the latest guidelines are necessary to improve clinical outcomes in CHF patients.

**P5976 | BEDSIDE**

Clinical outcomes and benefit of ambulatory pulmonary artery pressure monitoring in heart failure patients according to initial pulmonary artery diastolic pressure

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Background: Higher intracardiac filling pressures may identify heart failure (HF) patients at increased risk for hospitalization or death and represent a therapeutic target.

Results: In total, 533 CHF patients (mean age, 74.4 years; 54.6% men; NYHA class I, 9.6%; II, 30.7%; III, 31.5%; IV, 28.2%) were eligible for analysis. CAI for angiotensin-converting enzyme inhibitors or angiotensin receptor blocker was 63.6% (such patients were termed ‘adherers’). Of the patients, 89.7%, 61.0%, 58.2%, and 22.0% showed adherence to diuretics, beta-blockers, mineralocorticoid receptor blockers, and digitalis, respectively. Furthermore, 20.0%, 58.4% and 21.5% showed good, intermediate, and poor adherence, respectively. Kaplan-Meier curves with the log-rank test revealed that risks for re-hospitalization due to CHF worsening or due to any other cause within 360 days of discharge were higher in those with lower GAI-5 values.

Conclusions: To our knowledge, this is the first large-scale study on adherence to the Japanese CHF guidelines for treatment and its effects on outcomes. Similar to the reports of previous studies, CHF treatment in Japanese patients remained suboptimal. Our results suggest that poorer adherence to the guidelines may result in higher re-hospitalization rates. Thus, optimal pharmacological therapies that are in accordance with the latest guidelines are necessary to improve clinical outcomes in CHF patients.
Purpose: Assess clinical outcomes and efficacy of pulmonary artery (PA) pressure monitoring in HF patients with reduced (HFrEF) or preserved (HFpEF) ejection fraction according to initial PA diastolic pressure (PAD).

Methods: CHAMPION randomized patients with HFrEF (<40%, n=430) or HFpEF (<40%, n=119) to HF management with or without longitudinal guidance from a implantable PA pressure sensor. Clinicians had access to initial pressure measurements for all patients. The association between baseline PAD and risk of HF hospitalization (HHF) or death during the randomized access period and the interaction between baseline PAD and the efficacy of PA pressure-guided therapy were examined using the Andersen-Gill model.

Results: Over median follow-up of 18 months, there were 461 HHF hospitalizations (373 in HFrEF, 88 in HFpEF) and 114 deaths (93 in HFrEF, 21 in HFpEF). Median baseline PAD for HFrEF was 19 mm Hg (IQR 14–25) and for HFpEF was 15 mm Hg (IQR 11–20). For the entire population, higher baseline PAD was associated with higher risk for HHF and death even after adjustment for clinical predictors (HR 1.03 per 1 mm Hg, p=0.001). Baseline PAD above the median was associated with higher risk for HHF and death in patients with HFrEF (adjusted HR 1.93, 95% CI 1.55–2.40, p<0.001) and HFpEF (adjusted HR 2.10, 95% CI 1.26–3.49, p=0.004). For any PAD at baseline, PA-pressure guided management reduced the risk of HHF and death (Figure).

Conclusions: Higher PAD at baseline enhances risk for HHF and death in both HFrEF and HFpEF. HF management guided by ongoing PA pressure monitoring reduces HHF and death at all levels of baseline PAD.

PS977 | BEDSIDE
The effect of disease management on health-related quality of life and depression symptoms in patients with heart failure: A randomized controlled trial
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Purpose: To study the effect of a disease management (DM) program on health related quality of life (HRQoL) and depression symptoms during follow-up in heart failure (HF) patients.

Methods: Patients with HF [N=1,360; 27.5% women; mean age (SD) 71 (11) years], recruited either from the community or after recent hospital admission for HF exacerbation, were randomly assigned to DM group (N=682) or usual care (UC) control group (N=678). Patients assigned to DM were cared by multidisciplinary teams of cardiologists and nurses operating in ten HF centers and a central call center. The primary composite outcome of the trial was time-to-first hospital admission for HF exacerbation or death from any cause. HRQoL was measured with the short form (SF) 36-health survey and depression symptoms with the patient health questionnaire (PHQ-9). At baseline and every 6 months during follow-up. Adjusted odds ratios (ORs) for attaining a ≥2.5 points increase from baseline (minimal clinically important difference) in the physical component summary (PCS) and mental component summary (MCS) of SF-36 and having a PHQ-9 score ≥10 during follow-up, were calculated.

Results: Patients were followed for a median period of 2.7 years (range: 0–5). DM was not found to be superior to UC with respect to the primary composite outcome. Compared to patients assigned to UC, patients assigned to DM were more likely to attain a ≥2.5 points increases in PCS and MCS at SF-36, and less likely to have depression symptoms (PHQ-9 score ≥10) during follow-up; ORs (95% CI): 1.53 (1.16, 2.01), 1.57 (1.25, 1.97), and 0.69 (0.53, 0.90), respectively; adjusted for baseline score, age, sex, study center and study period, year at recruitment, baseline NYHA classification and 6-minute walking distance. The odds of attaining a ≥2.5 points increases in PCS and MCS, and a PHQ-9 score ≥10 during follow-up was positively associated with greater baseline 6-minute walking distance. Female sex was associated with lower HRQoL scores compared to men.

Conclusions: DM program improved significantly HRQoL and depression symptoms in HF patients.
However, the cost of each hospitalization was not significantly different (DMP: $3320.00±2785.00 vs. control: $4218.00±$4519.00), (P<0.14). The primary outcome of all cause readmissions at 6 months was significantly lower in the DMP (28.2% DMP group vs. 57.5% control group) (P<0.001). The secondary outcome of all cause mortality tends to be lower at 6 months in the DMP vs. control (99.9% vs. 99.0% respectively) (P<0.08). A multivariate analysis for the predictors of the readmissions at 6 months was only significant for the DMP vs. the control group (Adjusted OR (95% CI): 0.26 (0.12–0.56); (P=0.001). The use of digoxin and dopamine was associated with higher mortality (P<0.009).

Conclusion: A HF DMP that entails close follow-up after discharge with education, diet and exercise will decrease all cause readmission rates at 6 months and tends to lower mortality when compared to regular care.

TREATMENT OF HYPERCHOLESTEROLEMIA. A VISION TO THE FUTURE

PS5980 | BEDSIDE
Sustained treatment effect of alirocumab on Lp(a): pooled analyses from 4,915 patients in ten phase 3 trials in the ODYSSEY program
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Background: Lipoprotein (a) [Lp(a)] is an independent risk factor for cardiovascular (CV) disease. Current treatment options for elevated Lp(a) levels are limited. Statins have not shown any effect on Lp(a).

Purpose: To evaluate the treatment effect of alirocumab on serum Lp(a) using data from 10 Phase 3 trials of 24–78 week duration, conducted in patients with heterozygous familial hypercholesterolemia, high CV risk, and/or statin intolerance, as monotherapy or on a variety of background lipid-lowering therapies (LLTs).

Methods: Pooled analyses were conducted across 2 trials (LONG TERM, HIGH FH) and 8 trials with 2,429 patients receiving alirocumab 150 mg every 2 weeks (Q2W) versus placebo and 8 trials that evaluated alirocumab 75 mg Q2W (increasing to 150 mg Q2W at Week 12 if LDL-C goals not achieved at Week 8) versus control. In 5 trials (COMBO II, OPTIONS I and II, ALTERNATIVE and MONO, n=1,456) the comparator was ezetimibe and in 3 trials (COMBO I, FH I and II, n=1,043) the comparator was placebo.

Results: After 24 weeks, Lp(a) levels were reduced from baseline by 25% with alirocumab 150 mg Q2W (vs. control) and by up to 23.5% (Week 12, vs. control) in studies using 75 mg Q2W (p<0.0001; Table). Reductions were observed at Week 12 and sustained through the end of the observation period (either Week 24 or 52, depending on the study). Treatment-emergent adverse event (TEAE) rates were generally similar between alirocumab and control patients. Common TEAEs in alirocumab-treated patients include influenza, headache, myalgia, and myopathy: an updated (2015) meta-analysis of randomized controlled trials.

Conclusion: Across the ODYSSEY program, alirocumab therapy resulted in a significant reduction in Lp(a) maintained for at least 1 year inde-

PS5981 | BEDSIDE
Futility of supplementation with Coenzyme Q10 for statin-induced myopathy: an updated (2015) meta-analysis of randomized controlled trials
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Introduction: Coenzyme Q10 (CoQ10) is a key antioxidant and coenzyme for energy production. It is used as a dietary supplement to protect against statin-induced myopathy, which is the most common myopathy of statin use. A previous meta-analysis has not suggested any benefit of CoQ10 supplementation in improving statin-induced myopathy, even using higher CoQ10 doses.

Purpose: To re-evaluate the efficacy of CoQ10 supplementation on SIM.

Methods: We searched the MEDLINE, Cochrane Library, Scopus, and EMBASE databases (up to 10 February 2015) to identify RCTs investigating the impact of CoQ10 on muscle pain and plasma CK activity.

Results: We included 10 RCTs with 446 participants. The results of the meta-analysis did not provide compelling evidence as to a significant effect of CoQ10 supplementation in reducing either the severity of myopathic pain (SMD: 0.36, 95% CI: -0.82–0.09, p=0.117) or plasma CK activity (WMD: 0.34 U/L, 95% CI: 0.23–0.46, p=0.290). These findings were robust in the leave-one-out analysis, and the calculated effect sizes were not sensitive to any single study included in the meta-analysis. A sensitivity group analysis was performed to assess the impact of placebo (n=160 vs >200 mg/day) and duration (<12 weeks vs >12 weeks) of supplementation with CoQ10 on the calculated effect sizes. The results suggest that changes in both efficacy measures were independent of dose and duration of supplementation. Likewise, large doses of CoQ10 (-400 and >400 mg) had also no significant effect both on myalgia and plasma CK activity (SMD: 0.45, 95% CI: -1.02–0.13; p=0.13 and 0.08; 95% CI: -0.52–0.36; p=0.721, and WMD 5.06 U/L, 95% CI: -5.34–15.46; p=0.34, and -3.52 U/L _72.04–65.00; p=0.92, respectively).

Conclusion: The results of this meta-analysis support the lack of any significant benefit of CoQ10 supplementation in improving statin-induced myopathy, even using higher CoQ10 doses.

PS5982 | BEDSIDE
Effect of K-877, a potent and selective PPAR alpha modulator (SPPARalpha), on cholesterol efflux from macrophages in dyslipidemic patients
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Introduction: Plasma concentration of high-density lipoprotein cholesterol (HDL-C) is inversely associated with the risk of atherosclerotic cardiovascular disease (ASCVD). The protection against atherosclerosis is largely mediated by stimulating the removal of cholesterol from macrophages by HDL and its component, APOA1. K-877 is a potent and selective peroxisome proliferator-activated receptor alpha (PAPARalpha) modulator, which improves lipids profiles including HDL-C. APOA1 and APOC3. Here, we hypothesized that K-877 increases cholesterol efflux capacity (CEC), which could be translated into ASCVD risk reduction.

Purpose: To investigate whether CEC is increased by K-877 in dyslipidemic pa-

Methods: This was a double-blind, randomized cross-over study. A total of 33 dyslipidemic patients with fasting hypertriglyceridemia (≥150, <400 mg/dL) and low HDL-C (<40, ≥50 mg/dL for males, <50, ≥55 mg/dL for females) were randomized to twice-daily, K-877 0.4 mg/d or placebo groups for 4 weeks. Each group was switched to the other treatment group and treated for another 4 weeks. Plasma lipids, lipoproteins, apolipoproteins and pref-1-HDL were measured. CEC was measured by validated method; after pre-labeling with [3H] cholesterol, J774 cells were incubated with a media containing HDL fraction isolated by ultracen-
trigitation from the patients. CEC was calculated from the ratio of [3H] cholesterol quantity in the LDL fraction.

Results: Treatment with K-877 increased HDL-C and ApoA1 and decreased ApoC3 from the baseline (16.1, 8.34 and −31.35%, respectively; p < 0.01), but placebo did not. Treatment with K-877 also increased HDL-C and pref1-HDL from the baseline (28.3 and 37.36%, respectively; p < 0.01), but placebo did not.

HPLC analysis showed that K-877 increased medium, small and very small HDL-C (22.34, 37.90 and 23.69%, respectively) and reduced large and very large HDL-C (−47.58 and −11.45%, respectively). HDL from patients treated with K-877 stimulated CEC more than that with placebo (2.57%, p < 0.045). Positive correlation with CEC was observed in HDL-C and ApoA1.

Conclusions: This study revealed that K-877 exerted a positive influence on HDL-C in both quantity and quality based on the assessment on ApoA1, ApoC3 and ApoC1 levels. However, the suggestion that K-877 could reduce the risk of increasing CEC along with an increase of ApoA1, pref1-HDL and HDL-C to this degree is known. Thus K-877 may inhibit the progression and even promote the regression of atherosclerosis.

P5983 | BEDSIDE
K-877, a selective PPAR alpha modulator (SPPARM alpha), ameliorates dyslipidaemia in patients with well-controlled LDL Cholesterol levels on statin therapy, without increases in serum creatinine
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Background: Patients treated with statins, particularly those with elevated TG and reduced HDL-C, are still at risk of cardiovascular disease (CVD) even when LDL-C levels are controlled. Additional therapy is sometimes necessary to alter the lipid profile further, therefore warranted. K-877 is a SPPARM alpha, designed to be highly selective for PPARs, co-administerable with statins, and to modulate PPAR activity without undesirable effects.

Purpose: To assess the efficacy and safety of K-877 in dyslipidemia patients whose LDL-C levels are adequately controlled with statins.

Methods: This was a multi-country, placebo-controlled, randomised, double-blind, parallel-group study in patients on atorvastatin, rosuvastatin or simvastatin with significant residual dyslipidemia. Principal efficacy endpoints were % changes in TG and non-HDL-C, and principal safety endpoints were changes in serum creatinine and homocysteine. Male and female patients with controlled LDL-C were eligible for inclusion if concentrations of TG were 175–500 mg/dL (1.9–5.7 mmol/L) and HDL-C were 50 mg/dL (1.3 mmol/L) or 55 mg/dL (1.4 mmol/L) or less in men and women, respectively. The study was conducted in compliance with the principles of the Declaration of Helsinki.

Results: 408 patients were randomised to 7 treatment groups (placebo, 0.05 mg BID, 0.1 mg BID, 0.2 mg BID, 0.1 mg QD, 0.2 mg QD and 0.4 mg QD and 0.4 mg QD) for 12 weeks. 95.6% of the patients completed treatment. Baseline TG, HDL-C and LDL-C levels were 245.3 mg/dL (median), 39.2 mg/dL (mean) and 88.4 mg/dL (mean), respectively. Compared to placebo, K-877 significantly reduced TG by 9.4–19.5% in all the treatment groups except 0.1 mg QD and LDL-C by 5.2–25.5% in all the treatment groups except 0.05 mg BID. Serum creatinine was not changed significantly in any of the treatment groups. Homocysteine were significantly elevated at 0.2 mg BID and 0.4 mg QD by 2.3 and 2.4 μmol/L, respectively. Adverse events occurred in 56.7% of patients on placebo, but 46.4% of those in the K-877 groups. No other safety concerns were found during this 12-week study.

Conclusion: K-877 was well tolerated by statin-treated subjects with well-controlled LDL-C levels over 12 weeks. K-877 significantly reduced TG, non-HDL-C, remnant cholesterol and Apo CIII without significant increases in serum creatinine.

P5984 | BEDSIDE
Relationship of body weight and dosing of Evolocumab (EVO) for the treatment of hypercholesterolemia
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Background: Recent clinical trials have evaluated monoclonal antibodies (mAbs) directed against proprotein convertase subtilisin/kexin type 9 (PCSK9) (PCSK9-mAbs) as a novel treatment for hypercholesterolemia. Optimal dosing remains a subject of investigation. In particular, the effect of body weight (BW) has been incompletely analyzed.

Purpose: To evaluate whether BW leads to differences in the effects of evolocumab (EVO), an investigational mAb directed against PCSK9.

Methods: Data from eleven Phase 2 and 3 clinical trials were analyzed by quartiles of BW. This data included unpublished information correlating EVO concentration, free PCSK9 levels, LDL-cholesterol response, and adverse events (AEs) by baseline BW. Biweekly versus monthly dosing regimens were separately analyzed.

Results: Circulating concentrations of EVO were highest in patients with the lowest BW and lowest in the highest patients. However, this difference resulted in only minor differences in free PCSK9 levels and no discernible effects on LDL reduction. In all groups, EVO led to robust LDL reductions between 58.0% and 69.1% on top of that achieved by baseline therapy. AEs occurred at similar rates across quartiles of BW.

PKPD data by quartile of body weight

<table>
<thead>
<tr>
<th>Dose</th>
<th>Body weight</th>
<th>EVO conc.</th>
<th>PCSK9</th>
<th>LDL-C</th>
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<td>140 mg b.i.w.</td>
<td>N</td>
<td>1055</td>
<td>1103</td>
<td>1131</td>
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<tr>
<td>39 to 69</td>
<td>11.2 (1.8 to 32)</td>
<td>−79.4 (−95.2 to −39.5)</td>
<td>−69.1 (−92.3 to −33.7)</td>
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</tr>
<tr>
<td>70 to 89</td>
<td>8.3 (1.3 to 32)</td>
<td>−79.4 (−92.6 to −38.7)</td>
<td>−69.9 (−93.6 to −37.4)</td>
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<tr>
<td>90 to 110</td>
<td>4.6 (1.0 to 15.1)</td>
<td>−63.3 (−83.3 to −23.4)</td>
<td>−65.2 (−88.0 to −24.7)</td>
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<tr>
<td>94 to 160</td>
<td>2.7 (1.0 to 10.7)</td>
<td>−56.7 (−89.2 to −30.2)</td>
<td>−62.9 (−87.0 to −16.6)</td>
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<tr>
<td>1040 mg b.i.w.</td>
<td>N</td>
<td>1756</td>
<td>1795</td>
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<tr>
<td>39 to 69</td>
<td>15.9 (3.0 to 45.8)</td>
<td>−52.6 (−86.8 to −22.7)</td>
<td>−63.1 (−85.5 to −28.2)</td>
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<tr>
<td>70 to 89</td>
<td>8.9 (1.8 to 28.1)</td>
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<td>−58.0 (−79.9 to −19.4)</td>
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</tr>
</tbody>
</table>

Median (90% CI) EVO concentration, PCSK9, and LDL-C at week 12.

Conclusion: EVO is a highly efficacious therapy for hypercholesterolemia across patients with different BW. Nonetheless, the lower levels of EVO found in the heaviest patients suggest that these individuals may experience a more rapid increase in LDL-C during delays in dosing or when discontinuing therapy. Therefore, heavier patients may have a narrower time window for optimal dosing.

P5985 | BEDSIDE
K-877, a selective PPAR alpha modulator (SPPARM alpha), improves dyslipidaemia in statin-treated patients with type 2 diabetes mellitus
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Background: Diabetic dyslipidaemia, characterised by elevated levels of TG and remnant cholesterol together with reduced concentrations of HDL-C is common in patients with type 2 diabetes mellitus (T2DM), even on statin therapy, and poses residual cardiovascular disease (CVD). K-877 is a SPPARM alpha, designed to be highly selective for PPARalpha, co-administerable with statins, and to modulate PPAR activity without undesirable effects.

Purpose: To assess the efficacy and safety of K-877 in patients with T2DM who were adequately treated with statins.

Methods: We conducted a post-hoc subgroup analysis of patients with a pre-existing diagnosis of T2DM who participated in a larger multi-country, placebo-controlled, randomised, double-blind, parallel group study in patients in statin therapy and poses residual cardiovascular disease (CVD). K-877 is a SPPARM alpha, designed to be highly selective for PPARalpha, co-administerable with statins, and to modulate PPAR activity without undesirable effects.

Conclusion: K-877, administered for 12 weeks in patients with significant dyslipidaemia despite statin-controlled LDL-C, was well tolerated by patients with T2DM and significantly reduced atherogenic lipids including TG, Apo CIII, remnant cholesterol and non-HDL-C, with no increase in serum creatinine.

P5986 | BEDSIDE
Impaired acetylsalicylic acid antplatelet effects caused by dipyrone (metamizole) comedication can be prevented by order of intake
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Background: Acetylsalicylic acid (ASA) is the backbone of primary and sec-
ordinary prevention of cardiovascular events. Impaired ASA antplatelet effects are associated with increased incidence of events. Acute and chronic pain is frequent in patients with coronary artery disease (CAD). The majority of these patients rely on drugs for pain control. It is known, that non-steroidal anti-inflammatory drugs interact with ASA resulting in inhibition of ASA antplatelet effects. Dipyridamole (metamizole) is a non-opioid analgesic with favorable analgesic and antiplatelet effects. We have recently shown that dipyridine interacts with ASA antplatelet effects.

**Purpose:** We investigated the ASA and dipyridine interaction in patients with CAD and analyzed the drug-drug interaction to develop strategies to prevent the interaction.

**Methods:** We conducted an observational study in 56 CAD patients on permanent ASA medication. 36 of these patients had additional dipyridine medication because of various forms of pain. Furthermore a parallel group trial in twelve healthy individuals was performed to investigate if order of intake influences the incidence of ASA and dipyridine interaction. In-vitro analyses in seven healthy individuals were conducted to investigate the drug-drug interaction. Antplatelet effects were measured by light-transmission aggregometry and thromboxane formation. Dipyridine plasma levels by high-performance-liquid-chromatography.

**Results:** ASA antplatelet effects were sufficient in all ASA treated CAD patients without dipyridine comedication. However residual platelet reactivity despite ASA medication occurred in 50% of ASA and dipyridine comedicated CAD patients. Dipyridine plasma levels coincide with the ASA induced inhibition of thromboxane formation. In-vitro increasement of ASA concentrations restores the inhibited antplatelet effects of ASA. In healthy individuals, ASA medication 30 minutes prior to dipyridine medication prevents the inhibition of ASA antplatelet effects by dipyridine whereas dipyridine medication prior to ASA blunts ASA antplatelet effects.

**Conclusion:** Dipyridine medication inhibits ASA antplatelet effects in CAD patients. This pharmacodynamic drug-drug interaction can be prevented by a strict order of intake with ASA medication prior to dipyridine intake.

**PERCUTANEOUS VERSUS SURGICAL MANAGEMENT OF VALVULAR AORTIC STENOSIS: BOUNDARIES VERSUS OPPORTUNITIES**

6016 | BEDSIDE

**Improved outcomes following TAVI for aortic stenosis in low and intermediate risk high risk patients: results from a multi-center Israeli TAVI registry**

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**Background:** Transcatheter aortic valve implantation (TAVI) for high risk aortic stenosis patients is comparable to surgical replacement. Despite a lack of data regarding the safety and efficacy of TAVI in lower risk patients they are already being treated by TAVI in many countries.

**Aim:** To assess safety and efficacy of TAVI in low risk patients.

**Methods:** Patients undergoing TAVI during 2008–2014 were enrolled (n=1349). Procedural outcomes were adjudicated according to VARC-2 definitions. Patients were stratified according to their STS score into 3 groups: High (STS >6, n=279, 21%), Intermediate (STS 4–6, n=494, 37%) or Low risk (STS <4, n=576, 42%).

**Results:** Low risk patients were younger and more likely to be males compared to intermediate/high risk patients. Baseline characteristics differed significantly between the groups with gradual increase in rates of prior CABG, stroke, PVD, renal failure, COPD and frailty, from low to high risk groups. Low-risk patients were more likely to undergo TAVI via transfemoral route (72% vs. 88% vs. 95%, p<0.0001) and under conscious sedation (59% vs. 72% vs. 81%, p<0.0001). Interestingly, there were no significant differences in the rates of procedural complications apart from bleeding. Short- and long-term mortality (Figure) were significantly lower for intermediate- and even more, for low-risk patients as compared to high-risk patients (p<0.001). Lower mortality for intermediate (HR 0.44, 95% CI 0.29–0.67) and low risk patients (HR 0.27, 95% CI 0.17–0.43) was maintained also after multivariable adjustment.

**Conclusions:** TAVI for intermediate or low risk patients is safe and associated with improved outcome compared to high risk patients. These data support the hypothesis that TAVI may achieve results comparable to surgical AVR also in lower risk patients.

6017 | BEDSIDE

The long-term outcome of patients after TAVI remains un influenced by pacemaker implantation in case of AV-block third degree

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**Introduction:** The transfemoral aortic valve implantation (TAVI) has established itself as a common therapy in patients with severe aortic stenosis and high surgical risk. Currently, different prosthesis types are available. A typical complication is AV block third degree with need for pacemaker implantation (PM). Our aim is to investigate whether the choice of the prosthesis type has an impact on the long-term outcome of patients.

**Methods:** From July 2008 to February 2014 560 TAVIs have been implanted at our Heart Center. 48.9% (n=269) received a Medtronic Core Valve (CV), 44.3% (n=248) an Edwards Sapien XT (SA), 4.8% (n=27) a Direct Flow, 2, 3% (n=13) a Portico and 0.5% (n=3) an Edwards Sapien S3. In 15.4% (n=86) of the patients the implantation of a pacemaker was indicated due to intracardiac conduction disturbances. The patients were followed during routine clinic visits and received a pacemaker inspection with regard to the existence of an intrinsic rhythm (Ventricular pacing (VP) <50%). Additionally, a Kaplan-Meier survival analysis was performed.

**Results:** The 1-year mortality rate for patients with CV and SA is up to 15.0%. The mortality in the group of SA with PM, containing a small-sized number of cases, is slightly higher but not significantly different after 1 year and is balanced after 2 years. In 53% of the patients the intrinsic AV conduction recovered. There was no significant difference in the valve type between patients with or without recovering intrinsic AV conduction. The prosthesis diameter showed significant difference between these two groups. The smaller the valve diameter of the used valve prosthesis, the higher was the amount of patients with an intrinsic activity in the follow-up (p=0.046).

**Conclusions:** The long-term outcome seems to be independent of the type of prosthesis (SA vs. CV) and the presence of a pacemaker. The recovery of the AV node function due to perinterventional AV block applies to more than half of the patients and appears to be mainly dependent on the prosthesis diameter but not the valve type.

6018 | BEDSIDE

Outcomes from surgical para-valvular leak repair versus percutaneous closure


**Background:** Para-valvular leak (PVL) is a complication after valve replacement surgery due to incomplete apposition from the suture ring to the native tissue. It has an incidence of 2–10% and 7–17% in the aortic and mitral position respectively. It has serious clinical consequences such as heart failure and hemolytic anemia. Redo-surgery mortality is high (10–15%), and rises even more with the number of previous sternotomies. Percutaneous treatment of PVL has emerged during last years as an alternative to surgery.

**Purpose:** To compare the in-hospital and one-year outcomes between surgical and percutaneous treatment of isolated PVL.

**Methods:** Patients who underwent either surgery or percutaneous treatment for PVL were included in the study. Those with additional surgical or percutaneous treatment other than isolated PVL were excluded from the analysis.

**Results:** Between 2006 and 2014 a total of 35 patients (mean age of 69.5±18.2 years and 43% of males) were included in the study. Of those, 18 (52%) and 17 (48%) underwent percutaneous and surgical techniques respectively. Among them, 10 (28.5%) were located in the aortic and 25 (71.5%) in the mitral valve without differences between groups. Similarly, no differences in age, gender, cardiovascular risk factors, left ventricular ejection fraction, renal function and pulmonary pressure were observed among groups. Euro-score 2 was 20.1±18.9 and 14.7±25 in the percutaneous and surgical group respectively, p=0.124. Successful treatment was achieved in all percutaneous patients and 94.1% of those with surgical techniques. In-hospital mortality was 5.5% in the percutaneous branch and 29.4% in the surgical group; p=0.061. Patients with percutaneous techniques had a shorter in-hospital admission than those surgically treated (6.0±6.5 vs. 32.5±33.0 days; p<0.004). At one year follow-up, cardiovascular mortality was lower in the percutaneous group (5.5% versus 31.2%; p=0.05). In addition, re-intervention rates were 5.8% and 27.3% in the percutaneous and surgical groups respectively, p=0.114.

**Conclusions:** In this series of patients, percutaneous treatment of isolated PVL...
Background: There are several scoring systems available for risk stratification in cardiac surgery, the most important of which are the EuroSCORE-II, the STS-PROM and the American College of Cardiology/ American Heart Association (ACC/AHA) score. However, in patients undergoing TAVI these scores have shown only a low accuracy for predicting both mid- and long-term all-cause mortality. Postoperative acute kidney injury significantly worsens prognosis after TAVI. We aimed to assess the prognostic value of ACEF-7, a new score which includes the highest creatinine level detected within 7 days after the procedure, in predicting 6-month and 1-year mortality after TAVI.

Methods: 253 consecutive patients undergoing transcatheter aortic valve replacement (transmembrane n=210; transfenstral n=43) were enrolled. ACEF score, EuroSCORE II, STS score were calculated pre TAVI for all enrolled patients. ACEF-7 was calculated for all 1-week survivors (n=245, 97%) based on peak creatinine values post TAVI. The first analysis compared established scores (EuroSCORE-II, STS, ACEF) for all-cause mortality at 6-month and 1 year. In a second analysis we compared the predictive value of ACEF-7 to all the other scores for the same outcome. Patients were further stratified according to tertiles of ACEF-7.

Results: Overall mortality at 6 months and 1-year was 6.7% and 19% accordingly. The Euro-Score II, STS Score, and ACEF showed similar low accuracy for prediction of mortality at 6-month (AUC: 0.638±0.07; 0.632±0.01 and 0.664±0.01 respectively) and 1-year mortality (AUC: 0.635±0.01; 0.625±0.02 and 0.672±0.02 respectively).

In survivors at 1 week post TAVI (n=245) only ACEF scores showed significant accuracy in prediction of 6-month (AUC: 0.648±0.009) and 1-year mortality (AUC: 0.674±0.007). Most importantly, the ACEF-7 score further improved this predictive validity for all-cause mortality at 6 month (AUC: 0.742±0.001) and 1 year (AUC: 0.750±0.001) as compared to the ACEF score. Multivariate analysis demonstrated that ACEF-7 was an independent predictor of both 6-month (HR: 1.70; CI: 1.052-2.75; p=0.03) and 1-year mortality (HR 2.28; CI: 1.55–3.363; p<0.001).

Finally the predefined tertiles of ACEF-7 allowed an accurate risk stratification with a predicted 6-month survival of 91.1% in the ACEF-7mid tertile and of 65.7% in the ACEF-7high tertile. Most interestingly, ACEF-7 score further improved this predictive validity for all-cause mortality at 6 month (AUC: 0.742±0.001) and 1 year (AUC: 0.750±0.001) as compared to the ACEF score. Multivariate analysis demonstrated that ACEF-7 was an independent predictor of both 6-month (HR: 1.70; CI: 1.052-2.75; p=0.03) and 1-year mortality (HR 2.28; CI: 1.55–3.363; p<0.001).

Conclusions: The ACEF-7 score improves accuracy of mid and long term predictability of all-cause mortality beyond the currently used scores in patients undergoing TAVI.

Impact of right ventricular dysfunction on short- and long-term mortality for the PM implanting transcatheter aortic valve implantation

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Introduction: Impaired right ventricular (RV) function is an established predictor of adverse events after open-heart surgery for treatment of left-sided heart valve disease. The relevance of RV dysfunction on clinical outcomes following transcatheter aortic valve implantation (TAVI) is unknown.

Methods: Before undergoing TAVI for treatment of symptomatic severe aortic stenosis, 273 unselected patients had quantitative assessment of RV function by transthoracic echocardiography using tricuspid annular plane systolic excursion (TAPSE) and/or tricuspid annular velocity by Doppler tissue imaging (DTIV). The patients were divided into two groups: normal RV function (TAPSE>16 mm and/or DTIV>14 cm/s, n=190) and RV dysfunction (TAPSE<16 mm and/or DTIV<10 cm/s, n=83). Primary endpoints were all-cause and cardiovascular mortality at 30 days and 1 year.

Results: RV dysfunction was detected in 83/273 patients (30%). At baseline, patients with RV dysfunction were at higher surgical risk (mean STS score 9.7±7.5 vs. 6.8±4.6; p<0.001), had lower LVEF (42% vs. 54%; p<0.001) and had more often untreated coronary artery bypass grafting (18% vs. 6%; p=0.008). Concomitant moderate or severe mitral regurgitation was detected in 43% of patients with impaired RV function as compared to 20% of patients with normal RV function (p<0.001). Right heart catheterization revealed significantly higher pulmonary artery pressures in the RV dysfunction group (mean PA pressure 39 vs. 32 mmHg; p<0.001). After multivariable adjustment, higher rates of all-cause (4% vs. 13%; HR 3.44, 95% CI 1.25–9.45; p=0.017) and cardiovascular mortality (3% vs. 12%; HR 3.84, 95% CI 1.40–10.34; p=0.011) were observed at 30 days among patients with RV dysfunction. However, this difference was no longer significant at 1 year of follow-up.

Conclusion: Patients with RV dysfunction as determined by transthoracic echo-cardiography at baseline have higher short-term, but not long-term mortality after TAVI. This observation may have important implications for patient selection and peri-procedural management.
6023 | BEDSIDE
Prognostic effect of permanent pacemaker implantation on mortality after transcatheter aortic valve replacement


Background: Transcatheter aortic valve implantation (TAVI) is now an established treatment for high-grade aortic valve stenosis in patients found unfit for open heart surgery, but has been shown to cause cardiac conduction disorders requiring permanent pacemaker (PPM) implantation. Long-term effect of PPM implantation in this setting remains ambiguous.

Purpose: To investigate the association between post-TAVI PPM implantation and long-term all-cause mortality.

Methods: In a single-center study, we included 168 consecutive patients who underwent TAVI from 2008 to 2012 and were followed until mid-2014. Patient characteristics, ECGs (prior to and within 4 days of TAVI) and PM data were collected retrospectively through electronic medical records. Kaplan-Meier plots and Cox regression analysis were performed.

Results: 40 subjects were excluded due to PPM prior to TAVI or missing ECGs, leaving 128 patients for final inclusion. 41 (32%) patients received a PPM (mean age 82 vs. 80 in patients without PPM, p=0.06) within 30d of the TAVI procedure. The PO- and ORS-interval increased significantly from 162±37 and 107±27 pre-TAVI to 200±55 and 132±41 ms post-TAVI. Median follow-up time was 1387d (691–2335) and 37 (29%) patients died. One-year mortality was 14% for non-PPM patients vs. 2% in PPM patients, and mortality at 5 yrs 70% vs. 54% (Figure). Independent mortality predictors were: not receiving a PPM (HR 3.4, p=0.01), post-procedural atrial fibrillation (HR 8.7, p=0.01) and a prior diagnosis of chronic obstructive pulmonary disease (HR 3.3, p=0.003). Left bundle branch block was not statistically significant (HR 1.9, p=0.11).

Survival curves by PPM-status

Conclusion: In this study TAVI-patients with a PPM implanted had better long-term survival than in whom a PPM was not implanted.

6024 | BEDSIDE
Impact of small annulus on reverse remodeling of left ventricular hypertrophy and mid-term outcome following transcatheter aortic valve implantation compared with surgical aortic valve replacement

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Background: The extent and effect of Left ventricular (LV) reverse remodeling in aortic stenosis (AS) patients with small annulus remains unclear. And the impact of small annulus on those outcome after transcatheter aortic valve implantation (TAVI) compared with surgical aortic valve replacement (SAVR) also remains equivocal.

Purpose: The aim of this study was to investigate the impact of small annulus on reverse remodeling of LV hypertrophy and mid-term outcome in patients with severe AS following TAVI compared with SAVR.

Methods: From Jan. 2013 to Aug. 2014, a total of 206 consecutive patients underwent aortic valve replacement were retrospectively enrolled. We defined annulus with 20mm or less as small annulus and the ratio between the measured LV mass index (LVMi) to the pre-procedural LVMi as LVM ratio.

Results: The age of the 75 severe AS patients with small annulus ranged from 63 to 95 years (meanSD, 80.7±7.0 years). In analysis of small annulus, aortic valve intervention reduced LVMi immediate after the procedure and kept decreasing to 6months follow-up. In comparison with each procedure, post-procedural LVMi, LVM ratio were significantly lower in the SAVR group than in the TAVI group, and these difference remained to 6months follow-up. However, clinical efficacy endpoint 30 days after procedure was similar between the two groups (P=0.40).

Change of LV mass index

6025 | BEDSIDE
High-sensitivity troponin and diagnosis of myocardial infarction after combined aortic valve replacement and coronary artery bypass grafting

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Background: The Universal Definition for type 5 myocardial infarction (MI) applies to coronary artery bypass grafting (CABG), while perioperative MI for other cardiac surgeries are rarely studied and not specifically defined. Our previous studies found isolated aortic valve replacement (AVR) to have higher troponin rise than CABG.

Purpose: We assessed whether post-operative high-sensitivity troponin (hs-TnT) at pre-specified thresholds, with or without concurrent ischaemic changes on ECG or echocardiogram, predicted mortality and morbidity after AVR+CABG.

Methods: Patients undergoing AVR+CABG during July 2010-December 2012 were identified (n=167), and hs-TnT routinely measured 12–24 hours postoperatively were collected. We pre-specified 140ng/L (10 times 99th percentile upper reference limit [URL]), 500ng/L and 95 (67.4%) at 500ng/L, while 27 (19.1%) had new ECG or echocardiographic changes. C-statistics and 95% confidence interval for operative mortality were hs-TnT alone 0.711 (0.576–0.845), ECG and/or echocardiographic changes alone 0.703 (0.527–0.893) and combined hs-TnT–ECG/Echocardiogram 0.764 (0.599–0.924). In multivariate analyses, the MI criteria to independently and most strongly predicting operative mortality was hs-TnT≥500ng/L+Ecg and/or echocardiographic changes odds ratio 15.9 (95% confidence interval 2.33–109) and for mortality during follow-up the same criteria hazards ratio 7.05 (2.40–20.7).

Conclusion: HS-TnT≥500ng/L+Ecg and/or echocardiographic criteria was strongly prognostic of short and long-term mortality after AVR+CABG. Our findings suggest higher hs-TnT thresholds for defining MI after AVR+CABG than isolated CABG to be more appropriate.

NOVEL INSIGHTS IS PATHOPHYSIOLOGY

6037 | BEDSIDE
Hypotension in patients with acute heart failure: Insights from RELAX-AHF


Background: Hypotension during treatment of acute heart failure (AHF) is an important adverse event linked to worse outcomes. The clinical variables associated with in-hospital hypotension, and whether its outcomes differ with serelaxin are unknown.
Methods: RELAX-AHF was a randomized trial of selresulin vs. placebo in 1161 AHF patients (pts) with systolic blood pressure (SBP) <125 mmHg. We assessed the baseline (BL) clinical characteristics associated with in-hospital confirmed BP decrease events (CBPDE). The protocol definition for CBPDE was either a decrease in SBP to <100 mmHg or a >40 decrease from BL or both. Study drug dose was reduced by 50% in those who dropped by 40 vs BL and were still >100. Pts with SBP decrease <100 had to discontinue study drug. In post-hoc multivariate analysis, we evaluated biologic correlates and outcomes of pts with and without CBPDE, as well as the impact of selresulin. Outcomes included in-hospital worsening heart failure (WHF), cardiovascular (CV) death or HFreferral rehospitalization (60-day), and CV mortality (180-day).

Results: Of 1150 AHF pts with complete CBPDE data, 272 (24%) had a CBPDE of which 93% were asymptomatic. Clinical variables associated with CBPDE were older age, increased BL respiratory rate, worse BL dyspnea, lower hemoglobin and sodium, and increased bilirubin and alkaline phosphatase. Event rates for in-hospital WHF and 180-day CV mortality were lower in selresulin-treated pts compared with placebo-treated pts regardless of whether a CBPDE occurred (Table).

Table 1. Unadjusted and adjusted association of CBPDE with and without treatment with serelaxin.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>No CBPDE (N=679)</th>
<th>CBPDE (N=472)</th>
<th>Adjusted interaction p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum creatinine</td>
<td>0.9 (N=405)</td>
<td>1.0 (N=473)</td>
<td>0.44</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>0.9 (N=168)</td>
<td>0.9 (N=104)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Conclusion: Blood pressure decrease events occurred in nearly a quarter of AHF pts during hospitalization and were associated with older age, baseline dyspnea severity, and elevated laboratory values. WHF and 180-day CV mortality were lower in selresulin-treated pts compared with placebo-treated pts regardless of whether a blood pressure decrease event occurred.

6038 | BENCH

Neutralophil-dependent cardiac post-infarct remodeling in mice is mainly mediated by myeloperoxidase

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Background: Polymorphonuclear neutrophils (PMNs) play a pivotal role within the orchestra of inflammation, oxidative stress and structural remodeling in response to cardiac injury following myocardial infarction (MI). Neutrophil depletion reduces post-MI infarct size and the extent of cardiac injury. However, the mechanisms by which PMNs mediate MI-induced LV remodeling remains to be fully elucidated. Myeloperoxidase (MPO) is primarily released by activated PMNs and influences structural remodeling in a redox-sensitive manner. In order to improve our understanding on how PMNs influence post-MI LV remodeling and cardiac function, we compared the effect of PMN-depletion and MPO-knockout on LV remodeling and cardiac function in a murine model of MI.

Purpose: Understanding how PMNs influence post-MI LV remodeling and cardiac function might give rise to new therapeutic options for post-MI patients.

Methods and results: PMN-depleted mice, MPO-knockout (MPO−/−) mice and wild type (WT) mice were subjected to left ventricular infarction by ligation of the left anterior descending artery. Depletion of PMNs was performed two days before LAD ligation by Ly6G antibody injection. FACS analysis revealed complete absence of Ly-6G positive plasma cells for at least 14 days. Functional analysis demonstrated attenuated structural remodeling, indicated by significantly reduced LV fibrosis (78±2% in WT vs 65±2% in MPO−/−, p <0.001). Histological analysis demonstrated attenuated structural remodeling, indicated by significantly reduced LV fibrosis (78±2% in WT vs 65±2% in MPO−/−, p <0.001). Histological analysis demonstrated attenuated structural remodeling, indicated by significantly reduced LV fibrosis (78±2% in WT vs 65±2% in MPO−/−, p <0.001).

Conclusion: Myeloperoxidase-deficiency was as effective as PMN-depletion in the attenuation of post-MI LV dysfunction and structural LV remodeling. Thus, MPO appears to be an important mediator of PMN-induced LV remodeling and cardiac dysfunction after myocardial infarction. The role of MPO in the development of heart failure in human studies remains to be elucidated. The results of this study may provide new insights.
**6041 | BEDSIDE**

Gremlin-1 expression correlates with cardiac fibrosis and left ventricular dysfunction visualized by cardiac magnetic resonance imaging in non-ischemic heart failure

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**Background:** Gremlin-1 (Grem1), an antagonist of bone morphogenetic proteins, is involved in fibrotic tissue formation in kidney and lung. Recently, it was shown that Grem1 correlates with the degree of myocardial fibrosis on endomyocardial biopsy and adverse prognosis. However, the correlation of endomyocardial Grem1 expression and cardiovascular system enhancement (LGE) in cardiac magnetic resonance imaging (MRI) is unknown.

**Methods:** 210 patients with non-ischemic heart failure underwent endomyocardial biopsy with Grem1 staining and contrast-enhanced cardiac MRI (1.5 Tesla scanner; Siemens Medical Systems, Germany). Grem1 staining was classified as "negative" (score 1 or 2) or "positive" (score 3 or 4). Scores for Grem1 were obtained in a blinded manner from 1–2 sections per staining by 2 investigators. For LGE imaging a two-dimensional inversion-recovery segmented k-space gradient-echo MR sequence was performed. MRI images were acquired in short- and long-axis views 10–15 minutes after intravenous injection of 0.15 mmol per kilogram body weight gadobutrol (Gadovist, Bayer Healthcare, Germany). End-diastolic volumes and end-systolic volumes were used to determine left ventricular ejection fraction.

**Results:** 140 out of 211 patients (66.4%) had Grem1 positive endomyocardial biopsies. Grem1 positive patients had a significantly higher rate of LGE-positive cardiac MFRs (65% vs. 51% in Grem1 negative patients, respectively, p<0.045). Further, Grem1 positive patients were in higher NYHA-class (mean 2.2±0.8 vs. 1.9±0.7; p=0.010), had a lower LVEF (51±14.6 vs. 46±15.3%; p=0.002), a higher LVEDD (55.1±9.4 vs. 51.9±9.5, p=0.013) and higher serum levels of BNP (246±2335 mg/dl vs. 936±1508 mg/dl, p=0.003).

**Conclusions:** Patients with a higher expression of Grem1 in their endomyocardial biopsy demonstrate a higher amount of cardiac fibrosis visualized by contrast-enhanced cardiac MRI. Grem1 positive patients show more severe clinical signs of heart failure.

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**6042 | BEDSIDE**

Biomarkers of heart failure in exhaled breath

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**Purpose:** Heart failure (HF) is a widely prevalent disease that have multiple causes. Patients with HF often present with signs and symptoms that are often non-specific. The purpose of this study was to find out novel biomarkers of HF in exhaled breath.

**Methods:** From October 2013 to February 2015, we included 46 patients with LV EF less than 45% in heart failure group and 15 patients without HF in control group. We collected fasting exhaled breath samples of all patients in 1L Tedlar bags. Exhaled breath was analyzed using PTR-MS (Compact PTR-MS, Ionicon, Austria).

**Results:** The baseline characteristics were similar in both groups. The mean EF in HF group was 34±28%. In compare with control group several biomarkers were significantly higher in HF group. They are acetone, acetic acid, ethanol, propylene and xylool (Table 1). The greatest difference was observed in the concentrations of acetone (p<0.0001) and propylene (p<0.002). Receiver operator characteristic (ROC) analyses were performed to assess optimal cutoff points for these biomarkers and to calculate sensitivity and specificity. The areas under the ROC curve for acetone and propylene were 0.809 and 0.77, respectively. The optimal cutoff concentrations of acetone and propylene for heart failure. These estimated cutoff concentrations of acetone and propylene for heart failure. These biomarkers possessed tolerable sensitivity and low specificity.

**Acknowledgement/Funding:** This study was supported by Russian Academy of Science

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**6043 | BEDSIDE**

The novel cardiovascular biomarker secretoneurin predicts mortality and shock in critical ill patients with infections


**Methods:** We measured circulating SN levels in 232 patients with severe sepsis (FINNSEPSIS Study) and validated the results in 94 patients with acute respiratory failure and infections (FINNALI substudy). SN was compared to established risk factors and biomarkers, including high-sensitivity troponin T (hs-TnT) and N-terminal pro-B-type natriuretic peptide (NT-proBNP).

**Results:** SN levels measured on intensive care unit (ICU) admission in both cohorts were correlated with established risk indices in patients with critical illness, including SOFA and SAPS II scores, and with hospital mortality (Fig). In patients with severe sepsis, admission SN levels (logarithmically transformed) were associated with hospital mortality (OR 3.17 [95% CI 1.12–9.00], p=0.030) and shock during the hospitalization (OR 2.17 [1.06–4.46], p=0.034) in analyses that adjusted for the other risk factors, including cardiovascular biomarkers. SN levels were also associated with hospital mortality after adjusting for other risk factors in the validation cohort, while neither hs-TnT nor NT-proBNP were associated with mortality or shock in multivariable analyses in the two cohorts. In both cohorts the optimal cutoff levels on ICU admission to predict hospital mortality was ~175 pmol/L, and higher levels were associated with mortality also when adjusting for SAPS II and SOFA scores.

**Conclusion:** SN levels provide incremental information to established risk indices for the prediction of mortality and shock in critically ill patients with severe infections.

**Acknowledgement/Funding:** This study was funded by Akershus University Hospital.

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**6044 | BEDSIDE**

Myocardial fibrosis at cardiovascular magnetic resonance predicts left ventricular reverse remodelling

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**Purpose:** In nonischaemic dilated cardiomyopathy (NICM), myocardial fibrosis at cardiovascular magnetic resonance (CMR) is associated with worse prognosis. The aim of the study was to investigate whether myocardial fibrosis progresses during follow-up and whether its absence is associated with left ventricular reverse remodelling (LV-RR).

**Methods:** One-hundred-and-twenty-five NICM patients (age 51±16 years, 82 male) were enrolled and underwent baseline CMR; patients with ischaemic, valvular, congenital heart disease, other cardiomyopathies or conotruncal abnormalities were excluded from study entry. After a 24-month follow-up on optimal medical therapy of patients underwent CMR at 24 months. LV volumes and end-systolic volumes were used to determine left ventricular ejection fraction (LVEF) at follow-up. LV-RR was defined as an increase in LVEF 10±6% and ≥10% at follow-up.

**Results:** Mean LVEF at baseline was 41±11% at baseline, 47±12% at follow-up. LV-RR was observed in 59 patients (47%), with no age or gender difference (p=0.8). LGE was present in 48 (38%) patients at baseline (mean extent 5±6% of LV mass), in 76 (61%) patients at follow-up (mean extent 7±7%, p<0.01 vs. base-line). Patients experiencing LV-RR during follow-up presented a baseline worse LV ejection fraction (36±12%) than no-LV-RR patients (45±9%, p<0.01, greater

**Conclusion:** SN levels provide incremental information to established risk indices for the prediction of mortality and shock in critically ill patients with severe infections.
Methods and results: aged patients. 
Acute heart failure (AHF) might be different between the elderly and the general 
subjects with systolic HF and in the total population. (Figure)

Background: The clinical characteristics and prognostic factors of patients with acute heart failure (AHF) might be different between the elderly and the general population. We attempted to explore the determinants of outcomes in the extremely aged patients.

Methods and results: Based on the data of an intramural registry, patients aged ≥80 years and hospitalized for AHF were eligible for this analysis. A guideline adherence score of medications (GASM) was calculated by the prescriptions of β-blocker, spironolactone, and ACEi/ARB, each medicine was count 1 point. A total of 1295 extremely aged subjects (86±4 years, 34.1% systolic HF) were enrolled. During an mean follow-up duration of 26.7±24.3 months, 532 subjects (41.1%) died. The dead were even older, had lower hemoglobin, sodium level and eGFR, and higher LVEF, RVSP, uric acid (UA) and NT-proBNP levels. With adjustments of age, gender and eGFR, Hgb (β=-0.07, p=0.03), sodium (β=-0.14, p<0.001), and NT-proBNP (β=0.29, p<0.001) were independent predictors of LV-RV. The Kaplan-Meier survival analysis clearly demonstrated a trend toward better survival along with the increase of NT-proBNP in subjects with systolic HF and in the total population. (Figure)

Conclusion: The proposed prognostic factors remained associated with mortality in the extremely aged patients hospitalized for AHF. Adherence to the guideline was still essential to improve their clinical outcomes.

5604 | BEDSIDE
Determinants of long-term outcomes in the extremely aged patients hospitalized for acute heart failure
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Background: The clinical characteristics and prognostic factors of patients with acute heart failure (AHF) might be different between the elderly and the general population. We attempted to explore the determinants of outcomes in the extremely aged patients.

Methods and results: Based on the data of an intramural registry, patients aged ≥80 years and hospitalized for AHF were eligible for this analysis. A guideline adherence score of medications (GASM) was calculated by the prescriptions of β-blocker, spironolactone, and ACEi/ARB, each medicine was count 1 point. A total of 1295 extremely aged subjects (86±4 years, 34.1% systolic HF) were enrolled. During an mean follow-up duration of 26.7±24.3 months, 532 subjects (41.1%) died. The dead were even older, had lower hemoglobin, sodium level and eGFR, and higher LVEF, RVSP, uric acid (UA) and NT-proBNP levels. With adjustments of age, gender and eGFR, Hgb (β=-0.07, p=0.03), sodium (β=-0.14, p<0.001), and NT-proBNP (β=0.29, p<0.001) were independent predictors of LV-RV. The Kaplan-Meier survival analysis clearly demonstrated a trend toward better survival along with the increase of NT-proBNP in subjects with systolic HF and in the total population. (Figure)

Conclusion: The proposed prognostic factors remained associated with mortality in the extremely aged patients hospitalized for AHF. Adherence to the guideline was still essential to improve their clinical outcomes.

5604 | BEDSIDE
Predictors of insulin resistance in chronic systolic heart failure
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Background: Insulin resistance (IR) is a common finding in symptomatic systolic chronic heart failure (CHF). Nevertheless, there is lack of data about clinical and pathophysiological features of patients (pts) of this group.

Objective: To establish clinical factors associated with presence of IR in systolic CHF.

Methods: 107 stable CHF pts (NYHA class II-IV, left ventricular ejection fraction <40%) were examined (vital signs, routine laboratory tests, echocardiography, flow-mediated vasodilatation (FMD) of brachial artery, fasting insulin and glucose levels). The HOMA index was calculated by standard formula. Plasma levels of tumor-necrotic factor (TNF-α), interleukin 6 (IL) and adiponectin (A) were determined by enzymatic method. FMD of brachial artery was calculated by the standard cuff test. The L/A ratio was determined too.

Results: IR (defined as HOMA >2.77) was observed in 45 (42%) pts, the HOMA index median (Me) in IR group was 3.58 [2.96; 5.74] vs 1.85 [0.95; 2.31] in non-IR group. No significant differences were observed between IR and non-IR groups were observed by age, sex distribution, CHF etiology, NYHA class, body mass index, heart rate, blood pressure, echo parameters and the A ratio. Simultaneously, pts with IR demonstrated higher levels of IL (Me=6.30 [3.69;22.01] ng/ml vs 5.53 [3.16;16.97] ng/ml, respectively, p=0.044); TNF-α (Me=3.40 [1.35;19.25, pg/ml] vs Me=2.80 [0.82;5.38, pg/ml, respectively, p=0.041); plasma uric acid (549.37±153.23, pg/ml, vs 463.55±131.15, mmol/l, respectively, p=0.003, and poorer FMD (Me=5.40 [4.63;7.95] vs Me=7.99 [5.21;11.50], %; respectively, p=0.033) in comparison with pts of non-IR group.

Conclusion: IR is present in 42% pts with stable systolic CHF and is associated with higher plasma levels of leptin, TNF-α, uric acid and poor FMD of brachial artery.

5605 | BENCH
PMCA4 ablation in cardiac fibroblasts protects the heart from pathological hypertrophy

The plasma membrane calcium ATPase 4 (PMCA4) is a ubiquitously expressed calcium pump that is important in mediating molecular signalling in the heart. Here we investigated a novel role of PMCA4 in cardiac fibroblasts that is important in controlling myocardial hypertrophy.

We generated three PMCA4 conditional knockout mouse strains: i) PMCA4 systemic knockout (PMCA4−/−); ii) PMCA4 cardiomyocyte-specific knockout (PMCA4cko); iii) PMCA4 fibroblast-specific knockout (PMCA4fko). Following transverse aortic constriction (TAC) for 5 weeks PMCA4−/− and PMCA4fko mice displayed a significantly reduced hypertrophy compared with control mice. This was accompanied by less fibrosis and a lower expression of hypertrophic marker ANP. However, PMCA4cko mice did not show any protective effect following TAC prompting us to hypothesise that the protective effect might be due to PMCA4 ablation in fibroblasts. Microarray analysis revealed a ∼100 fold up-regulation of the secreted frizzled-related protein 2 (sFRP2) in PMCA4−/− fibroblasts, which was confirmed by qRT-PCR and Western blot. sFRP2 is a potent inhibitor of the Wnt/β-catenin pathway. We then cultured isolated wild type (WT) cardiomyocytes with conditioned medium from either PMCA4−/− or WT fibroblasts. In response to phenylephrine stimulation cardiomyocytes cultured in PMCA4−/− fibroblasts conditioned medium displayed 88% less hypertrophy when compared with cultures in PMCA4+/- or WT fibroblasts conditioned medium (P<0.01). Mechanistically, PMCA4−/− fibroblasts showed a significant elevation in NFκB activity, a transcription factor regulating sFRP2 expression. Inhibition of NFκB activity significantly reduced the expression of sFRP2 in PMCA4−/− fibroblasts to the level comparable with WT fibroblasts. A chemical library screen identified a novel PMCA4 inhibitor, aminohexoxyacidic acid (ATA). ATA treatment enhanced sFRP2 expression in mouse heart. Importantly, ATA inhibited and reversed TAC-induced cardiac hypertrophy in mice showing its efficacy in both preventive and therapeutic setting.

In conclusion, our data shows that PMCA4-mediated signaling in cardiac fibroblast plays a key role in controlling hypertrophy. Thus, PMCA4 might be a target for the treatment of cardiac hypertrophy in the future.

5605 | BENCH
Genetic ablation of the G-protein coupled receptor 99 (GPR99) increases pressure overload-induced hypertrophy in mice
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The G-protein coupled receptors (GPCRs) family of proteins play essential roles in the heart, including in the regulation of cardiac hypertrophy. One member of this family, the GPR99, may have a crucial role in the heart because it acts as a receptor for α-ketoglutarate, a metabolite that is elevated in heart failure patients. GPR99 is expressed in the heart but its precise function during cardiac pathophysiological process is unknown. In this study we used both in vivo and in vitro approaches to investigate the role of GPR99 during cardiac hypertrophy.

Genetic ablation of GPR99 in mice (GPR99−/−) resulted in a significant increase in hypertrophy following two weeks transverse aortic constriction (TAC), as indicated by heart weight/tibia length ratio (HW/TL; GPR99−/− / TAC: 7.1±0.24 mg/mm; n=7–8, P<0.05). GPR99−/− mice displayed an increased cardiomyocyte cross-sectional area and expressions of hypertrophic markers ANP and BNP. Moreover, interstitial fibrosis was increased by 11.3% in GPR99−/− mice compared to wild type (WT) controls following TAC. Using yeast two hybrid screening analysis we identified novel interacting partner and downstream signalling pathways that are regulated by the GPR99. First, we found that GPR99 forms a
molecular complex with TTK2, an upstream regulator of pro-hypertrophic factors, STAT1 and STAT3. Adenoviral mediated overexpression of GPR9R in neonatal rat cardiomyocytes significantly reduced TTK2 and STAT1/3 phosphorylation. Conversely, this pathway was over-activated in GPR9R−/− mice following TAC. Secondly, we found that through interaction with CSNS, GPR9R regulates the ubiquitination of Interferon Regulatory Factor 5 (IRF5) and IRF8, which are known as pro-hypertrophic factors. Overexpression of GPR9R enhanced ubiquitination of both IRF5 and IRF8 whereas deletion of this receptor reduced IRF5/8 ubiquitination.

In conclusion, our study has identified GPR9R as a novel regulator of pathological hypertrophy via the regulation of the STAT pathway and the ubiquitination of IRF5/8. Identification of molecules that can specifically activate or inhibit this receptor may be very useful in the development of new therapeutic approach for cardiac hypertrophy.

6058 | BENCH
Urocortin-2 improves right ventricular function in pulmonary arterial hypertension
Urocortin (UCN)-2 has shown promising therapeutic effects in humans and animal models with heart failure (HF). This study analyzed the effects of UCN-2 treatment in an animal model of right ventricle (RV) HF, secondary to pulmonary arterial hypertension (PAH).

Male Wistar rats received monocrotaline (MCT, 60mg/kg) or vehicle. After 2 weeks, animals were randomly assigned to receive UCN-2 (5μg/kg/day) or vehicle. The study resulted in 4 groups: CTRL (n=9); CTRL-UCN-2 (n=9); MCT (n=7) and MCT+UCN-2 (n=10). Hemodynamic studies and sample collections were performed 4 weeks after MCT injection. Only significant results (mean±SEM, p<0.05) are given.

Hemodynamic studies revealed that MCT group developed PAH, as shown by increased RV end-systolic pressure (MCT vs CTRL: 63±2 vs 22±1mmHg), end-diastolic pressure (6.0±0.7 vs 7.5±0.3mmHg), RV dilation (end-diastolic volume (288±14 vs 222±11mm3) and decreased cardiac output (35±6 vs 64±3mL/min) and ejection fraction (32±4 vs 72±3%). UCN-2 treatment resulted in attenuation of these changes (48±4mmHg; 4.2±3.3mmHg: 213±12L; 47.5±2mL/min and 60±3%, respectively). Moreover, the survival rate for UCN-2 treated rats was higher (76%) than for MCT rats (44%). PAH rats presented RV hypertrophy as shown by the morphometric analysis (RV weight/tibia length ratio, MCT vs CTRL: 0.01±0.00 vs 0.04±0.00g/cm) and by histology (cardiomyocyte cross-sectional area: 366±25 vs 255±27μm2).

UCN-2 treatment attenuated RV remodeling (0.06±0.00g/cm and 288±26μm2, respectively). The MCT group presented increased UCN-2 expression (MCT vs CTRL: 2.5±0.9 vs 1.0±0.3AU) and decreased CRHR2 expression (0.5±0.1 vs 1.0±0.1AU) in the RV, that were reversed by UCN-2 treatment (0.2±0.1 and 0.9±0.1AU, respectively).

Expression of pathology markers in MCT animals, such as BNP (15.3±2.5 vs 90 patients (31–82 years, mean age 65±10 years, 5±1 antihypertensive drugs) suffering from resistant arterial hypertension were included in two centers following the Symplicity HTN-3 criteria. Secondary arterial hypertension, including obstructive sleep apnea, was excluded. The 1st generation of the Arterial/Medtronic RDN radiofrequency ablation catheter system was used for treatment. An I.E.M. device was used for 24h blood pressure and stiffness measurements. For pulse wave velocities (PVW) a multivariate analysis of variance (t-test) was performed.

Results: RDN was successfully performed in all patients without complications. Office systolic blood pressure (SBP) showed a significant decrease over 24 months. Response rate, defined as a reduction of 10 mmHg SBP, was 66% after 12 months and 65% after 24 months, respectively. SBP improved significantly from 147±21 mmHg after 3 months to 128±12 mmHg after 12 months and to 129±12 mmHg after 24 months (p<0.001) and to 129±12 mmHg after 24 months (p<0.001). PWV improved at daytime by 0.24 m/s after 12 months (p<0.017) and by 0.36 m/s after 24 months (p<0.007), respectively, whereas no significant effects were observed during nighttime.

Conclusions: This study proved for the first time a sustained effect of RDN on established cardiovascular surrogate endpoints. An extensively exclusion of a secondary arterial hypertension is crucial for RDN patient selection and might, at least in part, explain some differences as compared to Symplicity HTN-3.

6067 | BENCH
Neuropeptide Y as an indicator of successful alterations in sympathetic nervous activity after renal sympathetic denervation
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Background: Previous studies on renal sympathetic denervation (RDN) investigated treatment effects on arterial stiffness and central blood pressure parameters in patients with resistant arterial hypertension. The present study aims to evaluate the effects of RDN on these parameters in ambulatory 24h measurements.

Methods: 90 patients (31–82 years, mean age 65±10 years, 5±1 antihypertensive drugs) suffering from resistant arterial hypertension were included in two centers following the Symplicity HTN-3 criteria. Secondary arterial hypertension, including obstructive sleep apnea, was excluded. The 1st generation of the Arterial/Medtronic RDN radiofrequency ablation catheter system was used for treatment. An I.E.M. device was used for 24h blood pressure and stiffness measurements. For pulse wave velocities (PVW) a multivariate analysis of variance (t-test) was performed.

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Conclusions: This study proved for the first time a sustained effect of RDN on established cardiovascular surrogate endpoints. An extensively exclusion of a secondary arterial hypertension is crucial for RDN patient selection and might, at least in part, explain some differences as compared to Symplicity HTN-3.
a specific biomarker of sympathetic activity. Further, the association between changes in NPY levels and blood pressure reduction after RSD was analyzed.

**Methods:** A total of 150 consecutive patients (age: 64.9±10.2 y) from 3 clinical centers undergoing RSD were included in this study. Response to RSD was defined as an office systolic blood pressure (SBP) reduction of >10 mmHg 6 months after RSD. Venous blood samples for measurement of NPY in serum were collected prior to and 6 months after RSD.

**Results:** A significant reduction in the office SBP of 23.0 mmHg (SBP baseline: 168.6 mmHg [SD: 20.8], p<0.001) was observed 6 months after RSD. In addition NPY serum levels were significantly reduced by 0.24 ng/mL, after 6 months follow-up, when compared to baseline values (NPY baseline: 7.1 [IQR: 2.6–8.7], p<0.01). There was a significant correlation between baseline SBP and RSD-related systolic BP reduction (r=-0.43, p<0.001) and between serum NPY baseline values and NPY level changes (r=-0.52, p<0.001) after the 6-month follow-up. Successful SBP reduction after RSD (responders) was associated with a significantly greater NPY level reduction when compared with BP non-responders (p=0.002).

**Conclusion:** In addition to the blood pressure reduction in response to RSD, this study demonstrates an effect of RSD on serum NPY levels, as a specific marker for sympathetic activity. The association between RSD-related changes in SBP and NPY levels provide further evidence of the effect of RSD on the SNS.

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**TRANSLATIONAL ELECTROPHYSIOLOGY OF ATRIAL FIBRILLATION**

**6074 | BEDSIDE**

**Serum YKL-40 as a novel marker of left atrial fibrosis assessed by delayed enhancement MRI in lone atrial fibrillation**

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**Background:** Assessment of the presence and extent of left atrial (LA) fibrosis by using delayed-enhanced magnetic resonance imaging (DE-MRI) in AF patients is a pioneering non-invasive method. Serum YKL-40 is a novel marker for inflammation and known to play a role in ongoing tissue fibrosis. However, its role in LA fibrosis is unclear.

**Objective:** We aimed to investigate the association of serum YKL-40 level with both the presence and extent of LA fibrosis by using DE-MRI.

**Methods:** A total of 50 patients with lone paroxysmal AF (62% male; age:47±27.0) underwent cardiac DE-MRI as a study protocol. Cardiac DE-MRI at 1.5T scanner to quantify LA fibrosis, serum YKL-40 levels, clinical and echocardiographic data were recorded. Fibrosis degree was categorized according to Utah class defined in the DECAAF study.

**Results:** DE-MRI revealed any degree of LA fibrosis in 31 (62%) patients with a median enhancement of 15% of the LA surface area. Median serum YKL-40 was significantly higher (p<0.008) and UEF was lower (p=0.047) in patients with LA fibrosis as compared to patients without LA fibrosis. Extent of LA fibrosis was significantly correlated with age, duration of AF history, serum CRP and serum YKL-40 levels. Only log (YKL-40) level was found as independent predictor for the presence of LA fibrosis (OR: 1.626, p=0.003). Multivariate linear regression analysis pointed out that duration of AF history (p=0.330, p=0.003) and serum log (YKL-40) levels (p=0.546, p<0.001) were significantly and independently associated with the extent of LA fibrosis.

**Conclusion:** Higher levels of serum YKL-40 are associated with both the presence and more extensive LA fibrosis in patients with lone AF. As a novel marker of inflammation, serum YKL-40 may also be used as an indicator for the degree of LA fibrosis.

**6075 | BEDSIDE**

**Exercise-induced left atrial hypertension in patients with non-valvular atrial fibrillation: prevalence and impact on clinical outcome of catheter ablation**

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**Purpose:** We investigated whether static handgrip exercise would induce left atrial hypertension (LAH) in the patients with non-valvular atrial fibrillation (AF) and whether the exercise-induced LAH would project worse outcome of catheter ablation for the AF.

**Methods:** LA pressure was measured directly after transseptal puncture at rest and during static handgrip exercise (40% maximal voluntary contraction) in 225 patients undergoing radiofrequency ablation for non-valvular AF (paroxysmal/persistent AF, 66/33%). Functional limitation was assessed at baseline and at 3 months after the ablation by the SF-36 questionnaire. Patients were followed for AF recurrence for 10±6 months.

**Results:** Mean LA pressure increased during the handgrip by 3±4 mmHg (range 0–25 mmHg). LAH, defined as mean LA pressure >15 mmHg was present at rest and during the handgrip in 14% and 30% of the patients. The strongest risk factors (p<0.001) for the exercise-induced LAH were older age, increased afterload, reduced LA volume, decreased LA appendage doppler flow and lower LA bipolar voltage. AF recurred in 46% of the patients with LAH compared to 24% of the patients without LAH (p<0.002). The patients with LAH were more limited during physical activity before and also after the ablation, even after adjusting for the heart rhythm and heart rate (p<0.001 by the SF-36). However, the LAH patients who maintained sinus rhythm after the ablation improved their physical functioning by 24% (p<0.02).

**Conclusions:** Exercise-induced LAH is common in the patients with non-valvular AF. Presence of the LAH doubles the risk of AF recurrence and impedes complete functional recovery after ablation. On the other hand, managing AF by ablation in the patients with LAH may substantially improve their physical functioning.

**6076 | BEDSIDE**

**Lower and high resting heart rate is associated with an increased risk of incident atrial fibrillation**

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**Background:** A recent meta-analysis of randomized clinical trials investigating the heart rate-reducing agent ibradirelin in patients with cardiovascular disease has shown an increased risk of atrial fibrillation (AF) when treated with ibradirelin compared to placebo. However, whether the increased risk of AF observed is due to ibradirelin per se or due to ibradirelin-induced bradycardia remains to be established.

**Purpose:** We aimed to describe the association between resting heart rate and the risk of AF in an observational setting of primary care patients referred for electrocardiogram (ECG) recording. Moreover, as secondary endpoints, we aimed to describe the association between resting heart rate and the risk of death from all causes as well as stroke.

**Methods:** Using computerized ECG analysis, resting heart rate was obtained from 282,015 individuals referred for ECG recording at a general practitioner’s core facility from 2001 to 2011. Data on drug use, comorbidity, and outcomes were collected from administrative healthcare registries. Among several things, we were able to adjust for treatment with heart rate-modulating medication.

**Results:** During a median follow-up time of 5.6 years, 7,607 developed AF, of which 875 developed lone AF. Having a resting heart rate below the 5th percentile (<51 beats/min) was associated with a multivariable-adjusted hazard ratio of 1.15 (95% CI 1.01–1.30; P=0.031) for developing AF compared with the reference group (40th to <60th percentile, 66–72 beats/min). From the reference group and upward, the risk of AF increased with increasing heart rate, reaching a multivariable-adjusted hazard ratio 1.31 (95% CI 1.19–1.45; P<0.001) for those with a heart rate above the 95th percentile (>95 beats/min). The association was accentuated when looking only at lone AF, as evidenced by a hazard ratio of 1.49 (95% CI 1.08–2.07; P=0.017) and 1.97 (95% CI 1.46–2.66; P<0.001) for those with a heart rate below the 5th percentile (<51 beats/min) and above the 95th percentile (>93 beats/min), respectively. Regarding secondary end-points, the multivariable-adjusted analysis revealed that the risk of death and stroke increased almost linearly with increasing heart rate.

**Conclusions:** In this large ECG study, we found that both low and high resting heart rate is associated with an increased risk of AF independently of treatment with heart rate-modulating medication. This association was even stronger for the
outcome of lone AF. For death and stroke, we found almost linear increased risks for increasing resting heart rate.

### ADVANCES IN SCIENCES: PERIPHERAL CIRCULATION

#### 6084 | BEDSIDE

**Defining the value of the toe-brachial index for normal, mild, moderate and severe PAD**


**Background:** The ankle-brachial index (ABI) has been used to define peripheral arterial disease (PAD) as either mild (ABI, <0.9), moderate (ABI, 0.90–0.80) or severe (ABI, <0.50). The toe-brachial index (TBI) has traditionally been reserved for those patients with a high ABI (>1.30) where it feels that incompressibility due to peripheral arterial calcification impairs the reliability of the ABI for the diagnosis of obstructive PAD. While there has been data to categorize a TBI as either normal or abnormal, to our knowledge there has never been a similar categorization of values for mild, moderate or severe using the TBI. The purpose of our investigation was to define the cutoffs for PAD severity for the TBI using the ABI cutoffs of severity.

**Methods:** Our database was searched for all patients who had both ABI and TBI measured. There were 7,490 legs where both ABI and TBI were recorded. ROC curves were constructed using the ABI cutoffs for mild, moderate and severe as described above. All ROC graphs and statistical calculations were performed using the MedCalc statistics program.

**Results:** The TBI that best separated those without PAD and those with mild PAD was ≤0.68 (sensitivity 93.1%, specificity 80.8%, AUC, 0.932 [95% CI, 0.926–0.938], P value <0.001). The TBI that best separated those with moderate PAD was ≤0.81 (sensitivity 92.2%, specificity 84.2%, AUC, 0.941 [95% CI, 0.936–0.947], P value <0.001). The TBI that best separated those severe PAD was ≤0.54 (sensitivity 97.2%, specificity 87.4%, AUC, 0.969 [95% CI, 0.965–0.973], P value <0.001). The ROC curves for mild and severe PAD are shown in the figure below.

**Conclusions:** We can now categorize the severity of PAD based on the TBI alone. A normal TBI is ≤0.68, mild disease is 0.62–0.68, moderate disease 0.50–0.61 and severe disease ≤0.49.

#### 6085 | BEDSIDE

**Burden of subclinical atherosclerosis assessed by carotid and femoral 3D vascular ultrasound: the PESGA (Progression of Early Subclinical Atherosclerosis) study**

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**Introduction:** Plaque volume assessment with real 3D vascular ultrasound (r3D-US) is a novel approach to detecting and quantifying atherosclerosis. Here we characterize, for the first time, carotid and femoral plaque burden in an asymptomatic middle-aged population.

**Methods:** PESA is an observational, prospective, cohort study of bank employees aged 40 to 54 that evaluates the presence and progression of subclinical atherosclerosis. We report data from the first 1970 participants screened with r3D-US. Atherosclerotic burden was defined as the sum of all plaque volumes in the carotid and femoral arteries. Linear regression models were used to explore the association between burden and age.

**Results:** Atherosclerosis was detected in 47% of the participants (46±4yo, 35%female). Atherosclerotic burden was greater in men (median (IQR) 79mm3 (179–31) vs 32mm3 (72–13) in women) and in the femoral arteries (median (IQR) 78mm3 (170–36) vs 28mm3 (58–14) in carotids). Stratifying by age (Figure) revealed a significant increase in femoral burden (FB) in men (β coefficient 5.59; p<0.001), whereas carotid burden (CB) showed no age association (β coefficient 0.16; p=0.852). In contrast, women showed a significant age-related increase in CB (β coefficient 2.59; p=0.002) but no association for FB (β coefficient 0.86; p=0.579). Age-related differences between the development of FB and CB were significant in men (p=0.004) but not in women (p=0.298).

**Conclusions:** In this first report on carotid and femoral plaque volume with r3D-US we detected higher atherosclerotic burden in men and in the femoral arteries. Interestingly, men showed rapid development of femoral burden over the studied age range. Assessment of plaque burden by r3D-US is a valuable tool for screening subclinical atherosclerosis in the carotid and femoral arteries.

### IMAGING MODALITIES FOR PULMONARY HYPERTENSION

#### 6103 | BEDSIDE

**A feasible method for non-invasive measurement of pulmonary vascular resistance in pulmonary arterial hypertension: combined use of transthoracic Doppler-echoangiography and cardiac magnetic resonance**

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**Background:** Transthoracic Doppler-echoangiography (TTE) can estimate mean pulmonary arterial pressure (MPAP) and pulmonary capillary wedge pressure (PCWP) reliably, and cardiac magnetic resonance (CMR) is the best modality for non-invasive measurement of cardiac output (CO). Therefore, TTE and CMR
can complement each other in the evaluation of pulmonary vascular resistance (PVR).

Purpose: The study was performed to investigate whether combined use of TTE and CMR provided a feasible method for non-invasive measurement of PVR in pulmonary arterial hypertension (PAH).

Methods: Right heart catheterization (RHC) was undertaken in 77 patients (17M/60F) with PAH, and simultaneous TTE was carried out to evaluate MPAP, PCWP and CO. Within 2 days, CO was measured again with CMR in similar physiological status. Then, PVR was calculated with the integrated non-invasive method: TTE-derived (MPAP-PCWP)-CMR-derived CO and the isolated TTE method: TTE-derived (MPAP-PCWP)/TTE-derived CO, respectively. The results were compared with RHC-calculated PVR using the Bland-Altman analysis.

Results: The PVR calculated with integrated non-invasive method correlated well with RHC-calculated PVR (r = 0.931, 95% confidence interval 0.893 to 0.956). Between the integrated non-invasive PVR and RHC-calculated PVR, the Bland-Altman analysis showed the satisfactory limits of agreement (mean value: −0.89±2.59). In comparison, the limits of agreement were less satisfactory between TTE-calculated PVR and RHC-calculated PVR (mean value: −1.85±3.33). Furthermore, there were excellent intra- and inter-observer correlations for the measurements of TTE and CMR (P < 0.001 for all).

Conclusions: The combined use of TTE and CMR provides a clinically reliable method to determine PVR non-invasively. In comparison with RHC, the integrated method seems more accurate, which suggests the potential for the evaluation and serial follow-up in patients with PAH.

6104 | BEDSIDE

Atrial volume and function during exercise in chronic thromboembolic pulmonary hypertension

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Background: Although atrial volume and function have prognostic significance in many cardiovascular conditions, their changes with exercise are not well known.

Purpose: The aim of this study was to evaluate left and right atrial (LA and RA) volume and function during incremental exercise, both in normal individuals, after athletic remodeling, and in patients with chronic thromboembolic pulmonary hypertension (CTEPH).

Methods: Fifteen healthy non-athletes, 15 athletes and 15 CTEPH patients underwent exercise cardiac magnetic resonance imaging with simultaneous invasive hemodynamic measurements.

Results: At rest, athletes had larger indexed maximal RA and LA volumes (iRAV-max, iLAVmmax) than CTEPH patients and non-athletes, the latter two groups having similar values. CTEPH patients had lower RA and LA ejection fraction (EF) at rest. During exercise, RA volumes (maximum and minimum) increased in CTEPH patients, whilst decreasing in athletes and non-athletes (P < 0.0001). The exercise-induced change in iLAVmmax was similar between groups, but iLAVmin decreased in CTEPH patients. Thus exercise-induced increases in RAEF and iLAVmax were not different in the CTEPH patients and control. Conclusions: SRPA was useful to visualize decreased and narrowed pulmonary microvasculature in the PAH rats compared with the control. Microvascular density in the PAH rats was significantly decreased and the internal diameter of pulmonary arterioles in the PAH rats was 77±12 μm compared with 149±16 μm of control. eNOS expression was significantly decreased in the PAH rats compared with control (2.12±0.59 vs 2.91±0.66, p < 0.05). ET-1 expression was significantly increased in the PAH rats compared with control (1.53±0.45 vs 0.83±1.14, p < 0.05), although, VEGF expression was not different in the PAH rats and control.

Conclusions: SRPA was useful to visualize decreased and narrowed pulmonary micro-vasculature in the PAH rats. Increased ET-1 expression may contribute to a proliferation and remodeling of pulmonary arterioles. Also decreased eNOS expression may associate with vasospasm of pulmonary arterioles induced by endothelial dysfunction due to increased shear stress in PAH. Further study for detailed endothelial function would be necessary to investigate the mechanism of vascular remodeling associated with PAH. This newly developed SRPA technique makes it possible to visualize the micro-vasculature remodeling and could provide insights regarding the correlation between endothelial function and vascular remodeling in PAH.

Acknowledgement/Funding: JSFPS KAKENHI Grant Number 23791560

BEST POSTERS SESSION 7

BEST POSTERS IN CATHETER ABLATION

P6112 | BEDSIDE

The utility, efficacy and safety of a new rapid high-resolution mapping system in the catheter ablation of atrial and ventricular arrhythmias in humans

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Background: A novel 3D electroanatomical mapping system, capable of rapidly acquiring detailed maps based on automatic annotation of thousands of points was recently released for clinical use. We present our initial clinical experience.

Methods: The first 20 catheter ablation procedures (7 atrial tachycardia, 8 atrial fibrillation, 3 ventricular tachycardia and 2 ventricular ectopic beat ablation) based on standard indications are described. The system uses a bidirectional deflectable basket catheter with 64 closely spaced mini-electrodes (A). It automatically accepts and annotates electrograms when a number of predefined criteria that filter out the non-relevant signals are met.

Results: Thirty right atrial maps were acquired in median 11 (4–15) min consisting of 7220 (3467–10947) points, 22 left atrial maps in 11 (14–43) min consisting of 7818 (4379–12262) points and 10 left ventricular maps in 37 (14–43) min consisting of 8709 (2605–15514) points. The mini-basket catheter could reach all areas of interest without deflectable sheaths. Noembolic events, bleeding complications or endocardial structure damage was observed. Correction of the automatic annotation was performed in 0.02% of points in 4/62 maps. The system revealed re-entry circuits of atrial tachyarrhythmias (B), identified gaps on linear...
lesions (C) and correctly identified and annotated the clinical ventricular ectopic beats and channels of slow conduction within ventricular scar (D).

**Conclusions:** The novel automatic mapping system was rapid, safe and efficacious in mapping a variety of cardiac arrhythmias in humans. Further clinical research is needed to optimise its use in the ablation of complex arrhythmias.

**P6113 | BEDSIDE**

**Ablation of hemodynamically unstable VT with support of a microaxial pump, early experience**


**Introduction:** Besides progress in the ablation of ventricular arrhythmias with precise definition of the arrhythmic substrate, with its precise localization by three dimensional mapping and additional LAVA ablation there are still patients that cannot be treated successful by these means alone. In these cases the induction of the clinical VT is essential. In patients with severely depressed LV function or with immediate syncope the poor tolerability of these VT can be overcome by using a hemodynamic support by a microaxial pump. With this support an ablation is possible even under light sedation with a high success rate. We here report the results our first 11 procedures.

**Methods and results:** Retrospective analysis of consecutive patients admitted for VT ablation with an ejection fraction well below 25% or with immediate syncope. All patients were treated by RF-Ablation under hemodynamic support with a microaxial pump. With this support an ablation was possible even under light sedation with a high success rate. We here report the results of our first 11 procedures.

**Results:** Procedural success rate was 90% for NavX and 91% for RTG ablation. Time to first application 23±15 vs 27±18 min., time to last application 47±31 vs 52±33 min, as evidenced by an increased pressure to 11 mmhg. Unintended RV perforation occurred in 1 pts (4%) and was detected by the device (figure). No drainable fluid was observed.

**Conclusion:** Epicardial access with the novel EpiAccess™ needle and real time pressure monitoring is feasible and safe. The pressure monitoring identifies successful epicardial access and minimizes complications. This has relevant clinical implications.

**BEST POSTERS IN MEDICAL THERAPY OF STABLE CORONARY ARTERY DISEASE**

**P6114 | BEDSIDE**

**The impact of NavX in pediatric arrhythmia ablation on safety, procedure duration and number of RF lesions. Is it a time to change approach?**

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Non-fluoroscopic approach to pediatric ablation gets broad acceptance as it reduces the x-ray exposition. The only limitation is that it in most reports increases the duration of procedure.

Our objective is to compare the standard x-ray ablation (X) with nearly-0 fluoroscopy ablation with NavX (NavX) in pediatric population undergoing ablation. From the cohort of 538 consecutive patients we excluded 16 patients with complicated medical history after surgical correction. From the NavX group the procedure was started from RA reconstruction, followed by CS, tricuspid valve and His bundle. Left sided WPW ablation was performed retrogradely or transeptally. Short fluoroscopy was used during transseptal puncture, when VT originated close to aortic valve or when CS diverticulum was suspected. We analyzed the procedural (duration of GA and procedure), x-ray (fluoroscopy, dose) and ablation parameters (time to 1st and the last application, the number of applications and the cumulative duration of energy delivered as well and procedural success rates).

We included 522 patients (age 13.4±6.2 years, 238F) with SVT (202), WPW+AVRT/PAF (183), asympotomatic WPW (41), AT (26) and VEs/VT (44) or documented palpitations. Finally AVNRT ablation was performed in 131 patients, WPW in 287 patients, AT in 22 and VEs/VT in 44 cases. The NavX was used in 278 patients. In patients with AVNRT the “0” fluoroscopy was possible in 82%, in WPW: 47%, in AT: 50% and for VEs/VT: 41%. Generally, the majority of ablations were completed with “0” fluoroscopy (162, 58%). For the NavX in comparison to X, the procedural parameters were significantly shorter (procedural time 65.3±33 min, GA time 89±36 min, DAP 103±24 vs 92±15m2, and fluoro time 2.6±5 vs 17±14 min.). Ablation parameters were also in favour of NavX (time to 1st application 23±15 vs 27±18 min., time to last application 47±31 vs 52±33 min, as well as the number of applications 7.7±7 vs 8.7±9 and total RF time 253±274 vs 284±271 sec) however this did not reach statistical significance. Procedural success rate was 90% for NavX and 91% for RTG ablation.

We conclude that nonfluoroscopic approach with NavX is safe and successful method for pediatric ablation. If the method is used systematically it leads not only to reduced radiation burden but also to shorter procedural and GA time and the application lesions.

**P6115 | BEDSIDE**

**Initial international multicenter human experience of a novel epicardial access tuohy needle embedded with a real time pressure/frequency monitoring to facilitate epicardial access**

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**Introduction:** Epicardial (epi) ablation is often necessary for the treatment of challenging arrhythmias refractory to endocardial ablation. The subxiphoid approach is the most used method for epi access. However, major and minor complications may occur even in experienced centers with reported rates of 4–7%.

We evaluated the feasibility and safety of the EpiAccess™ Needle by EpiEP Inc., a novel “tuohy” epi access needle in a multicenter study.

**Methods:** 25 patients with a clinical need for epi access were enrolled. Epi access was obtained with the EpiAccess Needle whose tip is embedded with a pressure sensor able to report the pressure waveform in real time. Successful epi access was assessed through the device and confirmed by fluoro and contrast injection.

**Results:** Patients were male (92%) with a mean age of 65.6±13.9. Epi access due to VT ablation occurred in 84% of the patients. Successful epi access was obtained in 64% of cases. Mean access time was 280 sec ± 98.9 sec. Mean peri-cardial pressure/pulsation was 4.7±2.1 mmHg. Pressure monitoring identified pericardial wire access in 100% of the cases. In 2 cases (8%) the needle sensor suggested tenting of the pericardial space but not access to pericardial space was confirmed by an increase pressure of 11%.

**Conclusion:** Epicardial access with the novel EpiAccess™ tuohy needle and real time pressure monitoring is feasible and safe. The pressure monitoring identifies successful epi access and minimizes complications. This has relevant clinical implications.
tient characteristics and procedural profiles were comparable between the two groups. Coronary vasconstricting responses to ACh were most enhanced at the distal edge of EES as compared with non-stented vessel, and were significantly inhibited in the nifedipine group (Figure). Furthermore, the inflammatory profiles, including serum levels of hsCRP and adiponectin, were also improved in the nifedipine group (Figure).

Conclusions: These results indicate that long-acting nifedipine suppresses DES-induced coronary hyperconstricting responses in humans.

P6118 | BENCH
Atorvastatin downregulates in vivo the immediate-early response gene EGR1 in patients with acute coronary syndromes
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Background: Statins have anti-inflammatory and immune-regulatory effects besides lowering lipids that may, at least partially, account for their beneficial effects. In a previous ex vivo study, atorvastatin improves the functional profile of CD4+T-cells isolated from statin-naïve acute coronary syndrome (ACS) patients and, among the other genes, markedly down-regulates early growth response 1 (EGR1) gene expression, as assessed by PCR array analysis. EGR-1 is an immediate-early response gene, based on rapid kinetics of its expression and induction. EGR1 up-regulation alters a wide array of EGR1 target downstream genes such pro-inflammatory cytokines, and also negatively regulates the expression of the anti-inflammatory interleukin-10 at post-transcriptional level. Thus, we hypothesized that EGR1 might mediate the immune-regulatory effects of atorvastatin in ACS.

Purpose: To verify in the vivo effects of atorvastatin on EGR1, we analyzed EGR1 gene expression and protein levels in CD4+T-cells isolated from 10 statin-free ACS patients at baseline (before atorvastatin therapy, T0), and after 24h (T24) and 48h (T48) of atorvastatin therapy (80 mg/daily).

Results: qRT-PCR results show that EGR1 expression in vivo was reduced after 24h of atorvastatin therapy, from a mean value of 28.7±5.7 (mean ± SEM) at T0 to 8.5±1.9 (mean ± SEM) at T24 (P=0.01) and to 5.9±2.1 (mean ± SEM) at 48h (P=0.005). Moreover, EGR1 protein levels were significantly downregulated 48h after 80 mg statin assumption (T0 vs T48 P=0.03) (Fig. 1).

Conclusion: The anti-inflammatory effects of atorvastatin in patients with ACS might be related, at least partially, to direct inhibition of the master regulator EGR1. Our finding might offer a causal explanation on why statins have early beneficial effects in ACS.

P6119 | BENCH
Differential benefit of statin in secondary prevention of acute myocardial infarction according to the level of triglyceride and high-density lipoprotein cholesterol
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Background: Although substantial portion of patients with myocardial infarction (MI) were diagnosed as dyslipidemia, the differential benefit of statin according to the state of dyslipidemia was sparsely investigated. We sought to address the efficacy of statin in secondary prevention of MI according to the level of triglyceride and high-density lipoprotein (HDL) cholesterol on admission.

Methods: The 24653 acute MI patients were enrolled and total patients were divided according to level of triglyceride and HDL cholesterol on admission; Group A (HDL ≥40mg/dL & triglyceride >150mg/dL; n=11189), Group B (HDL ≥40mg/dL & triglyceride >150mg/dL; n=3329), Group C (HDL <40mg/dL & triglyceride >150mg/dL; n=6062) and Group D (HDL <40mg/dL & triglyceride ≥150mg/dL; n=3443). We evaluated differential efficacy of statin according to the presence or absence of component of dyslipidemia. The primary end point was major adverse cardiac event (MACE) s and MACE was defined as composite of cardiac death, non-fatal MI, target-vessel revascularization and coronary artery bypass surgery for 2 years.

Results: Statin therapy significantly reduced the risk of MACEs in Group A (HR=0.85 (95% CI: 0.802–0.905); p=0.001). Especially, the benefit of statin in Group A was different compared with Group D (Interaction p=0.042).

Conclusions: The benefit of statin in patients with MI and dyslipidemia, different lipid-lowering strategy is necessary in these patients.
Conclusions: evaluate the long-term prognosis by Kaplan–Meier survival curves.

≥

<

significantly higher in HTX patients (56±12 vs 46±9%, p

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Longitudinal shortening is considered to be the most important motion determining right ventricular (RV) function. However, the radial direction (“bellowls effect”) can gain particular importance in certain conditions. Our aim was to quantify the longitudinal and the radial components of RV performance using three-dimensional (3D) echocardiography and assess their relative contribution in normal subjects versus patients after heart transplantation (HTX).

Thirty HTX patients and 30 healthy volunteers were enrolled. Using dedicated software for RV 3D and speckle tracking analysis (4D RV-Function 2), beutel model was computed and exported volume by-volume throughout the cardiac cycle.

Beside end-diastolic (EDV) volume and total ejection fraction (TEF), we quantified longitudinal (LEF) and radial ejection fraction (REF) by decomposing the motion of each vertex of the reconstructed 3D beutel model along three orthogonal axes and omitting the other two directions.

EDV did not differ between the groups (HTX vs control: 87±22 vs 80±26mL). In HTX patients TEF was lower, but tricuspid annular plane systolic excursion (TAPSE) was decreased to a greater extent (TEF: 45±7 vs 51±4% [−12%], TAPSE: 35±10 vs 39±11% [−12%], p<0.01). LEF correlated robustly with TAPSE (r=−0.75) and free wall longitudinal strain (r=−0.69, p<0.01). In healthy subjects, TEF correlated with REF (r=0.50) and RR for (r=0.37, p<0.05). In HTX patients, TEF correlated with REF (r=0.80, p<0.001), but not with LEF. REF/TEF ratio was significantly higher in HTX patients (56±12 vs 46±9%, p<0.001).

Our software allows to quantify longitudinal and radial motion of the RV separately using 3D analysis. Current results confirm the empirical phenomenon on the superiority of radial motion in determining RV function in HTX patients.

P6121 | BEDSIDE

Right ventricular post systolic shortening using speckle-tracking echocardiography associated with prognosis in patients with pulmonary artery hypertension

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Purpose: Right Ventricular (RV) free-wall longitudinal peak systolic strain is a predictor of the clinical outcome of patients with pulmonary artery hypertension (PAH). RV dyssynchrony including post systolic shortening (PSS) in RV free-wall appeared and associated with RV systolic function in patients with RV pressure overload. We sought to investigate the association between the degree of PSS in RV free-wall using speckle-tracking echocardiography (STE) and prognosis in patients with PAH.

Methods: We performed speckle-tracking echocardiography and right heart catheterization in 91 PAH patients (age: 42±13 years). We measured RV free-wall peak longitudinal systolic strain (PLSS) and PSS index (PSSsyn舒张期 peak strain/peak strain) by STE. Mean right atrial pressure (mRAP), pulmonary vascular resistance (PVR), and cardiac index (CI) by right heart catheterization, and serum BNP were measured.

Results: Sixteen patients (17.6%) died within three years. PSS appeared in all systolic echocardiography patients. PSS index was higher in non-survivors patients compared with survivors patients (16.7% vs. 3.7%; p<0.001). There were significant correlations between CI and PLSS (r=0.71, p<0.01), PSS index (r=0.69, p<0.01). There were significant correlations between mRAP and PLSS (r=0.72, p<0.01), and PSS index (r=0.70, p<0.01). There were significant correlations between PVR and PLSS (r=0.70, p<0.01), PSS index (r=0.67, p<0.01). BNP level was correlated with PLSS (r=0.72, p<0.01), PSS index (r=0.68, p<0.01). PLSS >−10 (p<0.01) and PSS index >13.5% (p<0.01) was independent predictor to evaluate the long-term prognosis by Kaplan–Meier survival curves.

Conclusions: PSS in RV free-wall using STE was important factor for noninvasive evaluation of severity and prognosis in patients with PAH as well as PLSS.
Conclusions: Systemically regulated pVAT inflammation characterized by persistent cholesterol depletion by activation of PKC, NF-κB and STAT1. These pro-inflammatory activities on macrophages could at least partly underlie the disappoiting therapeutic potential of HDL raising therapy in current cardiovascular clinical trials.

P6129 | BENCH
STAT3 in vascular smooth muscle cells protects aorta from dissection
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Aortic dissection (AD) is a common and fatal disease for which pathogenesis is largely unknown. Recently we and others reported that Jak/Stat3-activating cytokines are highly expressed in human and mouse models of AD. In this study, we first examined the activation of STAT3 in human AD. We found that STAT3 was activated (phosphorylated) both in inflammatory cells and in vascular smooth muscle cells (VSMCs) in AD tissue. We used a mouse model of AD that was induced by continuous infusion of beta-aminopropionitrile, an inhibitor of lysyl oxidase that cross-links collagen and elastin, and angiotensin II (BAPN+AngII). BAPN+AngII caused thoracic and suprarenal AD starting at 7 days of the administration, and most of the mice developed AD within 14 days. To investigate into the function of STAT3 in VSMCs, we used the smooth muscle-specific knockout mice for SOCS3, a negative feedback regulator of STAT3 (smSOCS3-KO). The smSOCS3-KO mice developed less severe AD in the aortic arch (WT; 0.99±0.18 vs. smSOCS3-KO; 0.019±0.03 mm/g body weight, P<0.014), as determined by the lesion length with enlarged aortic diameter. Immunofluorescence staining of phospho-STAT3 showed activation of STAT3 by BAPN+AngII, which was more prominent in smSOCS3-KO as expected. Unexpectedly, smSOCS3-KO aorta showed more collagen fibers and non-nucleus cells in adventitia, suggesting deletion of smSOCS3 in VSMCs disrupts the balance between BMPR2 and IL-6, reduced the inflammation measured by the levels of IL-6 and CX3CL1 (both P<0.001). Therefore, activation of STAT3 in VSMCs reinforces the aortic wall by enhancing collagen synthesis in adventitia, thus protecting aorta from dissection. Understanding of the protection mechanism of the aortic wall from dissection would be better to understanding of the molecular pathogenesis, which is essential for developing novel therapeutic strategy for AD.

P6130 | BENCH
Gp130 inhibitor reduces inflammation and reverses pulmonary arterial remodeling of monocrotaline-induced pulmonary arterial hypertension
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Background: The pathogenesis of pulmonary arterial hypertension (PAH) is characterized by three major processes including vasoconstriction, vascular remodeling and microthrombotic events. Accumulating evidences point to inflammatory cytokine interleukin (IL)-6 as a major contributor to the development of PAH. Glycoprotein130 (Gp130) is a unique signal-transducing subunit involved in the biologic activities of IL-6.

Purpose: To test the hypothesis that Gp130 inhibitor reduces inflammation and reverses pulmonary vascular remodeling of monocrotaline (MCT)-induced PAH in rats.

Methods: Sixty male Sprague-Dawley rats weighing 240 to 250 g were randomly divided into three groups: Saline-treated control, MCT-exposed and MCT-exposed plus Gp130 inhibitor. Three groups were evaluated at day 28 for haemodynamic parameters, right ventricular hypertrophy, morphometry, immunohistochemistry, IL6, phosphorylated signal transducer and activator of transcription 3 (PYSTAT3), proliferating cell nuclear antigen (PCNA), bone morphogenetic protein receptor-2 (BMPR2) expression, and proangiogenic factor, vascular endothelial growth factor (VEGF), and the propropofol kinase extracellular signal-regulated kinase (ERK), and the antipapoptotic proteins survivin and Bcl-2 and Bax.

Results: Compared to the MCT group, the administration of Gp130 inhibitor significantly reduced MCT-induced pulmonary arterial remodeling. Accumulating evidences point to inflammatory cytokine interleukin (IL)-6 as a major contributor to the development of PAH. Glycoprotein130 (Gp130) is a unique signal-transducing subunit involved in the biologic activities of IL-6.

Conclusion: Gp130 inhibitor upregulated MCT-exposed BMPR2 expression, restored the balance between BMPR2 and IL-6, reduced the inflammation associated with IL-6, significantly inhibited the proliferation of pulmonary arterial smooth muscle cells and reversed pulmonary vascular remodeling of MCT-induced PAH in rats.

Best Posters in Rheumatic Heart Disease 2019

P6132 | BEDSIDE
Prevalence of rheumatic heart disease in north Madagascar: an echocardiographic screening study
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Background: Rheumatic Heart Disease (RHD) is one of the major causes of morbidity and mortality all over the world. Especially in developing countries it is a significant public health concern. Historically, sub-Saharan Africa has the greatest burden. In epidemiologic research, echocardiographic RHD screening significantly reduced the severity of inflammation measured by the levels of IL-6 and CXCL1 (both P<0.001), and reversed pulmonary arterial remodeling assessed by the medial wall thickness (P<0.0001). The Gp130 inhibitor upregulated BMPR2 expression of MCT-exposed lungs (P<0.001). Also, it decreased the expression of PCNA, VEGF, ERK and survivin (all P<0.05).

Conclusions: Gp130 inhibitor upregulated the MCT-exposed pulmonary BMPR2 expression, restored the balance between BMPR2 and IL-6, reduced the inflammation associated with IL-6, significantly inhibited the proliferation of pulmonary arterial smooth muscle cells and reversed pulmonary vascular remodeling of MCT-induced PAH in rats.

Best Posters in Vascular Signal Transduction / Best Posters in Rheumatic Heart Disease 2019

P6129 | BENCH
High Density Lipoproteins exert pro-inflammatory effects on macrophages via passive cholesterol depletion and PKC-dependent NF-κB/STAT1 activation
M. Donners 1, E.P.C. Van Der Vorst1, K. Theodorou 1, M.A. Hoeksema 2, M. Donners 1, E.P.C. Van Der Vorst1, K. Theodorou 1, M.A. Hoeksema 2, Z.W. Huang, Z.H. Liu, O. Luo, Z.H. Zhao, Q. Zhao, Y.G. Zheng, Q.Y. Xi on behalf of Chinese pulmonary vascular disease research group. Fuwai Hospital, CAMS, PUMC, cardiology, Beijing, China, People's Republic of China

Background: Membrane cholesterol is known to modulate a variety of cell signal-
Prevalence of clinically silent and manifest rheumatic heart disease among children in Nepal


Background: Rheumatic heart disease continues to be a major contributor to morbidity and mortality in developing countries. Detection of clinically silent disease and timely secondary prevention may prevent progression of disease.

Objective: The objective of the study was to assess prevalence of clinically silent and manifest rheumatic heart disease, and to determine risk factors associated with diagnosis.

Methods: A multistage sampling strategy was used to randomly select public and private schools in urban and rural areas in the Sunsari district situated on the foothills of the lower Himalayan range in Nepal. All children from a selected school between the ages of 5 to 15 years underwent a standardized interview, and independent clinical and echocardiographic examination. Echocardiographic diagnosis of at least one of rheumatic heart disease was based on the World Heart Federation criteria. Clinically silent disease was recorded in the absence of a cardiac murmur.

Results: Between December 2012 and September 2014 a total of 5467 eligible children from 26 randomly selected schools were enrolled in an observational survey. 2498 children due to incomplete documentation, 5179 children remained for the purpose of this analysis. The median age of the children was 10 years (IQR 8–13) and 48% were female. Prevalence of borderline or definite rheumatic heart disease amounted to 10.2/1000. 36 children had definite rheumatic heart disease and 17 had borderline disease. Prevalence increased across age categories from 5.5/1000 among children 5 years of age to 16.0/1000 among children aged 15 years. Silent disease (n=44) was 5 times more common than clinically manifest disease (n=9). Children with silent rheumatic heart disease were younger than children with clinically manifest disease (10.5 years QR 9–13 versus 14 (IQR 11–15) years, p<0.05). Children with rheumatic heart disease more commonly went to governmental schools (40.76% versus 278.55%, p=0.002), were older (11 years, IQR 9–14 versus 10 years, IQR 8–13, p=0.031) and more commonly girls (54.64% versus 19.36%, p=0.021). In a multivariate analysis, older age, female gender, and governmental school were identified as independent predictors of RHD.

Conclusion: Prevalence of rheumatic heart disease continues to be high in Eastern Nepal. Prevalence increases with advancing age, and clinically silent disease is more common than clinically manifest disease. All three components of cardiology examination and transthoracic echocardiogram focused on the 4 valves, by a portable ultrasound machine. In addition, children underwent oropharyngeal swab by rapid kit analysis and adults blood sample for Anti-Streptolisyn O (ASO) titer.

Results: Of the overall population 42% were children, 60% females, 64% from a rural context. The total prevalence of RHD was 3.2% (16 cases). Of the 209 children (mean age 13.5 years), 7 (3.3%) were found to have RHD disease. Of these, 7 had mitral disease, one had both left heart valves disease, and of the 5 available ASO titer none was positive. Only 3 (33%) of the 9 RHD were positive on cardiac auscultation and 22% had past history of GAS infections.

Conclusion: This is the first study collecting epidemiologic data about RHD in Non-subsaharan Africa, where RHD prevalence is similar to that of other African countries. Use of echocardiography, advanced technique in a developing country, permits to identify more subclinical cases. Moreover, we confirm the low accuracy of laboratory tests and clinical examination in RHD screening. However, new data are needed to describe the real dimension of the problem for future therapeutic and preventive strategies.

Echocardiographic screening among schoolchildren in Peru: Prevalence of rheumatic heart disease according to different definitions and incidental findings

E. Spitzer1, J. Mercado2, F. Islas3, M. Rothenbuehler4, R. Kurnmann5, F. Zuercher1, P. Kraehenmann1, P. Juni5, P. Torres3, T. Pilgrim1.

Background: Rheumatic heart disease (RHD) remains a major challenge in low and middle income countries. Echocardiographic screening facilitates early detection of clinically silent valvular disease. The implications of different echocardiographic criteria for diagnosis of RHD, and the burden of incidental findings from echocardiographic screening need to be determined.

Methods: We report the prevalence of RHD using the proposed WHF echocardiographic criteria. The prevalence of RHD varies widely across India and programs to control RHD should focus on high prevalence zones.

Prevalence of RHD in school children

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Manipur</th>
<th>Goa</th>
<th>Navsari</th>
<th>Ballabgarh</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=288</td>
<td>n=202</td>
<td>n=490</td>
<td>n=4452</td>
</tr>
<tr>
<td>Clinical RHD</td>
<td>3</td>
<td>1</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Prevalence of clinical RHD</td>
<td>0.29/1000</td>
<td>1.48/1000</td>
<td>0.40/1000</td>
<td>0.71/1000</td>
</tr>
<tr>
<td>Subclinical RHD</td>
<td>16</td>
<td>22</td>
<td>22</td>
<td>16</td>
</tr>
<tr>
<td>Prevalence of subclinical RHD</td>
<td>0.14/1000</td>
<td>0.07/1000</td>
<td>0.04/1000</td>
<td>0.07/1000</td>
</tr>
<tr>
<td>Borderline RHD</td>
<td>14</td>
<td>17</td>
<td>16</td>
<td>45</td>
</tr>
<tr>
<td>Prevalence of borderline RHD</td>
<td>0.14/1000</td>
<td>0.07/1000</td>
<td>0.04/1000</td>
<td>0.07/1000</td>
</tr>
</tbody>
</table>

Conclusions: The prevalence of RHD is several folds higher using WHF echocardiographic criteria. The prevalence of RHD varies widely across India and programs to control RHD should focus on high prevalence zones.
Conclusions: Prevalence of rheumatic heart disease ranged from 3.9/1000 children to 17.7/1000 children and was paralleled by a comparable number of undetected congenital heart disease. Strategies to address collateral findings from echocardiographic screening are necessary in the setup of active preventive surveillance programs for rheumatic heart disease.

BEST POSTERS IN CARDIOVASCULAR PREVENTION: INTERVENTIONS AND OUTCOMES

P6137 | BEDSIDE Clinical characteristics and outcomes of dialysis patients with atrial fibrillation: The Fushimi AF Registry
Y. Yamashita, Y. Hamatani, M. Esato, Y. Chun, H. Itoh, M. Nishimura, H. Wada, K. Hasegawa, M. Abe, M. Akao on behalf of the Fushimi AF Registry investigators. 1Kyoto Medical Center, National Hospital Organization, Kyoto, Japan; 2Takeda Hospital, Kyōto, Japan; 3Itoh Hemodialysis Clinic, Kyoto, Japan; 4Toujinkai Hospital, Cardiovascular Division, Kyōto, Japan

Background: Oral anticoagulants (OAC) are available for stroke prevention in patients with atrial fibrillation (AF). AF is a common arrhythmia in dialysis patients, and the use of warfarin for those patients is controversial.

Purpose: To evaluate clinical characteristics and outcomes in dialysis patients with AF in ‘real-world’ clinical practice.

Methods: The Fushimi AF Registry is a community-based prospective survey of AF patients who visited the participating medical institutions in Fushimi-ku, Kagamiishi, Fushimi-ku, and Hogon-ku, Kyoto city. The INR values were collected and TTR was calculated with linear interpolation method (Rosendaal method) using specialized software. The patients, whose TTR value was above 65%, were accepted as patient on effective warfarin treatment. Minimum 6 months period of warfarin usage required and warfarin interruptions with any reason was excluded. Minimum 4 INR estimations over 2 months interval have been recorded. In hospitals with having only one cardiologist and patients warfarin treatment was monitored by the same physician, the data were grouped as ‘single physician’. In hospitals with multiple cardiologists, patients have admitted to different physicians in each visit, the data were grouped as “multiple physicians”

Results: In this study, 24.9% of the patients (n=156) were followed by single physician. Mean age, comorbidities and indications of warfarin usage of the patients were not different between groups. Mean TTR values of the single physician group were higher than multiple physicians group (80.2±6.6 vs 54.9±27.6, P=0.009). The proportion of the effective TTR was higher in single physician group that was statistically significant (51% vs 39% p=0.026). Minor bleeding and cerebral embolism complications were lower in single doctor group (p<0.001). Level of confidence about warfarin usage was also higher in single doctor group (p<0.001).

Characteristics and complications of patient

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Single physician</th>
<th>Multiple physician</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>61.0±12.0</td>
<td>60.2±13.2</td>
<td>0.312</td>
</tr>
<tr>
<td>Cerebral embolism during warfarin use (n, %)</td>
<td>6 (3.8)</td>
<td>43 (9.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean time in therapeutic range, TTR (%)</td>
<td>62.0±26.6</td>
<td>54.9±27.6</td>
<td>0.009</td>
</tr>
<tr>
<td>Patients with TTR ≤ 65% (n, %)</td>
<td>80 (51.2)</td>
<td>186 (39.7)</td>
<td>0.027</td>
</tr>
<tr>
<td>Level of confidence about warfarin usage (n, %)</td>
<td>16 (10.3)</td>
<td>55 (11.7)</td>
<td>0.767</td>
</tr>
<tr>
<td>Patients with TTR &lt; 40% (n, %)</td>
<td>13 (8.3)</td>
<td>147 (31.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Moderate</td>
<td>44 (28.2)</td>
<td>112 (23.9)</td>
<td></td>
</tr>
<tr>
<td>Level to high</td>
<td>51 (32.7)</td>
<td>92 (19.6)</td>
<td></td>
</tr>
<tr>
<td>TTR in therapeutic range.</td>
<td>32 (20.5)</td>
<td>54 (11.5)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Mean TTR and effective TTR is higher in single physician group. Cerebral embolism and minor bleeding was also lower in this group.

P6138 | BEDSIDE Mortality in takotsubo syndrome is similar to mortality in myocardial infarction - a report from the SWEDHEART registry

Background: Takotsubo syndrome is an acute cardiovascular condition that predominately affects women.

Purpose: In this study, we compared patients with takotsubo syndrome and those with acute myocardial infarction with respect to patient characteristics, angiographic findings, and short- and long-term mortality.

Methods: From the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) and the Register of Information and Knowledge about Swedish Heart Interventions (RIKS-HIA), we obtained and merged data on patients undergoing coronary angiography in Västra Götaland County in western Sweden between January 2005 and May 2013. Short- and long-term mortality in patients with takotsubo (n=302) and patients with ST-elevation myocardial infarction (STEMI), (n=8207) were compared by modeling unadjusted and propensity score—adjusted logistic and Cox proportional-hazards regression.

Results: The proportion of the patients diagnosed with takotsubo increased from 0.16% in 2005 to 2.2% in 2012 (P < 0.05); 14% of these patients also had significant coronary artery disease. Cardiogenic shock developed more frequently in patients with takotsubo than NSTEMI (adjusted OR 3.08, 95% CI 1.80–5.28, P < 0.001). Thirty-day mortality was 4.1% and was comparable to STEMI and NSTEMI. The long-term risk of dying in takotsubo (median follow-up 25 months) was also comparable to NSTEMI (adjusted HR 1.01, 95% CI 0.70–1.46, P=0.955) STEMI (adjusted HR 0.83, 95% CI 0.57–1.20, P=0.328).

Conclusions: The proportion of acute coronary syndromes attributed to takotsubo syndrome in Western Sweden has increased over the last decade. The prognosis of takotsubo syndrome is poor, with similar early and late mortality as STEMI and NSTEMI.
at high risk of having poor quality on OAC whilst on VKAs. We explore the predictive role of the SAME-TT2R2 score for assessing poor anticoagulant control in a prospective cohort of patients on VKA treatment.

Methods: We studied VKA treated non-valvular AF patients who were prospectively recruited in the multicentre Spanish observational registry FANTASIA. Estimated TTR was calculated from both direct and Rosendaal methods during a 6 month period. The SAME-TT2R2 score was calculated and TTR values compared for those patients with a SAME-TT2R2 score of 0 and >2.

Results: We studied 948 patients (mean age 73±9.4 years, 57.5% male). Mean TTR was 0.68±0.29 for the direct method and 0.57±0.23 for the Rosendaal method. Prevalence of poor anticoagulation control (TTR<65%) was 54%. As expected a progressive reduction of TTR was found as SAME-TT2R2 score values increased (Table). Those patients with SAME-TT2R2 score of 0–1 had better TTR as calculated by the Rosendaal method (62.5±24 vs 58.9±24.1; p<0.01).

Mean TTR for each SAME-TT2R2 value

<table>
<thead>
<tr>
<th>SAME-TT2R2 score</th>
<th>N</th>
<th>TTR direct</th>
<th>TTR Rosendaal</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>159</td>
<td>65.4±22.5</td>
<td>63.2±24.6</td>
</tr>
<tr>
<td>1</td>
<td>387</td>
<td>64.6±23.7</td>
<td>61.5±24.7</td>
</tr>
<tr>
<td>2</td>
<td>289</td>
<td>63.5±23.5</td>
<td>58.3±23.2</td>
</tr>
<tr>
<td>3</td>
<td>84</td>
<td>61.3±23.7</td>
<td>58.4±23.2</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>57.3±18.1</td>
<td>52.1±19.3</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>54.7±21.0</td>
<td>51.6±20.4</td>
</tr>
</tbody>
</table>

Conclusions: In a multicenter prospective registry, a high SAME-TT2R2 score (>2 points) is associated with poor quality anticoagulation in patients on VKA. Our registry demonstrates the potential role of this simple clinical risk score to predict the poor quality OAC with VKA in clinical practice, and helps decision making for additional strategies including use of the Non-VKA Oral Anticoagulants.

BEST POSTERS IN CIRCULATORY ASSIST AND OTHER

P6142 | BEDSIDE

Impact of preoperative pulmonary hypertension and right ventricular dysfunction on caridorectal interaction after left ventricular assist device implantation

S. Keymel1, S. Bueter1, D. Saeed2, U. Boeken2, C. Heiss1, A. Lichtenberg 2, K. Minatoya1, H. Sasaki 1, H. Tanaka 1, T. Itonaga 1, Y. Seike1, T. Oda 1, D. Saeed2, U. Boeken2, C. Heiss1, A. Lichtenberg 2, K. Minatoya1, H. Sasaki 1, H. Tanaka 1, T. Itonaga 1, Y. Seike1, T. Oda 1

Background: Incidence of advanced heart and renal failure (cardiorenal syndrome) (CRS) is associated with poor outcome. Timely left ventricular assist device implantation (LVAD) implantation may reverse renal dysfunction due to restoration of cardiac output (CO) and relief of venous congestion. Besides the mere reduction of CO, right ventricular dysfunction induced venous congestion is believed to be involved in the progression of renal failure in CRS.

Purpose: Preoperative pulmonary hypertension and right ventricular dysfunction influence the course of CRS after LVAD implantation.

Methods: We performed a retrospective analysis in patients with heart failure (HF) before and after LVAD implantation. Patients with early mortality (90 days) were excluded from the analysis. Renal function was assessed by glomerular filtration rate (GFR) before, after the procedure and 3 and 6 months after LVAD implantation. Right ventricular function was evaluated by preoperative echocardiography (tricuspid annular plane systolic excursion (TAPSE)) and right heart catheterization (cardiac index (CI)), mean pulmonary artery pressure (mPAP). GFR after 1 month and 6 month, respectively, were analysed versus baseline GFR by t test.

Results: 35 patients (age 53±14 years) with advanced HF were analysed. HeartWare LVAD (n=31) or HeartMate II LVAD (n=4) were implanted. Mean baseline GFR was 63±20 ml/min. After 1 month, a significant increase of GFR was observed (82±330 ml/min; p=0.002) which decreased after 6 month (65±21 ml/min; p=0.621). Subgroup analyses were performed regarding baseline GFR, preoperative CI, TAPSE or mPAP. Mean GFR did not change in patients with baseline GFR >60 ml/min with a significant improvement of GFR after 1 (47±8 vs 78±33 ml/min; p=0.001) and 6 month (55±16 ml/min; p=0.036). Patients with CI above median showed a significant increase of GFR after 1 month (62±21 vs 76±17 ml/min; p=0.033; 6 month 62±20 vs 76±17 ml/min; p=0.038) while no change was found in patients with CI below median. Patients with TAPSE <14 mm showed a significant increase of GFR after 1 month (61±24 vs 85±35 ml/min; p=0.035; 6 month 59±15 ml/min; p=0.645). Also, in patients with mPAP >37.5 mmHg a significant improvement after 1 month was found (66±25 vs 85±27 ml/min; p=0.037; 6 month 71±20 ml/min; p=0.443). No changes were observed in patients with TAPSE <14 mm or mPAP <37.5 mmHg.

Conclusion: In advanced HF, LVAD implantation improves CRS. Presence of pulmonary hypertension or right ventricular dysfunction seems to be more predictive than reduction of cardiac output for potential resolution of CRS after LVAD implantation.

P6143 | BEDSIDE

Is tricuspid annuloplasty really unnecessary at pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension?

K. Minatoya1, H. Sasaki1, H. Tanaka1, T. Itonaga1, Y. Seike1, T. Oda1

Background: Tricuspid regurgitation (TR) is detected in most patients with chronic thromboembolic pulmonary hypertension (CTEPH). TR with a dilated anulus is supposed to be improved without tricuspid annuloplasty (TAP) after significant reduction of pulmonary artery pressure (PAP) reduction with the pulmonary endarterectomy (PEA).

Purpose: The aim of this study is to investigate the improvement of significant TR with and without PAP after PEA for CTEPH.

Methods: Since 2000, 143 patients underwent surgery for CTEPH. Of them, survivors of preoperative TR grade 3 or 4 consist of study population. Fifty patients had TR grade 3 and 18 had grade 4. The mean PAP was 47±8 mmHg, and the mean pulmonary vascular resistance (PVR) was 120±404 dyne.s.cm-5. PEF was performed through median sternotomy using cycles of 15–20 minute intermittent circulatory arrest at 10–20 degrees Celsius. Of these patients (25.7%) had tricuspid valve annuloplasty (TAP), due to severe annulus prolapse. Results: Postoperative mean PAP was 25±12 mmHg, and postoperative PVR was 497±336 dyne.s.cm-5. Forty-nine patients (70.0%) showed postoperative TR grade less than grade 2 (38 pts. without TAP vs. 11 pts. with TAP, p=0.035), and 64 patients (91.4%) showed TR grade less than grade 3 (49 pts. without TAP vs 15 pts. with TAP; p=0.16). Among the 6 patients with more than postoperative TR grade 3, 3 without TAP showed TR grade 3 despite the reduction of PAP and 3 with TAP showed TR grade 3 with residual elevated PVR (Table).

Postoperative TR grade more than grade 3

<table>
<thead>
<tr>
<th>TAP</th>
<th>Postop TR</th>
<th>Postop mean PAP</th>
<th>Postop PVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>4</td>
<td>3</td>
<td>33</td>
</tr>
<tr>
<td>Yes</td>
<td>4</td>
<td>3</td>
<td>59</td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
<td>66</td>
<td>1864</td>
</tr>
<tr>
<td>No</td>
<td>4</td>
<td>3</td>
<td>49</td>
</tr>
<tr>
<td>No</td>
<td>3</td>
<td>3</td>
<td>42</td>
</tr>
<tr>
<td>No</td>
<td>3</td>
<td>3</td>
<td>62</td>
</tr>
</tbody>
</table>

TAP: tricuspid annuloplasty; TR: tricuspid regurgitation; PAP: pulmonary arterial pressure; PVR: pulmonary vascular resistance. Conclusions: Most patients with more than moderate TR showed significant reduction of TR grade after PEA, however, some showed no improvement after PEA. Although PAP was not a complete solution for the TR, routine TAP for severe TR in patients with CTEPH might be an option.
The efficacy and safety of novel hemostasis technique: ultrasound-guided thrombin injection with ballooning

H. Takimura, T. Muramatsu, R. Tsukahara, Y. Tto, T. Sakai, K. Hirano, M. Yamawaki, M. Araki, N. Kobayashi, Y. Sakamoto. Saiseikai Yokohama-city Eastern Hospital, Yokohama, Japan

Background: Recently percutaneous intervention via common femoral artery (CFA) has been used in not only percutaneous coronary intervention but also endovascular intervention. Transcatheter aortic valve replacement (TAVR), percutaneous Impella LVA-0. This technique requires use of large diameter sheath via CFA without a surgical cut-down. Complication of vascular access site has become a problem. So we have developed a novel hemostasis technique “Ultrasound-guided Thrombin Injection with Ballooning (UTIB)”. Our aim was to evaluate the efficacy and safety of UTIB technique.

Methods: From April 2012 to 2013 May, 20 consecutive patients underwent to balloon aortic valvuloplasty in our institution. 12 or 14 French size sheaths was inserted via CFA without cut-down. Ultrasound-guided thrombin injection with ballooning was performed after procedure. 5 Fr. IMA catheter was introduced over a wire via the contralateral CFA to the ipsilateral common iliac artery. 0.035 inch guide wire was then introduced to the ipsilateral CFA passed the sheath. A balloon of appropriate size was deployed at the level of puncture site in the CFA. The sheath was removed and then the balloon was inflated. We detected the non-bleeding by color doppler with ultrasonography (US) from body surface. Thrombin was injected with 2.5cc syringe and 21G needle on the CFA during ultrasound guided. And then we detect stopping bleeding with US, the balloon was deflated. Results: The mean patient age was 86±range 65-95 years old and 70.0% were male. 95.0% patients were on single or dual antiplatelet therapy. The CFA diameter was 7.7±0.8mm, balloon diameter was 7.3±0.9mm. The mean bovine thrombin dose was 3133IU (range 1000-5000IU). Success cases were all cases (100%). Hemostasis time was 4.6±1.8 min. No complications were observed including thromboembolism, limb ischemia, pseudo aneurysm, infection and bleeding.

Conclusions: In percutaneous intervention that large vessel vascular access was needed, UTIB was useful and safety for patients under antiplatelet therapy.

BEST POSTERS IN PROGNOSIS

P6148 | BEDSIDE
Nocturnal desaturation: a predictor of outcome in heart failure with reduced ejection fraction

1 University Hospital Henri Mondor, Department of Cardiology, Creteil, France; 2 University Hospital Henri Mondor, Public Health Department and Clinical Research Unit, Creteil, France; 3 University Hospital Henri Mondor, Department of Physiology, Creteil, France

Aims: Sleep disordered breathing (SDB) is common in HF with reduced ejection fraction (HFrEF). An increased apnea-hypopnea index (AHI) is predictive of poor outcomes. Our objective was to examine whether an analysis of ND can improve the risk stratification of HFrEF patients.

Methods and results: 376 consecutive patients with stable HFrEF and LVEF <45% were screened for SDB between 2005 and 2010 using polygraphy. SDB was defined as an AHI>5, and sleep apnea (SA) as an AHI>15. The mean age was 59±15, the mean LVEF was 30±16%, and the median AHI was 18 [IQR: 9.33]; 310 patients (82%) had SDB. The predefined composite primary end-points (death, heart transplantation or LV assistance) occurred in 98 patients (26%) within 3 years. Minimal oxygen saturation (MOS), the number of desaturations <90% of the time spent with oxygen saturation <90% were significantly associated with adverse events (adjusted HR [95% CI]: 1.25 [1.03–1.52], 1.25 [1.03–1.53], and 1.28 [1.04–1.59], respectively) after adjustment for confounders, whereas AHI was not (1.10 [0.86–1.39]). The best MOS cut-off value for poor outcomes was <88%. Patients with an MOS <88% without SA (32/100 patients) had similar event rates to those with an MOS <88% with SA (31/100). The patients with an MOS <88% had a significantly higher event rate (31/100) than those with an MOS >88% (15.6/100) (P<0.01). The risk assessment using a MOS of <88% in addition to established prognostic markers within the net reclassification improvement (NRI) of nearly 6% and was particularly useful in the subgroup of patients with events (NRI: 8.4%).

Conclusions: In HFrEF patients, ND<88% is an independent predictor of adverse events. The risk assessment in HFrEF should include ND and that SDB treatment may also focus on patients without SA who are presenting ND.

P6149 | BEDSIDE
Midregional pro-Adrenomedullin.Performance and risk stratification in patients with decompensated systolic heart failure

C. Morbach1, A. Marx1, M. Kaspar1, G. Gueder1, S. Brenner1, D. Berliner2, S. Stoenk1, J. Voller3, G. Erti1, G. Angermann1 on behalf of German Competence Network Heart Failure. 1 University of Wuerzburg, Dept. of Medicine and Comprehensive Heart Failure Centre, Wuerzburg, Germany; 2 Hannover Medical School, Clinic for Cardiology and Angiology, Hannover, Germany; 3Thermo Fischer Scientific, Hehningsdorf, Germany

Introduction and aim: Midregional pro-adrenomedullin (MR-proADM), the stable prohormone fragment of adrenomedullin, was shown to be elevated in acutely decompensated heart failure (ADHF), and proved superior to other biomarkers or risk models regarding prediction of outcomes in acute dyspnea regardless of aetiology. In the present post-hoc analysis from the Interdisciplinary Network Heart Failure (INH) Study we aimed to explore its performance as a biomarker and its predictive potential regarding short- and longer-term outcomes in patients hospitalised for ADHF.

Results: In 917 of 1022 study participants (72.2% male, mean age 68±12 years) MR-proADM was measured (KRYPTOR, detection limit 0.5nmol/L, intra- and inter-assay coefficients of variation <10%). In 905 of 917 (99.1%) patients with decompensated systolic heart failure (HF), the midregional pro-adrenomedullin (MR-proADM) concentration was significantly higher in HF patients with decompensated systolic heart failure (ADHF), and proved superior to other biomarkers or risk models predicting regard to outcomes in acute dyspnea regardless of aetiology. In 917 of 1022 study participants (72.2% male, mean age 68±12 years) MR-proADM was measured (KRYPTOR, detection limit 0.5nmol/L, sensitivity 0.25mmol/L) at discharge from hospital after best possible cardiac care. Otherwise, MR-proADM was significantly higher in patients hospitalised for ADHF within the entire FUP period (18 months), 185 patients (20%) died. In percutaneous intervention that large vessel vascular access was needed, UTIB was useful and safety for patients under antiplatelet therapy.

Event-free survival according to MOS

Conclusions: In HF patients, ND<88% is an independent predictor of adverse events. The risk assessment in HFrEF should include ND and that SDB treatment may also focus on patients without SA who are presenting ND.
coepetin (p<0.001 for inclusion of MR-proADM into all adjusted models). Further, in a multivariable model including the base model and both MR-proADM measurements, only the F6 value contributed significantly (p<0.001), whereas the BL value had no significant impact on survival during the following 12 months (p=0.419).

Conclusions: MR-proADM was strongly correlated with heart failure severity. It was a strong predictor for longer-term survival with a predictive power exceeding that of all other investigated novel biomarkers and NT-proBNP. Although MR-proADM values remained relatively stable over time, serial assessment after 6 months significantly improved risk stratification and helped to identify patients at highest risk.

BEST POSTERS IN HYPERTENSION TREATMENT

P6151 | BEDSIDE
Circulating endothelial progenitor cells in patients with essential hypertension
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Objective: The aim of study was to explore the quantity and properties circulating endothelial progenitor cells (CEPCs) function as well as their dynamics during antihypertensive treatment in patients (pts) of essential hypertension (EH).

Methods: 18 EH pts with LV hypertrophy (mean age 54.8±3.7 yrs, BMI 28.2±1.3 kg/m²) were enrolled. Pts received beta blockers and hydrochlorothiazide before the study pts. During the study all pts took lisinopril up 20 mg and then were re-examined through 12 weeks therapy. 19 normotensive healthy people were examined (40.5±1.7 yrs, BMI 24.9±0.6 kg/m²) as control group. 24-hour ABP monitoring, TTE, carotid intima-media thickness, flow-mediated dilatation (FMD) of brachial artery were done in all pts. The quantity of circulating CD34+CD133+ and CD34+CD133+VEGFR-2+ cells was assessed by flow cytometry. CEPCs function was evaluated by calculation of colony-forming units (CFU) with J.M.Hill's method. SA-beta-gal staining was used to evaluate the senescence.

Results: There were no differences in CEPCs number in EH pts and healthy control, but we revealed decreased number of CFU CEPC in EH pts. Pts with nocturnal hypertension had a lower CEPCs (r=-0.520, p=0.03) number and CFU (r=-0.563, p=0.01). Also, EPCs proliferate activity was associated with pts's age (r=-0.584, p=0.01) and SCORE index (r=-0.473, p=0.01). The same relations were observed between FMD of brachial artery and SCORE index (r=-0.468,p=0.05). In the end of study we found increasing CEPCs number and CFU, but the number of SA-beta-gal positive cells were decreased.

Conclusion: Hypertension has a negative impact on the CEPCs functional activity. Endothelial dysfunction may be connected with impaired function of CEPCs, which may be related to CEPCs senescence. ACE inhibitors therapy improves CEPCs functional activity.

P6152 | BENCH
TAK-085 is superior to eicosapentaenoic acid in ameliorating salt-sensitive hypertension in rats
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Objective: TAK-085 and eicosapentaenoic acid-ethyl ester (EPA-E) are clinically used for the treatment of hypertriglyceridemia. Unlike EPA-E products, TAK-085 contains not only EPA-E but also docosahexaenoic acid-ethyl ester (DHA-E). This product was developed for the treatment of hypertriglyceridemia. Unlike EPA-E products, TAK-085 seems to be effective for the prevention of salt-sensitive hypertension.

Methods: We enrolled 213 hypertensive patients with mild to moderate hypertension (systolic blood pressure (SBP) >140 and <180 mmHg and diastolic blood pressure (DBP) >90 and <105 mmHg). Patients were randomised to amiodidine 5 mg, or amiodidine 5 mg + ASA for three months; then, if adequate blood pressure was not achieved, patients were titrated up to amiodidine 10 mg. Both groups were followed for at least 3 months and compared to amiodidine 10 mg + ASA 100 mg.

Results: We assessed the effects of the two treatments on some inflammatory parameters evaluating, at baseline, after 3 and 6 months these markers: high sensitivity C-reactive protein (hs-CRP), adiponectin (ADN), tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), myeloperoxidase (MPO), soluble CD40 ligand (sCD40L).

Conclusion: There were no differences in CEPCs number in EH pts and healthy control, but we revealed decreased number of CFU CEPC in EH pts. Pts with nocturnal hypertension had a lower CEPCs (r=-0.520, p=0.03) number and CFU (r=-0.563, p=0.01). Also, EPCs proliferate activity was associated with pts's age (r=-0.584, p=0.01) and SCORE index (r=-0.473, p=0.01). The same relations were observed between FMD of brachial artery and SCORE index (r=-0.468, p=0.05). In the end of study we found increasing CEPCs number and CFU, but the number of SA-beta-gal positive cells were decreased.

Conclusion: Hypertension has a negative impact on the CEPCs functional activity. Endothelial dysfunction may be connected with impaired function of CEPCs, which may be related to CEPCs senescence. ACE inhibitors therapy improves CEPCs functional activity.

P6153 | BEDSIDE
Amiodidine alone compared to amiodidine + acetylsalicylic acid on inflammation and endothelial damage markers in hypertensive patients
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Background: The use of acetylsalicylic acid (ASA) in primary prevention is still debated.

Purpose: To evaluate the effects of amiodidine alone, compared to amiodidine + ASA, on some inflammatory and endothelial damage markers in patients affected by essential hypertension.

Methods: Inclusion criteria: We enrolled 213 hypertensive patients with mild to moderate hypertension (systolic blood pressure (SBP) >140 and <180 mmHg and diastolic blood pressure (DBP) >90 and <105 mmHg). Patients were randomised to amiodidine 5 mg, or amiodidine 5 mg + ASA for three months; then, if adequate blood pressure was not achieved, patients were titrated up to amiodidine 10 mg. Both groups were followed for at least 3 months and compared to amiodidine 10 mg + ASA 100 mg.

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Poster session 7

NEW INSIGHTS IN ARRHYTHMIAS: MECHANISMS AND TREATMENT

P6154 | BENCH
The combined effects of ranolazine and low dose dronedarone on atrial vs. ventricular electrophysiology; a novel therapeutic hope?
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Introduction: Pharmacological rhythm control of atrial fibrillation (AF) in patients with structural heart disease is limited. Ranolazine (Ran) in combination with low dose dronedarone (Dron) remarkably reduced the AF-burden of by 59% in the HARMONY Trial (Heart Rhythm congress 2014). We thus aimed to investigate the underlying causes of these trial results.

Results: Human atrial cardiomyocytes (CM) were isolated from 18 patients with AF versus 18 in sinus rhythm (SR). LV myocardium was taken from 9 human patients. The underlying causes of these trial results. Ranolazine (Ran) in combination with low dose dronedarone (Dron) remarkably reduced the AF-burden of by 59% in the HARMONY Trial (Heart Rhythm congress 2014). We thus aimed to investigate the underlying causes of these trial results.

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change the APD. Similar to its atrial effects Ran and the combination, but not Dron caused a hyperpolarisation of the resting membrane potential (p < 0.05) in human LV HF CM. The investigation of cellular arrhythmogenic triggers (EADs, DADs and spontaneous APs) in AF and in LV HF CM showed a reduction of DADs by the combination of Ran and Dron. The proarrhythmic SR-Ca2+-leak in SR and AF which underlies the occurrence of DADs was measured using confocal microscopy (Fluo 3). Ran alone caused a potent reduction of the SR-Ca2+-spark frequency (by 78.0%, p < 0.05) in SR CM. Comparable results could be obtained with the combination (by 78.2% p < 0.05) that also suppressed Ca2+ waves and spontaneous transients by ~60% (p < 0.05). In AF CM preliminary data show a significant reduction of the SR-Ca2+-spark frequency of Ran by 54% (p < 0.05) and the combination by 60% (p < 0.05).

Conclusion: Our electrophysiological measurements of Ran alone and in combination with low dose Dron show APD prolongation, cellular hyperpolarisation and a reduced SR-Ca2+-leak in human atrial CM. Therefore, the combined inhibitory action with low dose Dron show APD prolongation, cellular hyperpolarisation and a reduced SR-Ca2+-leak in human atrial CM. Therefore, the combined inhibitory action with low dose Dron show APD prolongation, cellular hyperpolarisation and a reduced SR-Ca2+-leak in human atrial CM. Therefore, the combined inhibitory action with low dose Dron show APD prolongation, cellular hyperpolarisation and a reduced SR-Ca2+-leak in human atrial CM.

P615 | BEDSIDE
Digoxin use is associated with higher mortality among patients with atrial fibrillation with and without heart failure: insights from the ARISTOTLE trial

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Background: Despite limited data from randomized controlled trial, digoxin is widely used in pts with atrial fibrillation (AF). Recent studies, exploring whether digoxin increases mortality, have reported conflicting results.

Purpose: To evaluate whether digoxin is associated with survival in pts with AF with or without heart failure (HF). We also assessed the treatment effect (apixaban vs. warfarin) on clinical outcomes according to digoxin use.

Methods: We studied ARISTOTLE pts where information about digoxin and HF status at baseline (n=17897) were available. Event-rates by digoxin use and HF status were computed and the association between digoxin and mortality was assessed.

Results: At baseline 5824 pts (32%) were treated with digoxin and 6693 (37%) had HF. Digoxin use was associated with a significant increase in the risk of all-cause mortality among pts with and without HF. The beneficial effects of apixaban vs. warfarin were similar in pts on and off digoxin.

<table>
<thead>
<tr>
<th>Event rates per 100 patient-year follow-up</th>
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<tr>
<td>Event rates by digoxin status</td>
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<tr>
<td>Digoxin No digoxin Adjusted HR (95% CI)</td>
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<tr>
<td>All-cause mortality</td>
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<tr>
<td>Overall population</td>
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<tr>
<td>No HF</td>
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<tr>
<td>HF</td>
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<td>Cardiovascular mortality</td>
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<td>Overall population</td>
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<td>Event rates by apixaban vs. warfarin</td>
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<td>Apixaban No warfarin</td>
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<tr>
<td>HR (95% CI)</td>
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<tr>
<td>Stroke/systemic embolism</td>
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<tr>
<td>Digoxin</td>
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<td>No digoxin</td>
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<tr>
<td>All cause mortality</td>
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<td>No digoxin</td>
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<td>ISTH major bleeding</td>
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<td>Digoxin</td>
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<td>No digoxin</td>
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*P for interaction: 0.866 for stroke/systemic embolism, 0.425 for all cause mortality and 0.461 for ISTH major bleeding.

Conclusions: Digoxin use was associated with a significant increased risk of mortality in AF, irrespective of the presence of HF. The benefits of apixaban vs. warfarin were consistent and preserved regardless of digoxin use.

P615 | BEDSIDE
Effects of combination therapy with nifekalant and mexiletine on electrical storm

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Background: Patients with electrical storm, which is a clinical emergency, are frequently required antarrhythmic drugs. Amiodarone has been widely used for the treatment of electrical storm, but is ineffective in a certain number of patients and evidence showing the efficacy of other antarrhythmic drugs for electrical storm is limited. Therefore, we aimed to study the efficacy of stepwise administration of nifekalant, a pure potassium channel blocker, and mexiletine as emergency treatment to control electrical storm.

Methods: This study included patients who received stepwise therapy with nifekalant and mexiletine for electrical storm. Nifekalant was initially administered, and mexiletine was subsequently added if nifekalant failed to control ventricular tachyarrhythmias.

Results: This study included 44 patients (age, 61±15 years; 10 women, 23% with repetitive ventricular tachyarrhythmias who were treated with nifekalant. Underlying heart diseases were, myocardial infarction (n=9, 20%), cardiomyopathy (n=27, 61%), and other diseases (n=8, 18%). Nifekalant completely suppressed recurrences of ventricular arrhythmias in 28 patients (64%). There was no severe side effect of nifekalant, which required the discontinuation of the drug. In 9 of 16 patients in whom nifekalant was partially effective but failed to suppress ventricular arrhythmias, mexiletine was added to nifekalant. The addition of mexiletine prevented recurrences of ventricular tachyarrhythmias in 5 of 9 patients (56%). Mexiletine was discontinued in two patients because of neurological side effect (n=1) and ventricular fibrillation (n=1). There was no death associated with electrical storm. In total, the stepwise treatment with nifekalant and mexiletine was effective in preventing ventricular tachyarrhythmias in 33 of 44 patients (75%). There was no difference in cycle length of ventricular tachycardia, QRS interval, QT interval, mexiletine dose, nifekalant dose, or left ventricular ejection fraction between patients who responded to antarrhythmic drugs and those who did not respond.

Conclusion: The stepwise therapy of nifekalant and mexiletine was highly effective in suppression of electrical storm.

P615 | BEDSIDE

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Background: An important decision in the management of atrial fibrillation (AF) is between a rate-control and rhythm-control strategy. If the latter is adopted options include oral anti-arrhythmic drugs (AADs) or catheter ablation. There have been increasing reports of the association between oral AADs (in particular Class Ia, Ic and III agents [Vaugan-Williams]) and higher mortality, which may affect prescribing behaviour.

Purpose: To describe the trend in oral AADs prescriptions in England 1998–2014.

Methods: We conducted a retrospective study using data from the Prescription Cost Analysis system, which holds information on every prescription dispensed in the community in England. We obtained data from 1998 to October 2014 for all Class Ia, Ic and III AADs. Beta blockers (Class II) were not studied as they are not exclusively used for rhythm control in AF.

Results: Amiodarone and sotalol remain the most commonly prescribed AADs in England, though the use of both is decreasing (Figure). Over the study period the two drugs have been discontinued: quinidine, tocainide and one introduced: dronedarone (2009). Dronedarone prescriptions peaked in September 2011 and our most recent data shows that amiodarone prescriptions are 25 fold those of dronedarone.

Conclusions: There is a decline in use of amiodarone and sotalol consistent with the growing safety concerns with these drugs. Dronedarone has failed to make an impact on AAD prescribing. In contrast, flecainide, which now has stronger evidence for safety has had a linear increase in use. There remains a dearth of safe and effective new oral AADs for AF, which needs attention.
null
In patients with a QTc probably related to the weight according to symptoms in the Schwartz score. The frequency of mutations is lower in the symptomatic with QTc<480ms group, probably related to the weight according to symptoms in the Schwartz score. In patients with a QTc>480ms, genetic analysis identified a high percentage of mutations independently of the presence of symptoms.

P6162 | BENCH
Single nucleotide polymorphisms discriminates between symptomatic and asymptomatic LQT2S patients: A DNA-based patient classification

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Aim: We evaluated if specific genomic signatures exist in LQT2S patients which could assist in discriminating disease severity between symptomatic and asymptomatic between symptomatic and asymptomatic LQT2S patients bearing heterozygous mutations in KCNH2 gene that encodes the IKr potassium ion channel. Using next generation sequencing (NGS), KCNH2 gene in LQT2S patients was sequenced along with healthy patient cohorts. Skin fibroblasts from selected patients were reprogrammed to generate transgene-free human induced pluripotent stem cells (hiPSCs). These hiPSCs were differentiated into cardiomyocytes for confirmation studies. Electrophysiological and electronic array analysis indicating corrected field potential duration (cFPD) demonstrated cardiomyocytes from LQT2S patients (asymptomatic and symptomatic, 628±73 ms, n=26) showed delayed repolarization as compared to controls (355±48 ms, n=15). Although symptomatic cardiomyocytes showed longer cFPD (689±89 ms, n=10) as compared to asymptomatic (601±190, n=16), no statistical difference was documented. Interestingly, NGS-based SNP analysis identified 11 SNPs within intragenic regions of KCNH2 gene only in LQT2S patients which were absent in controls. These NGS results were further validated by Sanger Sequencing across multiple LQT2S patients. More interestingly, there were 8 SNPs that could specifically discriminate between symptomatic and asymptomatic LQT2S patients based on their QTc interval and Schwartz score. These results provide insights in understanding the differences between symptomatic and asymptomatic LQT2S clinical presentations.

Conclusions: Understanding mechanisms governing subtle differences between symptomatic and asymptomatic patients would provide unparalleled insights in developing new diagnostic tools for patient management. Our study leverages on the presence of SNPs which could act as a genetic marker which could disprove the role of hERG and asymptomatic LQT2S patients and provide better clinical regimes as well as understanding disease penetrance in LQT2S.


P6163 | BENCH
Sustained QTc shortening by GS-6615 in patients with LQT3

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Introduction: In patients with LQT3, enhanced cardiac late sodium current (INa,L) causes prolongation of QT interval. GS-6615 is a selective inhibitor of INa,L that has been shown to shorten the action potential duration and QTc interval in experimental models of LQT3. We determined the effect of GS-6615 on QTc shortening and duration in patients with LQT3.

Methods: Five patients with LQT3 and QTc >480 msec at screening were admitted to the CRC of the University of Rochester. GS-6615 was administered orally at 50 mg on Day 1, 10 mg on Days 2–3, 20 mg on Days 4–7, and followed by washout on Days 8–11. Standard 12-lead ECG were collected over 12 hours each day. The daytime QTc interval for each day was calculated as AUC0–12/(QTc)/12 hours and the baseline was defined as the average of Days –2 and –1.

Results: The baseline mean (±SE) daytime QTc interval was 525±16 msec, which was shortened by 26–39 msec during seven days of dosing (Figure). After stopping GS-6615, QTc remained below baseline during the 4 days of washout, possibly due to the long half-life of GS-6615. On Day 1, the median (Q1, Q3) value for the maximal shortening of QTc interval relative to pre-dose was 53 (40, 70) msec, which was observed at 3 (3.5) hours post-dose. GS-6615 did not affect heart rate and blood pressure.

Conclusion: GS-6615 caused a sustained shortening of QTc in LQT3 patients and was well tolerated. A clinical study to evaluate the long-term safety and efficacy of GS-6615 in patients with LQT3 is currently ongoing.

Acknowledgement/Funding: Gilead Sciences Inc.

P6164 | BENCH
Inflammation in ARVC: new pathophysiological insights

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Introduction: Mutations in the DSC2 gene cause Arrhythmogenic Right Ventricular Dysplasia (ARVD). The mechanisms by which these mutations confer histologic substrate remain unknown. A metabolic function of inflammasome/casp1 in adipose tissue has been demonstrated.

Materials and methods: Fragments of cardiac tissue from 2 patients were collected after macroscopic and histopathological examination the patients’ hearts. A 63-year-old patient with ARVD caused by a DSC2 mutation (p.Arg132Cys) underwent heart transplantation. The diseased heart genome-wide expression profiling was compared with that of a non-diseased donor heart. The retained genes of interest were listed and classified according to their biological functions using Ingenuity Pathways Analysis (Ingenuity Systems Inc., Mountain View, CA). RT-qPCR and Western Blot (WB) were used to confirmed genes of interest.

Results: Transcriptomic and RT-qPCR data first revealed a down-expression of DSC2 mRNA and an unexpected overexpression of DSC3 mRNA in the posterior right ventricle of the ARVC patient (Fig) in the ARVD heart, DSC3 was found to be cleaved. Prediction software revealed that this cleavage could be due to Caspase-1. We observed an overexpression of Casp1 (fig) and other elements of inflammasome (CARD16, NLRP3) in the posterior RV of the ARVC patient. A down-expression of DSC2, DSP and RyR2 was also documented. Biological pathways analysis identified a relationship of Casp1 with apoptosis (BCL2, FOS), fibrogenesis (Col3A1, Col4A1, Col4A2, MMP9) and adipo genesis (IGF1, ADIPOQ) in the ARVC heart.

Conclusion: This is the first study that shows a switch DSC2/3SC3 in an ARVC patient with a DSC2 mutation. Casp1, activated owing to desmosome instability, could play a central role in ARVC pathophysiology.
stood out miR-919a, whose tissue levels were strongly correlated with the LAV (Pearson R=0.88; P < 0.001) and were significantly higher in patients with Pe-AF [median: 4.7 rpm; interquartile range (IQR): 3.1–5.2] than in those with Pxf-AF (1.2 rpm; IQR: 0.6–1.3) or SR (0.0 rpm; IQR: 0.0–0.4) = P<0.001. About 13,542 potential gene targets of the differentially expressed miRNAs were identified: 23 of them were simultaneous targets of at least 9 miRNAs, including KCNA1 (K+ voltage-gated channel) TAB1 (TGF-β activated kinase 1/ MAP3K7 binding protein 1), TCF21 (involved in cardiac morphogenesis) and ASPH (involved in Ca2+ storage and release by sarcoplasmic reticulum). The predicted gene targets are strongly associated with the regulation of tCO2 currents, muscle contraction, cell signalling pathways, cell programming, inflammation and thrombopotic propensity, and included genes known to be involved in long QT syndrome, dilated cardiomyopathy, neurological electrical disturbances, diabetes and thrombophilia.

Conclusions: 40% of the global expression profile of miRNA is significantly changed during AF progression. We identified a group of differentially expressed miRNAs with relevant predicted gene targets, suggesting the involvement of post-transcriptional regulation changes in the AF pathophysiology.

ARRHYTHMIAS AND CARDIOMYOPOIESIS

P6166 | BEDSIDE
Lamin A/C gene mutations underlie Arrhythmogenic Cardiomyopathy with atiro-ventricular block
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Background: Arrhythmogenic Cardiomyopathy (AC) is an inherited heart muscle disease characterized by ventricular arrhythmias and an increased risk of sudden death. Mutations in genes mainly encoding desmosomal components are involved in approximately 50% of AC cases, however mutations in extra-desmosomal genes can cause cardiomyopathies with overlapping AC features.

Methods: A 76 years-old man diagnosed with biventricular AC died in the Hospital for heart failure. Since young age he had frequent syncopal episodes, mainly during effort. The 12 lead- ECG showed low QRS voltages in limb leads and right precordial negative T-waves from V1 to V4, the color Doppler examinations evidenced severe right ventricular dilatation with global hypokinesia and mild left ventricular dilatation with mild systolic dysfunction. Angiography showed no lesions in the coronary arteries. At 72 yrs the patient was implanted with a pacemaker for complete AV block. At the age of 74 years he received an implantable cardioverter-defibrillator (ICD) for secondary prevention because he suffered by a syncopal episode due to ventricular tachycardia (VT) with left bundle branch morphology and superior axis. During the follow-up the patient received an appropriate ICD intervention in response to VT. Conventional genetic screening was performed by bidirectional Sanger sequencing of all major desmosomal encoding genes on an ABI310 Genetic analyzer and subsequently whole exome sequencing (WES) was carried out by using TruSeq technology on a Illumina HiSeq2000 platform.

Results: Conventional genetic screening failed to detect genetic variations in desmosomal genes associated with the disease. WES identified a heterozygous point mutation c.499G>A, p.E133K in the lamin A/C gene (LMNA). This genetic variant, absent in the 1000 Genomes and Exome Variant Server datasets and predicted to be deleterious by Polyphen and SIFT, has been previously associated with autosomal dominant dilated Cardiomyopathy and atrio-ventricular block.

Conclusion: A novel mutation (c.499G>A, p.E133K) in the LMNA gene was detected in the proband’s daughter and son, who exhibited an AC-like pattern.

P6167 | BEDSIDE
Prognostic potential cardiac arrhythmia in familial amyloidotic polynuropathy, portuguese type, after liver transplant

Background: Cardiovascular complications are common in Familial Amyloidotic Polynuropathy (FAP) and, although liver transplant (LT) has been shown to improve the survival of patients (pts), it has also been reported progression of the disease after the procedure.

Purpose: The aim of this study was to evaluate the progression of cardiac conduction disorders in pts with FAP, portuguese type, submitted to LT and prophylactic permanent pacemaker (PM) implantation before the procedure.

Methods: We enrolled 117 pts with FAP due to transthyretin Val30Met mutation, submitted to LT and prophylactic PM implantation, between 2001 and 2012, and that were evaluated in our institution between December 2013 and November 2014. We analyzed symptoms, ECG and PM records.

Results: At the median age at disease onset set was 32 years old (IQR 27–36) and median time between disease onset and LT was 4 years (IQR 2.5–5). By the time of LT, 90% were in stage 1 (according with Coutinho neurological clinical staging) and 43% already had clinical manifestations of cardiovascular involvement.Median time from disease onset to the follow-up visit was 11 years (IQR 8–15).

At the follow-up visit, only 8.8% had a normal ECG. One third had paced rhythm, 44% 1st degree AV block, 45% impaired intraventricular conduction (IIVC), 37% poor R wave progression and 18% low voltage QRS. Only 4 pts had atrial fibrillation or flutter. Compared with the ECG’s from previous years (median 4 years before), there was a significant increase in the frequency of 1st degree AV block (16% vs 44%, P<0.001), IIVC (24% vs 45%, P<0.001) and poor R wave progression (16% vs 37%, P<0.001).

All percentage of ventricular pacing was also associated with 1st degree AV block (80% vs 35%, P=0.002) and IIVC (86% vs 42%, P=0.043).

Conclusions: Cardiac conduction diseases progress in FAP pts in spite of LT, with the development of arrhythmia requiring PM.

P6168 | BEDSIDE
Characteristics of supra- and ventricular arrhythmias in 94 patients with genetically proven myotonic muscular dystrophy and no clinically overt cardiac dysfunction
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Purpose: Patients with myotonic muscular dystrophy (dystrophia myotonia, DM) are at risk for myocardium damage and sudden cardiac death due to diverse arrhythmias, especially progressive atrioventricular (AV) conduction abnormalities. However, there is limited data on potential life-threatening ventricular arrhythmias in DM patients, especially according to the type 1 and type 2 DM.

Methods: A group of 94 consecutive pts (47 F, 47 M) aged 42±14.0 yrs with genetically confirmed DM (mean disease duration 9.6 yrs) and 40 sex- and age-matched healthy controls underwent electrocardiography, echocardiography and 24-h Holter monitoring. Type 1 (DM1) was diagnosed in 51 pts, while type 2 (DM2) in 43 pts.

Results: All controls and 85 DM pts (91%) had preserved left ventricular function (LVEF = 55%, no valvaral dysfunctions). Due to previously detected advanced AV conduction defects 2 pts with DM had a pacemaker implantation. DM pts presented more frequently benign and potentially life threatening VA and also 1st degree AV block (AVB) than controls (Table). In opposite to AVB, all types of tachyarrhythmias were more frequently observed in DM2 than in DM1 patients. Moreover, 4 DM1 pts had persistent or paroxysmal atrial fibrillation.

Conclusions: In the large group of DM patients we observed significantly more frequent diverse arrhythmias (including potentially life-threatening ventricular arrhythmias) which warrants their close cardiac monitoring. Supraventricular and ventricular arrhythmias were more frequently observed in DM2 patients. However, DM1 subjects when compared to DM2 presented more AV conduction defects.

P6169 | BEDSIDE
Phenotype-genotype correlation of Lamin (LMNA A/C) associated dilated cardiomyopathy
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Dilated cardiomyopathy (DCM) caused by mutations in the lamin A/C (LMNA) gene is often associated with conduction disorders and cardiac arrhythmias. Aim: The purpose of this study was to identify LMNA mutations, estimate their prevalence among Belarus patients (pts) with sporadic DCM and phenotype-genotype correlation analysis.

Methods: We enrolled 173 pts with sporadic DCM. Of these 92 (53.2%) pts had a primary manifestation of conduction disorders and cardiac arrhythmias (aged 0.005.

Parameter DM Controls p DM 1 DM 2 p
(n=94) (n=40) (n=51) (n=43)

Short supraventricular tachycardia 18 2 0.043 15 3 0.005
Benign atrial fibrillation (atrial fibrillation and/or couplets) 22 3 0.033 7 15 0.03
Potentially malignant ventricular arrhythmia (non-sustained ventricular tachycardia and/or R-on-T prematurity ventricular contractions) 14 1 0.044 10 4 0.045
1st degree atrioventricular block 18 0 0.002 15 3 0.008
2nd degree atrioventricular block 5 2 0.9 4 1 0.4

Conclusions: In the large group of DM patients we observed significantly more frequent diverse arrhythmias (including potentially life-threatening ventricular arterial arrhythmias) which warrants their close cardiac monitoring. Supraventricular and ventricular arrhythmias were more frequently observed in DM2 patients. However, DM1 subjects when compared to DM2 presented more AV conduction defects.
42.3±11.7; men 89.1%; NYHA 2.7±0.4; LVEF 25.9±11.1%; LBBB 59.8%; AV block 21.7%; sVT+nST+VT 64.1%; AF 34.8%. Genetic analysis of 3,3,5,6–10 exons of LMNA was performed by SSCP and sequencing in 92 pts. Genetic testing, age, gender, NYHA, 6-MWT, serum CK, EchoCG and ECG/HM-ECG (QTdisp, HRT, microvot T-wave alternans (mTWA) were analyzed.

Results: Of those with DCM were identified changes in gene LMNA. So at 23 pts was detected replacement c.1698 C>T in exon 10, including two homoygous carriers T/T. Two different mutations were identified in 2 pts in exon 3: c.612G>A and c.569G>C; the latter is a result of substituted arginine by proline - Arg190Pro. Another nonsense mutation was identified in 9th exon Thr289X (c.1247-5T). In addition, two patients were identified as carriers simultaneously three nucleotide changes in the gene LMNA: c.639+730C>T and c.639+563G>A, located in intron and c.861T>G in exon 5. One patient had mutation extension -T>A -c.861T>G. These identified mutations could change the function of lamin A/C directly or indirectly and clinically manifest as “lamine-phenotypes” DCM. Genetic and phenotypic (clinical, morphofunctional) parameters were included in the correlation and univariate dispersive analysis. As a result, carriers of mutations in the LMNA gene were associated with a positive test mTWA (p < 0.005), 1° level of CK (p < 0.01), sVT positive (p < 0.05) and AV block (p < 0.01); a negative correlation was detected with LVEF (p < 0.05). As a result of univariate dispersive analysis, LVEF and nsVT were lost their significance (F = 2.95; p = 0.056), while AVblock and abnormal mTWA will allow to select a group of sporadic DCM pts for genetic and phenotypic (clinical, morphofunctional) analysis in both groups.

Conclusions: The 1/3 DCM pts of Belarus developed a phenotype with arrhythmias and conduction disorders caused by lamin A/C gene anomalies. Given the high risk of SCD pts with lamin-associated DCM, detection elevated level of sCK, AVblock and abnormal mTWA will allow to select a group of sporadic DCM pts for obligatory genetic screening in order to determine of risk stratification.

P6170 | BEDSIDE Cardiac magnetic resonance and arrhythmic risk stratification of cardiomyopathy associated with lamin A/C mutations: results from a 5 year study G. Peretto1, S. Sala1, S. Benedetti2, C. Di Resta3, M. Ferrari3, P. Delta Bella3, 1San Raffaele Hospital of Milan (IRCCS), Department of Arrhythmology and Electrophysiology, Milan, Italy; 2San Raffaele Hospital of Milan (IRCCS), Laboratory of Clinical Molecular Biology and Cytyogenetics, Milan, Italy

Background: Mutations in the LMNA gene, encoding nuclear proteins lamin A/C, have been associated with cardiac disease and high risk of sudden cardiac death (SCD) from both brady- and tachyarrhythmias. The implant of a cardioverter defibrillator (ICD) is to date the only effective intervention, but no specific guidelines are available.

Purpose: We designed a clinical protocol including extensive cardiovascular examination and strict follow-up (FU) of patients bearing LMNA gene mutations to define a risk stratification protocol for arrhythmic events.

Methods: To date, 17 patients (age 41±16; 59% males) bearing LMNA gene mutations have been enrolled in our center and followed for 5±2 years. All the patients had a baseline ECG and underwent cardiac magnetic resonance (CMR) at the time of genetic diagnosis. Patients fulfilling criteria for dilated cardiomyopathy -EF < 40%-, or those with severe or slight left ventricular (LV) dilatation were excluded (n = 4). We term early cardiomyopathy (ECM) the finding of late gadolinium enhancement (LGE) on CMR in the absence of the criteria defined above. Regular FU including 2year ECG, echocardiography and 24h Holter monitoring was obtained.

Results: All the patients were asymptomatic. Eight of them (47%) had a normal ECM. LCE phenotype was seen in the other 5 cases (38%), all with a midwall LGE distribution pattern involving mid-basal segments of interventricular septum (IVS) and posterior-inferior LV wall. At presentation, 4 patients in the ECM group (80%) had 1° degree atrioventricular (AV) block and/or QRS duration > 120 ms. Moreover, at 2.5±0.5 years FU, 2 of them developed 2° degree AV block. On the contrary, all the patients with normal CMR had no evidence of any conduction delay (p < 0.01). Due to history of family SCD, 7 patients (4 ECM + 3 normal) underwent ICD implantation in primary prevention. To date, no ICD shocks were seen in both groups. However, at 4.0±1.0 years, 3 patients in ECM group (60%) vs. 1 patient in normal group (13%) showed episodes of non-sustained ventricular tachycardia (NSVT) on Holter or ICD recording (p = n.s.). Interestingly, serial echocardiograms showed no significant changes in LV volumes and systolic function in both groups.

Conclusion: In carriers of LMNA mutations, CMR detects an early form of cardiomyopathy involving IVS. The presence of LGE identifies patients at a higher risk of both AV conduction defect, idiopathic ventricular fibrillation and sudden infant death syndrome (SIDS), and mixed arrhythmogenic syndromes. It was recently demonstrated that the phenotypic expression of SCNSA gene mutations could be expanded from electrical disorders with an apparently normal heart to cardiomyopathies. Currently, more than 10 mutations in the SCNSA gene have been described which lead to the development of DCM and/or atrial cardiomyopathy in conjunction with a wide range of cardiac arrhythmias and conduction disorders.

P6171 | BENCH Cardiac hypertrophy is associated with mutations in SCNSA gene A.G. Shestak1, S.L. Dzemeshkevich2, E.V. Zaklyazminskaya1, 1Russian Research Center of Surgery, Laboratory of Medical Genetics, Moscow, Russian Federation; 2Russian Research Center of Surgery, Moscow, Russian Federation

Background: The SCNSA gene encodes the alpha subunit of the Nav1.5 sodium channel, which is responsible for the inward sodium current (INa). Genetic alterations in the SCNSA gene may affect the structure, function or level of expression of the Nav1.5 sodium channel. These diverse and often functionally opposite alterations of cardiomyocyte electrical excitability result in various cardiac arrhythmias, such as long QT syndrome (LQTS), Brugada syndrome, sick sinus syndrome and progressive cardiac conduction defect. Idiopathic ventricular fibrillation in Japanese infants is a rare, inherited, familial heart disease, which suggests some genetic factors.

Results: We performed DNA diagnostics for primary arrhythmias since 1998 year, and 232 unrelated families underwent molecular genetic testing, including sequencing of SCNSA gene by Sanger or within PGM Ion Torrent target genes resequencing. Twenty-one mutations in 22 unrelated families in SCNSA gene were found, one proband have carried two mutations in two SCNSA alleles inherited from both parents. Detailed clinical and instrumental examinations including ECG, EchoCG, cardiac MRI, and neurological examination were performed for SCNSA mutation carriers (probands) regardless of underlying diagnosis of primary arrhythmia.

Results: The screening had revealed 4 patients (18%) with undoubted structural cardiac remodeling (Table 1).

Table 1. Cardiac remodeling in SCNSA-pos

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Age, y.o.</th>
<th>Gender</th>
<th>Primary diagnosis</th>
<th>Type of remodeling</th>
</tr>
</thead>
<tbody>
<tr>
<td>p1838F</td>
<td>32</td>
<td>F</td>
<td>PVC</td>
<td></td>
</tr>
<tr>
<td>p1543T</td>
<td>54</td>
<td>M</td>
<td>CCD</td>
<td>Dilated cardiomyopathy</td>
</tr>
<tr>
<td>p153813T</td>
<td>16</td>
<td>F</td>
<td>SSS</td>
<td></td>
</tr>
<tr>
<td>p20050A</td>
<td>20</td>
<td>F</td>
<td>LQTS, VF, SCD</td>
<td>Cardiac hypertrophy</td>
</tr>
</tbody>
</table>

Conclusion: It seems that the prevalence of different variants of cardiac remodeling in SCNSA-mutations carriers is higher than previously thought. In this study we did find hypertrophy in patients with SCNSA mutation what had not been published before.
P6173 | BENCH
Transcriptional profile and functional analysis of aged atrial fibrillation
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Background: Aging is known as a very important factor to increase the incidence of atrial fibrillation (AF) and to confer the risk of thromboembolism, however, the pathogenesis of aged atrial fibrillation remain poorly understood.

Methods and results: Samples of right atrial appendage were collected from patients undergoing aortic valve replacement. Patients with mitral valve diseases, rheumatic valve diseases, left atrial dimension > 50mm were not included. Patients were divided into six groups: aged 40 in sinus rhythm (SR-40), aged 50 in sinus rhythm (SR-50), aged 60 in sinus rhythm (SR-60), aged 70 in sinus rhythm (SR-70), aged 60 in AF (AF-60), and aged 70 in AF (AF-70). We performed genome-wide whole transcriptomic profiling using Illumina Human HT-12 mRNA microarrays. Among four SR groups, we found 257 genes associated with atrial aging were significantly up-regulated and 304 genes were significantly down-regulated. Among SR-60, SR-70, AF-60 and AF-70, 62 genes associated with atrial fibrillation were significantly up-regulated and 56 genes were significantly down-regulated. 10 genes were identified with both atrial aging and atrial fibrillation. Functional classification based on Gene Ontology Database were conducted and demonstrated these genes were strikingly associated with immunomodulation and electrophysiological remodeling.

Conclusion: Our study first revealed 10 genes and several signaling pathways significantly involved in aged AF-related transcriptional expression, which may yield novel insight into aged AF pathogenesis.

P6174 | BEDSIDE
Exercise-induced changes in Brugada ECG
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Purpose: Exercise is useful in radiofrequency catheter ablation for persistent atrial fibrillation (AF), and the effect of exercise in patient-specific in-silico modeling of left atrium (LA).

Introduction: Biomedical Engineering, Chuncheon, Korea, Republic of

Methods: Samples of right atrial appendage were collected from patients undergoing aortic valve replacement. Patients with mitral valve diseases, rheumatic valve diseases, left atrial dimension > 50mm were not included. Patients were divided into six groups: aged 40 in sinus rhythm (SR-40), aged 50 in sinus rhythm (SR-50), aged 60 in sinus rhythm (SR-60), aged 70 in sinus rhythm (SR-70), aged 60 in AF (AF-60), and aged 70 in AF (AF-70). We performed genome-wide whole transcriptomic profiling using Illumina Human HT-12 mRNA microarrays. Among four SR groups, we found 257 genes associated with atrial aging were significantly up-regulated and 304 genes were significantly down-regulated. Among SR-60, SR-70, AF-60 and AF-70, 62 genes associated with atrial fibrillation were significantly up-regulated and 56 genes were significantly down-regulated. 10 genes were identified with both atrial aging and atrial fibrillation. Functional classification based on Gene Ontology Database were conducted and demonstrated these genes were strikingly associated with immunomodulation and electrophysiological remodeling.

Conclusion: Our study first revealed 10 genes and several signaling pathways significantly involved in aged AF-related transcriptional expression, which may yield novel insight into aged AF pathogenesis.

P6175 | BENCH
PITX2 and atrial fibrillation: from palpitations to methylation
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Background: Pitx2 is a transcription factor located in proximity to the human 4q25 familial atrial fibrillation (AF) locus. The mechanisms underlying PITX2 regulation in AF remain unknown.

Purpose: To determine the role of methylation in PITX2 regulation in the left atrial muscle.

Methods: Transcriptomic analysis was used to identify the altered genes in myocardial left atrium (LA) of AF patients. Quantitative RT-PCR of PITX2 was also performed in fourteen subjects and in four aging spontaneously hypertensive rats (SHRs). Using bisulfite sequencing of DNA, the methylation status of the PITX2 promoter region was documented in 100% of AF patients and in 50% of SHRs. Quantitative RT-PCR confirmed the PITX2 demethylation in AF patients and in SHRs (significantly negatively correlated with age. Spearman r = −0.86, P < 0.01). Methylation of the PITX2 promoter region was documented in 100% of AF patients and in 50% of aging SHRs. Decitabine decreased the atrial tachycardia (AT) occurrence (three out of five) and reversed the hypermethylation of PITX2 promoter region in 3 out of 5 SHR rats.

Results: Microarray data showed that PITX2 was down-regulated in myocardial LA of AF patients (−5.40 fold changes AF patients/ controls). Quantitative RT-PCR confirmed the PITX2 demethylation in AF patients and in SHRs (significantly negatively correlated with age. Spearman r = −0.86, P < 0.01). Methylation of the PITX2 promoter region was documented in 100% of AF patients and in 50% of aging SHRs. Decitabine decreased the atrial tachycardia (AT) occurrence (three out of five) and reversed the hypermethylation of PITX2 promoter region in 3 out of 5 SHR rats.

Conclusions: These data suggest that in the left atria of AF patients and of SHRs, methylation of the PITX2 promoter region may underlie down-regulation of this gene. Additional studies are needed to confirm the anti-arrhythmic effect of PITX2 demethylation.

P6176 | BENCH
Flash-induced termination of anatomical reentry in optogenetically modified transverse rat ventricular tissue slices
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Background: Reentry is an important mechanism of ventricular arrhythmias in patients with structural heart disease. Termination often requires implantable cardioverter defibrillator shocks with significant impact on quality of life and prognosis. Optogenetics, which rely on light-gated ion channel expression and activation...
can modulate electrophysiological properties and may provide a new and unique means to analyze and counteract cardiac arrhythmias. Whether optogenetic interventions can influence anatomically determined reentry is unknown. We studied the effects of optogenetic interventions on reentry in a novel in situ model.

**Methods and results:** Hearts from 2-day-old Wistar rats and a dedicated vibration setup were used to produce 150 μm-thick transverse ventricular tissue slices, which were plated onto 0.4 μm-pore membranes (Millipore culture insert). Within 4 hours slices were genetically modified with lentiviral vectors encoding a depolarizing current-producing, light-activated Ca2+-translocating channelrhodopsin (CaCh). In eVFP as control, the effects of CaCh activation by 470 nm-light pulses from a LED which was positioned centrally below the specimen, was investigated by optical mapping using Di-4-ANEPPS as voltage-sensitive dye. During electrical stimulation action potential (APD) and conduction velocity (CV) showed no significant differences between controls and CatCh-group (129±37ms vs. 126±43ms; 6.91±0.0cm/s vs. 6.8±0.8cm/s). However, only in the CatCh-group, 10ms-LED flashes evoked action potentials up to 4 Hz. Reentry was induced in controls (80%, n=5) and in the CatCh-group (100%, n=6) by programmed electrical stimulation (51/52 protocol). Reentry cycle length was comparable (162±12ms vs.179±7ms, ns) and sustained unless terminated on purpose. Global illumination by longer duration LED flashes (500–1500ms) terminated reentry in 5 out of 6 slices in CatCh, but not in all of the controls (p<0.01). Localized illumination, targeting the critical part of the reentrant circuit, could also terminate the arrhythmia in CatCh-expressing slices. In both situations, depolarization-induced conduction block terminates the arrhythmia.

**Conclusion:** This is the first study to show that stable anatomically determined reentry in rat ventricular tissue slices can be terminated effectively by expression of light-gated ion channels that are subsequently activated by LED flashes. These results can provide novel practical and mechanistic insights into the optogenetic control of arrhythmic activity in ventricular tissue.

**ATRIAL FIBRILATION: BASIC MECHANISMS**

**P6178 | BENCH**

**Increased cellular inflammation and chemotactic activity of epicardial adipose tissue in atrial fibrillation**

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**Background:** There is growing evidence that epicardial adipose tissue (EAT) might be involved in the pathophysiology of atrial fibrillation (AF). We previously demonstrated a fibrotic remodeling of atrial EAT associated with AF.

**Purpose:** In this study we assessed inflammatory changes of atrial EAT induced by AF.

**Methods:** In a sheep model of long-term persistent AF, induced by atrial tachypacing, we specifically addressed the role of AF in altering EAT. First, the presence of inflammatory cells in the adipose tissue was assessed on Haematoxylin and Eosin stained sections. Second, atrial EAT was cultured and the conditioned medium was used in a chemotaxis assay (Figure A). Peripheral mononuclear cells (PBMC) were prepared from fresh blood and a total of 500 000 PBMCs were added to the upper chamber. The migration test was performed for 120 minutes in a cell culture incubator. 500 000 PBMCs were added to the upper chamber. The migration test was performed for 120 minutes in a cell culture incubator.

**Results:** Small lymphoid aggregates were observed in the fatty infiltrations (Figure B), more frequently in AF than control sheep (AF: 6 out of 15 sheep or 7% (14/211) of fatty infiltrations vs control: 1 out of 11 sheep or 1% (1/103) of fatty infiltrations in a cell culture incubator.

**Conclusion:** This study confirms that atrial fibrillation in sheep is associated with a strong induction of growth factors: 3-fold in CTGF (connective tissue growth factor), and 3.7-fold in CYR61. Interestingly this up-regulation was observed at the onset of diabetes. With the progression of diabetes, the expression of TGFβ, another marker of fibrosis, was significantly elevated. Surprisingly, the synthesis of new collagen was not induced. However, the advanced stage of diabetes was associated with rise in the expression of fibronectin (3.3±0.40; p<0.01), and MMP9 (2.2±0.34; p<0.05). Moreover, atrial myopathy in T2DM is characterized by increased levels of cytokines (IL-6, IL-8, TNFα), and adhesion molecules (ICAM-1). The exposure of atrial diabetic tissue slices to stimulation in the electrical field caused further up-regulation in the expression of fibronectin, IL-8, and TNFα compared to non-diabetic atrial diabetic slices. The augmented ratio of MMP/TIMP indicated that diabetic atrial tissue was more prone to degradation processes of ECM during pacing.

**Conclusions:** T2DM promote pro-fibrotic and pro-inflammatory atrial remodeling processes that might serve as a pro-arrhythmogenic substrate. The “in vitro” stimulation of diabetic atrial tissue further aggravates this inflammatory process.

**Acknowledgement/Funding:** European Union Seventh Framework Programme (FP7/2007-2013) under Grant Agreement HEALTH-F2-2010-261057

**P6180 | BENCH**

**Inhibitions of late sodium current and calmodulin kinase II terminate atrial fibrillation induced by isoproterenol**

L. Ren, S.H. Huang, Q.M. Yang, X.H. Wei, P.K. He, L.W. Peke, University First Hospital, Cardioiology Department, Beijing, China, People’s Republic of China

**Introduction:** Inhibitions of late sodium current and Ca2+-calmodulin-dependent protein kinase II (CaMK II) may be next targets in treating atrial fibrillation (AF).

**Purpose:** The objective of this study was to determine the role of late sodium current and CaMK II in prone AF rat model and their naturally occurred inhibitors (TIMPs).

**Methods:** Langendorff-perfused rabbit hearts were used to record right atrial monophasic action potentials (MAPs), ECG signals and 96-electrode atrial mapping. AF burden, AF inducible window and AERP (n=5, p>0.05). ISO (3, 6, 10, 15 nm) did not alter the intraatrial conduction time and mean activation time by 12±2 and 6±1 ms (n=5, p>0.05) and their non-diabetic controls, lean ZDF (n=24), were analysed at the age of 3 months (onset of diabetes) and 6 months (advanced stage). To study the molecular changes in response to pacing we prepared atrial slices and put into the cell culture and the membrane of the culture inserts. To resemble AF, the tissue slices were stimulated in the electrical field at 5 Hz (vs.0.6 Hz) up to 20h. Then, atrial tissue was examined using transcriptome analysis, and at the transcriptional and protein level. We focused our investigation on components of ECM including collagen, fibronectin, and adhesion molecules (ICAM-1), growth factors (TGFβ, CTGF, CYR61), metalloproteinases that remodel collagen (MMPs, ADAMs) and their naturally occurred inhibitors (TIMPs). Moreover the expression of tissue relevant cytokines was analysed.

**Results:** Transcriptome analysis revealed that atrial remodeling in T2DM is associated with a strong induction of growth factors: 3-fold in CTGF (connective tissue growth factor), and 3.7-fold in CYR61. Interestingly this up-regulation was observed at the onset of diabetes. With the progression of diabetes, the expression of TGFβ, another marker of fibrosis, was significantly elevated. Surprisingly, the synthesis of new collagen was not induced. However, the advanced stage of diabetes was associated with rise in the expression of fibronectin (3.3±0.40; p<0.01), and MMP9 (2.2±0.34; p<0.05). Moreover, atrial myopathy in T2DM is characterized by increased levels of cytokines (IL-6, IL-8, TNFα), and adhesion molecules (ICAM-1). The exposure of atrial diabetic tissue slices to stimulation in the electrical field caused further up-regulation in the expression of fibronectin, IL-8, and TNFα compared to non-diabetic atrial diabetic slices. The augmented ratio of MMP/TIMP indicated that diabetic atrial tissue was more prone to degradation processes of ECM during pacing.

**Conclusions:** T2DM promote pro-fibrotic and pro-inflammatory atrial remodeling processes that might serve as a pro-arrhythmogenic substrate. The “in vitro” stimulation of diabetic atrial tissue further aggravates this inflammatory process.

**Acknowledgement/Funding:** European Union Seventh Framework Programme (FP7/2007-2013) under Grant Agreement HEALTH-F2-2010-261057
Conclusions: Late sodium current and CaMK II pathways play important roles in the genesis of AF mediated by ISO. Inhibition of these pathways is effective in treating AF.

P6181 | BENCH
Pro-inflammatory skewing of inflammatory to regulatory T lymphocyte ratio in atrial fibrillation

Background: The precise role of inflammation in the development and perpetuation of atrial fibrillation (AF) is yet to be fully uncovered. T and B lymphocytes, the cells that populate in patients with adaptive immunity, have pivotal roles in orchestrating inflammation. Different subsets of lymphocytes either promote or prevent inflammation. We are investigating a unique subset of lymphocytes, the CD4+CD28null T cells that expand in patients with chronic inflammation. These cells secrete high levels of pro-inflammatory cytokones tumour necrosis factor-α (TNF-α) and interferon-γ (IFN-γ). The response of CD4+CD28null T cells is normally maintained under control by regulatory T cells (Tregs), a specialised subset of T lymphocytes with suppressive function that maintain immune homeostasis and prevent pathogenic immune responses. The role of CD4+CD28null and Treg cells has not been investigated in AF.

Purpose: We hypothesised that in AF the balance between pro-inflammatory and regulatory T lymphocytes is skewed in favour of inflammatory T cells.

Methods: We recruited 65 patients with idiopathic AF who lacked co-morbidities associated with inflammation (coronary artery disease, autoimmune diseases, diabetes, heart failure). Circulating CD4+CD28null T lymphocytes, Tregs and B cells were quantified by flow cytometry in AF patients and healthy controls (n=35). High sensitivity CRP, TNF-α and IFN-γ levels were quantified in serum.

Results: CD4+CD28null T lymphocytes were significantly increased in the circulation of AF patients compared to controls (p<0.0001). In addition, AF patients had a marked reduction (p<0.0001) in Treg cells. The ratio of CD4+CD28null/T lymphocytes to Tregs was also significantly increased. In contrast, no alterations were identified in circulating B cell subsets (total, mature and memory). The co-relation between CD4+CD28null or Treg lymphocytes and serum levels of CRP, TNF-α and IFN-γ was investigated.

Conclusions: Our findings demonstrate that specific subsets of T lymphocytes are upregulated in patients with AF. Pro-inflammatory CD4+CD28null T cells increase significantly in AF patients, whilst the anti-inflammatory Treg subset is markedly reduced. These innovative results suggest an imbalance in the mechanisms that maintain homeostasis in the immune response, which may provide new therapeutic strategies to re-establish the equilibrium between pro- and anti-inflammatory mechanisms at work in this disease.

P6182 | BENCH
Tissue expression levels of miRNAs associated with fibrosis in patients with paroxysmal and persistent atrial fibrillation
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Background: Atrial structural remodeling includes atrial enlargement and fibrosis and forms a key substrate for atrial fibrillation (AF). MicroRNAs (miRNAs) are likely modulators of atrial remodeling and are potential targets for diagnosis or therapies.

Purpose: This study aims to explore the differential expression of miRNAs associated with fibrosis in human left atrial tissue of patients with paroxysmal and persistent AF.

Methods: Left atrial appendages of 10 patients with paroxysmal (n=6) and persistent AF (n=4) were retrieved during thoracoscopic pulmonary vein isolation. Total RNA was extracted from tissue and miRNA sequencing was performed on the Illumina NextSeq500. The differential expression of 5 established miRNAs (miR-21, miR-29b, miR-30c, miR-133a, miR-98) known to suppress genes involved in structural remodeling was studied.

Results: miRNA sequencing revealed miR-29b-3p to be downregulated, consistently in AF compared to paroxysmal AF (LogFC −0.33, p 0.04). No differential expression was found for miRNA-21 (LogFC −0.4, p 0.21). miR-30c (LogFC 0.11, p 0.37), miR-133a (LogFC −0.03, p 0.83) and miR-98 (LogFC −0.15, p 0.78) and miR-590 (LogFC −0.01, p 0.92).

Conclusion: This is the first study to report on whole miRNA sequencing in human left atrial tissue. Our preliminary results show miR-29b-3p to be downregulated in persistent compared to paroxysmal AF. The consequent upregulation of extracellular matrix genes may induce atrial fibrosis and turns miR-29b-3p into a potential target of therapy. Other miRNAs were not differentially expressed. These data emphasize the relevance of miRNAs, but a larger study population including non-AF controls and the concomitant exploration of gene expression is needed to establish the pathophysiological role in AF.

Acknowledgement/Funding: Netherlands Organisation for Scientific Research (NWO); VIDI Grant nr.016.146.310

P6183 | BENCH
Atrial fibrillation altered hepatic gene expression profiles in human and rat model

Background: Atrial fibrillation (AF) increases the risk of stroke, and is accompanied by systemically enhanced coagulation. The liver is a major source of prothrombotic molecules. These evidences imply the role of the liver on pathophysiology of AF-related thromboembolism.

Purpose: The aim of this study was to identify the change of hepatic gene expression profiles associated with AF in human and rat model.

Methods and results: We screened 465 consecutive patients with non-alcoholic steatohepatitis, who underwent liver biopsy from 2003 to 2013, and identified 3 patients with AF. Patients in sinus rhythm matched for age, sex, hepatic histopathological stage, served as a control group. Using CDNA microarray, we compared gene expression profiles of the liver in 2 groups. Of 54675 genes on the array, 48950 filtered genes demonstrated clear clusters for AF or control. Interestingly, among 354 BioCarta Pathways, the extrinsic prothrombin activation pathway including fibrinogen and coagulation factor VII showed the most prominent change (Figure A). To assess whether rapid atrial excitation per se affects hepatic gene expression profile, we subjected healthy Sprague-Dawley rats to 12-hour rapid atrial pacing at 1200 bpm and analyzed their livers. Hierarchical clustering with 13463 filtered genes showed clear clusters for the pacing or sham group. As with human AF, rapid atrial pacing in rat significantly altered the hepatic gene expressions associated with extrinsic prothrombin activation pathway (Figure B). In contrast, the genes related to fibrinolysis were augmented in human, but not in rat.

Heatmap of extrinsic coagulation pathway

Conclusions: AF affected hepatic gene expressions, predominantly involved in coagulation. These findings suggest the cardio-hepatic interaction in the AF-related thromboembolism.

P6184 | BENCH
Differential expression of microRNAs associated with electrical remodeling in left atrial tissue of patients with paroxysmal versus persistent atrial fibrillation
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Background: The pathophysiological substrate of atrial fibrillation (AF) is complex and incompletely understood. Electrical remodeling contributes to arrhythmogenesis, and is reflected in the expression of microRNAs (miRNAs) in atrial tissue.

Table 1. Differential expression of miRNAs

<table>
<thead>
<tr>
<th>miRNA</th>
<th>Target gene</th>
<th>CPM paroxysmal</th>
<th>CPM persistent</th>
<th>Log fold change</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>miR-21</td>
<td>SPRY1</td>
<td>7.7±0.4</td>
<td>7.4±0.5</td>
<td>−0.4</td>
<td>0.21</td>
</tr>
<tr>
<td>miR-29b-3p</td>
<td>COL1A1, COL3A1, FBN</td>
<td>13.4±0.3</td>
<td>13.1±0.1</td>
<td>−0.33</td>
<td>0.04</td>
</tr>
<tr>
<td>miR-30c</td>
<td>CTGF</td>
<td>13.5±0.1</td>
<td>13.6±0.2</td>
<td>0.11</td>
<td>0.37</td>
</tr>
<tr>
<td>miR-133a</td>
<td>CTGF, CTGF-1, TGFβ2</td>
<td>15.8±0.2</td>
<td>15.8±0.2</td>
<td>−0.03−0.15</td>
<td>0.835-0.78</td>
</tr>
<tr>
<td>miR-98</td>
<td>TGFβ1, TGFβ2</td>
<td>4.9±0.2</td>
<td>4.7±0.2</td>
<td>−0.01</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Abbreviations: CPM, counts per million; SPRY1, sprouty-1; FBN, fibrillin; CTGF, connective tissue growth factor; TGFβ-1, transforming growth factor β1; TGFβ-2, transforming growth factor β receptor type 2.
Purpose: With this study to perform next-generation miRNA sequencing in human left atrial tissue we aim to determine whether miRNAs that are associated with electrical remodeling are differentially expressed in patients with paroxysmal versus persistent AF.

Methods: Left atrial appendages from patients with paroxysmal (n=6) and persistent AF (n=6) were retrieved during thoracoscopic surgery for AF. Total RNA was isolated and whole genome miRNA expression profiling was performed to evaluate differential miRNA expression. Seven miRNAs (miRNA-1, -26a/b, -133b, -208a, -328 and -499a) previously reported to be involved in electrical remodeling were studied.

Results: miRNA-499a showed lower expression in persistent AF patients with persistent AF compared to paroxysmal AF (log fold change (logFC) −0.8, p=0.01). The following miRNAs were not differentially expressed (table): miRNA-1 (logFC 0.1, p=0.8), miRNA-26a (logFC −0.1, p=0.3) and −26b (logFC −0.02, p=0.8), miRNA-133b (logFC −0.1, p=0.8), miRNA-208a (logFC −0.2, p=0.3) and miRNA-328 (logFC −0.01, p=1.0).

Conclusion: Expression of miRNA-499a, which downregulates the calcium-activated potassium channel 3 (SK3), is reduced in patients with persistent AF compared to paroxysmal AF. These data are consistent with upregulation of calcium-activated potassium current and action potential prolongation only during AF. However, to appreciate the functional role of miRNA-499a and its potential role as a diagnostic or therapeutic tool, a larger study sample, including atrial tissue of patients without AF, is required.

Acknowledgement/Funding: unrestricted grant from Atricure Inc.

P6168 | BENCH

Effect of idarucizumab on bleeding time associated with dabigatran in combination with antiplatelet agents aspirin, clopidogrel and ticagrelor in a rat tail bleeding model

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Introduction: Idarucizumab is a selective, humanized antibody fragment (Fab) that specifically reverses the anticoagulant activity of dabigatran, a selective and reversible direct thrombin inhibitor.

Purpose: To determine if idarucizumab can reverse the prolonged bleeding time after treatment with dabigatran etexilate (DE) and antiplatelets (AP), such as aspirin (ASA), clopidogrel and ticagrelor, in a rat tail bleeding model.

Methods: ASA (100 mg/kg), clopidogrel (4 mg/kg), ticagrelor (3 mg/kg) or vehicle was given orally to rats (~120 min). Ex vivo platelet aggregation was performed in platelet rich plasma with collagen (2 μM), ADP (5 μM) or arachidonic acid (AA) (100 μM). Idarucizumab (100 μg/kg) or saline was administered to the animals, and bleeding times were then measured. Eight animals were used for each treatment group.

Results:

<table>
<thead>
<tr>
<th>miRNA</th>
<th>Target-gene(s)</th>
<th>Effect</th>
<th>Expression levels (CFP)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>miRNA-1</td>
<td>KCNQ1, KCNQ2</td>
<td>Downregulating mK and Kᵥ2.2</td>
<td>12.4±0.3</td>
<td>12.5±0.4</td>
</tr>
<tr>
<td>miRNA-26a/b</td>
<td>KCNQ2</td>
<td>Increase in Iₖ and Kir 2.1 protein levels</td>
<td>15.9±0.2</td>
<td>12.7±0.1</td>
</tr>
<tr>
<td>miRNA-133b</td>
<td>KCNQ2</td>
<td>Increase TGFβ1 and TGFR-2</td>
<td>4.0±0.8</td>
<td>4.0±0.7</td>
</tr>
<tr>
<td>miRNA-208a</td>
<td>Unknown</td>
<td>Downregulating SK3</td>
<td>10.2±0.4</td>
<td>10.0±0.3</td>
</tr>
<tr>
<td>miRNA-328</td>
<td>CADNN1, CADNB1</td>
<td>Decrease in I_{CaL} reduced expression of Cav1.2 and Cavβ1 and APD shortening</td>
<td>6.4±0.4</td>
<td>6.4±0.3</td>
</tr>
<tr>
<td>miRNA-499a</td>
<td>KCNN3</td>
<td>Downregulating I_{K1}</td>
<td>3.7±0.3</td>
<td>3.0±0.5</td>
</tr>
</tbody>
</table>

miRNA, microRNA; FAF, paroxysmal atrial fibrillation; PersAF, persistent atrial fibrillation; CFP, counts per million.

Conclusion: Idarucizumab partially reversed the effect of dabigatran on bleeding time in rats treated with both dabigatran and each AP (p<0.05). Idarucizumab reversed the effect of dabigatran on bleeding time in rats treated with ASA, clopidogrel and ticagrelor, consistent with their mechanism of action. Dabigatran plasma concentration was increased by 40–60% using ADP for ticagrelor and clopidogrel and 100% for ASA in a rat tail bleeding model.


P6187 | BEDSIDE

Association of C34T AMP deaminase 1 gene polymorphism with permanent atrial fibrillation in patients with chronic heart failure

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Background: Association with heart failure (HF) is the most common persistent clinical tachyarrhythmia, is associated with altered gene expression resulting in functional loss and AF progression. Recent research showed Class I and Class IIa histone deacetylases (HDACs) to regulate pathologic and fetal gene expression causing cardiac contractile dysfunction and hypertrophy.

Purpose: Whether Class I and Class IIa HDACs are involved in AF progression is unknown. Therefore, we investigated their role in tachypacing-induced contractile dysfunction and pathological fetal gene expression in experimental model systems for AF and in clinical AF.

Methods: HL-1 cardiomyocytes were tachypaced (TP) at 500 ng/mL in DE-treated animals and similar across groups. Contraction was measured 15 min post-injection. Plasma levels of dabigatran were measured using diluted thrombin time (dTT, Hemoclot). Data presented as mean ± SE.

Results: TP of HL-1 atrial cardiomyocytes resulted in a CaT reduction. Overexpression of HDAC1 class I and HDAC7 class IIa deacetylases reduced CaT-induced CaT reduction, whereas overexpression of HDAC3 class IIa reduced CaT inhibition. Idarucizumab partially reversed the effect of dapagatran on bleeding time in rats treated with both dapagatran and tachypaced cardiomyocytes. Overexpression of Class IIa HDACs, HDAC3 and HDAC7, protected against TP-induced CaT reduction, while HDAC4 and HDAC9 did not. Notably, cardiomyocytes overexpressing a dominant negative HDAC5 or HDAC7 mutant, which bears a myosin enhancer factor 2 (MEF2) binding defect, were not protected against loss of CaT. Furthermore, TP increased phosphorylation of HDAC5, promoted its translocation from the nucleus to cytoplasm, and consequently increased MEF2-fetal related gene expression (p-MHC, BNP).

Conclusion: Overexpression of HDAC1, HDAC3 and HDAC7 protects against tachypacing-induced CaT reduction in HL-1 cardiomyocytes. Furthermore, tachypacing induces HDAC phosphorylation and its nuclear export, resulting in MEF2 regulated fetal gene expression. These features are also present in AF patients. As HDAC5 is abundantly expressed in the heart, in contrast to HDAC1 and HDAC7, HDAC5 is a promising therapeutic target in clinical AF to attenuate pathological fetal gene expression causing cardiac contractile dysfunction and hypertrophy.
higher tobacco use in patients without perm-AF. The prevalence of C34T was significantly higher in patients with perm-AF (45.2% vs 24.1% in no perm-AF patients, p=0.016). Multivariable logistic regression analysis adjusting for age, sex, EF; treatment and classical factors associated with a worse outcome in CHF and AF confirmed that age (HR 1.05 [1.01–1.10]) and C34T (HR 2.62 [1.14–6.02]) were the only variables independently associated with perm-AF.

Conclusions: C34T variant in AMPD1 was independently associated with the presence of perm-AF in a population of HF-patients. Impaired cardiomyocyte energetics and adenosine accumulation could be involved in AF promotion in patients with the C34T variant.

P6188 | BEDSIDE
Increased platelet toll-like receptor-2 and 4 expression in atrial fibrillation
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Background: Inflammation plays a major role in atrial fibrillation (AF) pathogenesis. Accumulating evidence suggest that platelets are of the immune cells involved in this process. Platelet responses, such as activation and aggregation, have been shown to be mediated by the Toll-like receptor (TLR)-2 and 4. However, platelet function mediated by TLR-2 and 4 have not been evaluated in AF patients, yet.

Purpose: In this study, we aim to compare platelet Toll-like receptor expression in patients with atrial fibrillation and sinus rhythm.

Methods: 30 patients with non-valvular AF and 31 healthy patients in sinus rhythm referred for routine check-up were included. Platelet TLR-2 and 4 expression were evaluated by flow cytometric analysis in peripheral venous blood samples.

Results: 61 subjects (55.7% male, 50.2±11.1 years) were included in the study. Platelet TLR-2 expression was higher in patients with AF when compared to those in sinus rhythm [20 (10–64) vs. 4 (1–21)%], p=0.001. Patients with AF also had higher expression of TLR-4 when compared to those with sinus rhythm [19 (8–65) vs. 4 (1–22)%], p<0.001 [Figure].

Conclusions: Our study shows that there is enhanced expression of the Toll-like receptor-2 and 4 on platelets in atrial fibrillation. Demonstrating whether the increased biological platelet activity via the TLRs is responsible for initiation and/or maintenance of AF or thrombogenesis merit further studies.

P6189 | BENCH
Novel HSP-inducing compounds restoring cardiomyocyte function in atrial fibrillation
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Background: Cardiac fibrillation (AF) is the most common clinical tachyarrhythmia associated with significant morbidity and mortality. AF is a persistent disease, caused by a progressive, often age-related, derangement of protein turnover resulting in structural remodeling and contractile dysfunction of cardiomyocytes. It has been widely acknowledged that the progressive nature of the disease hampers its effective functional conversion to sinus rhythm in patients and explains the limited efficacy of current drug therapies. Previously, we identified that inducers of heat shock proteins (HSps), such as glycerol-derived (GGA) by inducing Heat Shock Proteins (HSPs) expression, suppresses derangement of protein turnover and remodeling of cardiomyocytes. As a result, GGA attenuates the AF substrate in cellular, Drosophila melanogaster and animal experimental models. Clinical application of GGA is however hampered by the high dosage needed, because of its high logP value. Therefore, the aim of the current study was to identify novel HSP-inducing compounds, which protect against AF remodeling.

Methods and results: We synthesized 83 GGA-derivatives and explored their action (at 10μM) in HL-1 cardiomyocytes pretreated with a mild heat shock to activate heat shock factor-1 (HSF-1) (43°C 10 min, 10 min recovery 37°C). We identified 30 GGA-derivatives, that significantly induced HSP70 expression, and other HSF-1 related HSps, including HSP25, HSP90, HSP40, but not Grp78 (HSPA5, not HSF-1 related). The magnitude of induction was comparable or higher compared to GGA. Next, HL-1 cardiomyocytes were pretreated with the most potent HSP70-inducing GGA-derivatives (n=13) for 8 hrs, followed by 8 hrs tachypacing (5 Hz) or normal pacing (1 Hz) and contractile function was determined by measuring calcium transients (CaT). Tachypacing significantly reduced the amplitude of CaT, and 7 GGA-derivatives revealed a significant protective effect against CaT loss, which was improved or comparable to GGA.

Conclusion: We identified novel GGA derivatives with improved HSP-inducing and cardioprotective properties compared to GGA. Ultimately, these HSP-inducing compounds may prevent expansion of the structural remodeling during AF, resulting in improved outcome of cardioversion and/or delay in progression towards permanent AF.

Acknowledgement/Funding: Dutch Heart Foundation (2013T096, 2013T144), LSH-Impulse (40-43100-98-008)
coagulation before and after the procedure to minimise the risk of embolic stroke. Vitamin K antagonists (VKAs) have been the oral anticoagulants of choice for many years, but warfarin or acenocoumarol pharmacological effects are unpredictable and have a narrow therapeutic window. As a result ECV may be cancelled due to inadequate INR levels in the previous month. ECV cancellations lead to treatment delays and ECV waiting list at an increased hospital costs. The objective was to determine the frequency and cost of ECV cancellations due to inadequate anticoagulation in Spain.

Methods: Cost analysis and budget impact analysis were performed, from the Spanish National Health Service (NHS) perspective. Were considered as costs of ECV cancellation the day hospital cost and the procedure cost itself. The unit costs and population data were obtained from Spanish sources. ECV cancellation rates with rivaroxaban (0.2%) and VKA (44.2%) were obtained from the clinical trial of X-VeRT. Monte-Carlo simulations (one simulation per patient) were done to simulate the healthcare costs avoided with rivaroxaban versus VKA, simulating the effect of changes in different parameters to describe real-life distributions.

Results: The cost of a cancellation of cardioversion was estimated at €256.44 (95% CI €76.55 to €576.15). Considering that approximately 100% of the ECV are currently performed with VKA, 70% of AF are non-valvular AF and that all of these could be done with rivaroxaban, the annual budget saving for the NHS would be €292,124 (95% CI €88,155 to €663,476).

Conclusions: The cancellation rate of ECV is high and is costly with VKA. Replacing VKA with rivaroxaban with a predictable anticoagulation effect appears to be useful and cost saving.

Acknowledgement/Funding: Bayer HealthCare

**P6192 | BEDSIDE**

**Patient profile of oral anticoagulation (OAC) use in people with non-valvular atrial fibrillation (NVAF): Findings from REACT-AF2 study in UK primary care data**

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**Background:** Atrial fibrillation (AF) is the most common arrhythmia, affecting more than 4.5 million people in Europe, currently affecting approximately 2% of the UK population. Owing to recent developments in OAC treatment, there is a need to generate real-world evidence on patients prescribed OACs for AF.

**Purpose:** To describe the characteristics of patients with NVAF who are newly prescribed OACs in routine clinical practice in the UK.

**Methods:** This was a retrospective cohort study of patients with NVAF who were newly prescribed OAC treatment (apixaban, rivaroxaban, dabigatran and vitamin K antagonists (VKAs)) from 1st Dec 2012 to 31st Oct 2014 using UK primary care data from CPRD database. Newly prescribed OAC therapy was defined as initiation of OAC treatment during the study period and having had no prior prescriptions of the same OAC. Demographic and clinical characteristics (HAS-BLED score and CHA2DS2-Vasc score) were examined at the starting date of the new OAC (index date) in the overall cohort and within each cohort defined by the OAC treatment.

**Results:** In total, 16,067 patients were included in the study. 94.8% of patients received only one newly prescribed OAC therapy during the study period, of those 5.6% were treated with apixaban, 8.5% with dabigatran, 18.7% with rivaroxaban and 67.2% with VKA. 55.2% of patients were males. The mean age of the total cohort was 74.6 years. The distribution of age, previous OAC status, HAS-BLED, and 67.2% with VKA. 55.2% of patients were males. The mean age of the total cohort was 74.6 years. The distribution of age, previous OAC status, HAS-BLED, and CHA2DS2-VASc by OAC treatment groups are reported in table 1 below.

**Conclusion:** NVAF patients newly prescribed an OAC in the UK were predominantly males, over 70 years old. Overall, most patients had a high risk of stroke. The proportion of patients with high bleeding risk was slightly lower in those prescribed VKA compared to the other OACs.

**Acknowledgement/Funding:** The study was funded by the Alliance Pfizer/Bristol Myers-Squibb

**P6193 | BEDSIDE**

**CCP survey about management of thromboembolic events in atrial fibrillation prevention**

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**Purpose and methods:** To evaluate knowledge and application of 2012 ESC Atrial Fibrillation (AF) guidelines, we sent a questionnaire to 50840 cardiologists, subscribers of the CCP E-Journal, with 15 questions concerning anticoagulation management.

**Results:** The responders were 2428 (4.7% of total), 70.3% male, 51.8% from 30 to 50 years old, 70.3% from Europe, 56.1% working in hospital and 22.6% in out-of-hospital practice. 91.9% declare to use regularly the CHA2DS2-Vasc Score. Of the physicians not using the score 35.2% has difficulties in remembering it, and 23.1% lacks of knowledge. CHADS score was still used from 28.1%. HAS-BLED Score is not being used by 24.9% of the responders, mainly (35.4%) due to memory difficulties, or to lack of knowledge (22.8%). In patients with concomitant AF and stable CAD, 33.8% of physicians uses warfarin, 29.9% NOACs, 20.3% ASA and warfarin, 13.1% ASA and NOACs. 30.4% of physicians thinks anticoagulation compatible with an age > 90 years, but 14.8% believe 75 years the highest age compatible with OAC. The majority of responders (37.7%) uses NOACs as first line treatment, and 30.5% after VKA management problems. Patients wish is the reason for NOACs choiche for 21.9% of responders. 6.9% of responders is not using NOACs at all, mainly due to reimbursement problems in his country (31.5%) or lack of experience with this drugs (25.1%). 61.7% of responders declares to know and apply or to know and apply partially (35.9%) the 2012 ESC Guidelines on AF.

**Conclusions:** Many of the results of the questionnaire are quite satisfying. A large percentage of responders is using the CHA2DS2-Vasc Score. A good percentage of responders thinks anticoagulation compatible with very old ages, while only 14.8% consider the highest age 75 years. Realitively few responders don’t use NOACs, mainly due to lack of reimbursement of their NHSS. Finally a very large percentage knows the guidelines and applies them, at least partially. On the other hand about one fourth doesn’t use the HAS-BLED Score. The answer concerning the use of antithrombotic drugs in stable CAD is difficult to analyze: the choice of VKA and NOACs is adequate, while the association chosen by one third of responders of ASA and VKA or ASA and NOACs in stable conditions is not indicated in the guidelines. Our results indicate that 2012 AF ESC guidelines are accepted and known by the medical community. This is encouraging, however there is still a large room for improvement.
**P6195 | BEDSIDE**

Effect of renal function on the cost-effectiveness of high-dose edoxaban compared to adjusted-dose warfarin for stroke prevention in non-valvular atrial fibrillation patients

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**Background:** Post-hoc analysis suggests high-dose edoxaban may provide inferior anticoagulation to adjusted-dose warfarin in non-valvular atrial fibrillation (NVAF) patients with good renal function. To date, no cost-effectiveness analysis of edoxaban has taken these data into account.

**Purpose:** To assess the cost-effectiveness of high-dose edoxaban versus adjusted-dose warfarin for the prevention of stroke in patients with NVAF at differing categories of creatinine clearance (Ccr).

**Methods:** Our Markov model compared the cost-effectiveness of high-dose edoxaban (60 mg once daily, 30 mg once daily in patients with a Ccr < 50 mL/min) and adjusted-dose warfarin (target international normalized ratio (INR) range of 2.0–3.0) at Ccrs of > 80 mL/min, > 50–80 mL/min and Ccr ≤ 50 mL/min. The model was performed from a United States (US) societal perspective; and assumed NVAF patients initiated therapy at 70 years of age, had a moderate-to-high risk for ischemic stroke (mean CHADS2 of 3) and no contraindications to anticoagulation. Data sources included regulatory agency subgroup analyses of the Edoxaban versus Warfarin in Patients with Atrial Fibrillation (ENGAGE-AF) trial and other published anticoagulation studies. Outcome measures included lifetime costs (direct and indirect) in 2014 US dollars, quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios (ICERs). The robustness of our model's conclusions were tested using Monte Carlo simulations (MCS).

**Results:** High-dose edoxaban was found to be an economically dominant alternative to adjusted-dose warfarin in NVAF patients with a Ccr <80 mL/min (Table). In patients with a Ccr <80 mL/min, warfarin was the dominant strategy. Monte Carlo simulation suggested these conclusions were robust to uncertainty in included inputs.

**Conclusions:** Our Markov model suggests high-dose edoxaban is a dominant economic strategy when compared to adjusted-dose warfarin for the prevention of stroke in patients with NVAF, a moderate-to-high risk of stroke and a Ccr ≤ 80 mL/min.
P6198 | BEDSIDE
Guideline adherence to anticoagulation for atrial fibrillation: a study in indigenous and non-indigenous Australians

Background: Atrial fibrillation (AF) is a leading cause of preventable stroke in Australia. Given anticoagulation therapy can significantly reduce this stroke risk, we sought to characterise anticoagulation use in Indigenous and non-Indigenous Australians with AF.

Methods: Administrative, clinical and prescription data from patients with AF were linked. Anticoagulation use was characterised according to guideline-recommended risk scores and Indigenous status.

Results: 19,613 individuals with AF were studied. Despite a greater prevalence of other risk factors, Indigenous Australians were significantly younger than their non-Indigenous counterparts (p<0.001) and thus had lower CHADS2 (1.19±0.32 vs 1.99±0.47, p<0.001) and CHA2DS2VASc scores (1.47±0.03 vs 2.82±0.08, p<0.001). Correspondingly, the percentage of Indigenous Australians with CHADS2≥2 (36.9% vs 44.1%, p<0.001) and CHA2DS2VASc scores≥2 (62.9% vs 78.8%, p<0.001) was also lower. Indigenous Australians, however, had greater rates of under- and over-anticoagulation. Overall, 72.1% and 68.9% in this subgroup, correlation between TTR and duration of AF was significant (p<0.001). Exclusion criteria was the presence neurological disease, pregnancy, bleeding disorders, neoplasms. Presence of cardiovascular risk factors (hypertension, diabetes mel- litus type II, dyslipidemia, smoking status) and previous cardiovascular events (ischemic heart disease, stroke, and heart failure) were also collected. All patients were submitted to Short Portable Mental Status Questionnaire (SPMQS) (score from 0 to 10); significant dementia was defined as score ≥5.

Conclusion: Anticoagulation therapy is frequently not prescribed in accordance with guideline recommendations. Under- and over-anticoagulation in those at high stroke risk, and over-anticoagulation in those at low risk, is common and more likely in Indigenous patients with AF. Improving adherence to guideline recommendations for anticoagulation in AF may reduce both ischaemic and haemorrhagic strokes in Indigenous and non-Indigenous Australians.

P6199 | SPOTLIGHT
Inadequacy of oral anticoagulation is a crucial factor for development of dementia in patients with permanent atrial fibrillation
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Purpose: The aim of the present prospective study was to identify risk factors for significant dementia in patients with permanent atrial fibrillation (AF).

Methods: We enrolled 212 patients with at least 1 year of permanent AF referred to our unit between 2013-2017. Exclusion criteria were: age ≥75 years (45 cases), where the length of disease has not been found out of less than 1 year. In order to evaluate the influence of age and duration of AF on the risk of dementia, patients were split into two subgroups: age≤75 years (45 cases, where the length of disease has not been found out of less than 1 year). In the remaining 142 patients older than 75 years, the duration of AF was protective for dementia (OR=0.88, 0.83–0.94, p<0.001), probably due to better TTR. Intact, among 142 patients on warfarin ≥75 years, 60 with dementia showed lower TTR than 82 with dementia. Exclusion criteria was the presence of neurological disease, pregnancy, bleeding disorders, neoplasms. Presence of cardiovascular risk factors (hypertension, diabetes mellitus type II, dyslipidemia, smoking status) and previous cardiovascular events (ischemic heart disease, stroke, and heart failure) were also collected. All patients were submitted to Short Portable Mental Status Questionnaire (SPMQS) (score from 0 to 10); significant dementia was defined as score ≥5.

P6200 | BEDSIDE
Atrial fibrillation and anticoagulation therapy: a study in patients with atrial fibrillation
M. Nishino, N. Okamoto, A. Tanaka, N. Mori, Y. Yoshimura, N. Makino, Y. Egami, R. Shutta, J. Tanouchi, Osaka Rosai Hospital, Sakai, Osaka 591–8025, Japan

Background: It is unclear whether dabigatran and rivaroxaban have different risk factors for bleeding.

Methods: We enrolled consecutive patients with atrial fibrillation who received dabigatran or rivaroxaban. Selection of dabigatran or rivaroxaban depended on each physician's discretion. In this study, bleeding was defined as a reduction in the hemoglobin ≥2 g/dl. We compared the risk factors for bleeding including age, gender, incidence of custom dose and antipatelet therapy, CHADS2 and HAS-BLED scores, body weight, creatinine clearance, thrombin time (PT) and activated partial thromboplastin time between patients with and without bleeding in dabigatran and rivaroxaban groups, respectively. Uni and multivariate analyses were performed to determine the risk factors for bleeding.

Results: The dabigatran group consisted of 177 patients and the rivaroxaban group consisted of 197 patients. Multivariate analysis revealed that CLox was the only independent factor correlated with bleeding in the dabigatran group while in the rivaroxaban group, the CHADS2 score and use of antipatelet therapy were the independent factors correlating with bleeding (Table). Conclusion: To avoid bleeding, dabigatran should be prescribed with caution in patients with lower CLox and rivaroxaban should be prescribed with caution in patients with higher CHADS2 scores.

P6201 | BEDSIDE
Dabigatran and rivaroxaban have different risk factors for bleeding in atrial fibrillation patients
M. Nishino, N. Okamoto, A. Tanaka, N. Mori, Y. Yoshimura, N. Makino, Y. Egami, R. Shutta, J. Tanouchi, Osaka Rosai Hospital, Sakai, Osaka 591–8025, Japan

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Conclusions: To avoid bleeding, dabigatran should be prescribed with caution in patients with lower CLox and rivaroxaban should be prescribed with caution in patients with higher CHADS2 scores and patients using antipatelet therapy.
Conclusion: To the best of our knowledge, this is the first study to report the distribution of dabigatran concentrations in patients with NVAF under real-life conditions. Our study reveals that there are differences in the distribution of dabigatran concentrations between patients receiving dabigatran 110 mg bd and 150 mg bd. These differences can be attributed to inter-individual variability in drug clearance and to the lower dose of dabigatran 110 mg bd. However, the comparison of drug levels in patients with NVAF who received the 110 mg bd dose in the current study and patients who received the 150 mg bd dose in previous studies is limited by the different study designs and the lack of information on concomitant medications. The results of this study highlight the need for future studies to investigate the impact of individual patient characteristics on drug levels and the potential for dose optimization in NVAF patients.
or as categorical variable (low, moderate or high risk) were compared using the c-statistic with 95% CI.

**Results:** Among 8120 consecutive patients with AF including 46% elderly patients, 791 severe bleeding events were recorded during a follow-up of 877±1052 days. Bleeding occurred more commonly in patients with higher HAS-BLED, HEMORRHAGES and ATRIA scores. Overall, HAS-BLED significantly had higher c-statistics (0.60; 95% CI 0.59–0.61) than HEMORRHAGES (0.58; 95% CI 0.57–0.59; p=0.04) and ATRIA (0.58% 95% CI 0.57–0.59; p=0.04). In elderly patients, the c-statistic was lower for all 3 scores and was not significantly different between HAS-BLED (0.57; 95% CI 0.55–0.58), HEMORRHAGES (0.55% 95% CI 0.53–0.56; p=0.32) and ATRIA (0.55% 95% CI 0.53–0.56; p=0.13).

**Conclusion:** All 3 scores demonstrated only modest performance in predicting bleeding (c-stats from 0.53 to 0.80) although the HAS-BLED score performed better than HEMORRHAGES and ATRIA scores. In addition, all 3 scores showed lower performance in predicting bleeding within elderly population. HAS-BLED and other bleeding risk scores performed equally to predict bleeding events among elderly patients. Given its simplicity but similar performance, the HAS-BLED score may be an attractive alternative to HEMORRHAGES score for the estimation of bleeding risk in specific elderly population.

**P6206 | BEDSIDE**

**Differences in clinical outcome of patients with paroxysmal and sustained atrial fibrillation under oral anticoagulation therapy - results from the thromBEVAL study**

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**Background:** Oral anticoagulation therapy (OAC) for prophylaxis of stroke is recommended for patients at risk with paroxysmal (PAF) and sustained (SAF; ie, persistent and permanent) atrial fibrillation (AF). It is controversial whether AF pattern translates into differences in clinical outcome under OAC.

**Purpose:** We compared the outcomes in patients with paroxysmal and sustained AF in a regular medical care cohort under OAC.

**Methods:** ThromBEVAL is an investigator-initiated, prospective, multi-center cohort study (NCT01809015). Data were obtained from clinical visits and computer-assisted interviews according to standard operating procedures with a high-quality control. Study monitoring was carried out by an independent institution. Information on study endpoints was validated by medical records and adjudicated by a review committee.

**Results:** The analysis comprised 541 patients with PAF and 840 patients with SAF. Mean CHADS2 score was 2.3±1.3 for PAF and 2.5±1.3 for SAF. Mean follow-up time in both cohorts was 11.6±5.1 and 10.8±4.9 months respectively. There was a significant difference between event rates for net clinical benefit outcome (composite of thromboembolic events, major and clinically-relevant non-major bleeding, death) between both samples with 46 events/100 patient-years (7%) with SAF and 19 events/100 patient-years (3%) with PAF (OR: 0.52; 95% CI 0.41–0.67; p<0.001). Major bleeding events were less frequent in PAF patients (45.0%) as compared to SAF patients (33.8%). Overall stroke and bleeding risk-associated use of OAC included in the study was 0.57 (95% CI 0.48–0.70; p=0.001) for cardioembolic events and 0.57 (95% CI 0.48–0.70; p=0.001) for any stroke.

**Conclusion:** These preliminary results of a single-centre registry give interesting insights in promising characteristics of all three so far available OACs. These substances might enable effective anticoagulant therapy of patients with therapeutic failure of VKA therapy.

**P6208 | BEDSIDE**

**Stroke and bleeding risk-associated use of antithrombotic therapies for stroke prevention in atrial fibrillation in routine clinical practice: the BALKAN-AF Survey**

T.S. Potpara1, G.A. Dan2, E. Trendafilova3, V. Paparisto4, Z. Kuslijugo5, M.M. Polovina1, R. Musetescu6, S. Manola7, L.J. Music8, G.Y.H. Lip9 on behalf of the BALKAN-AF Study Group. 1Cardiology Clinic, Clinical Center of Serbia; 2University of Medicine, Belgrade University, Serbia, Belgrade, Serbia; 3University of Bucharest Carol Davila, Bucharest, Romania; 4National Heart Hospital, Sofia, Bulgaria; 5University Clinical Center Mostar, Bosnia and Herzegovina; 6University Clinical Center of Bucharest, Bucharest, Romania; 7University Clinical Center Tuzla, Tuzla, Bosnia and Herzegovina; 8Emergency County Hospital, Craiova, Romania; 9University Hospital Sestre Milosrdnice, Zagreb, Croatia; 9Cardiology Clinic for cardiology, Podgorica, Montenegro; 10Birmingham City Hospital, Centre for Cardiovascular Sciences, Birmingham, United Kingdom.

**Background:** In contrast to other European regions, real-world data on the management of atrial fibrillation (AF) in the Balkan countries are scarce.

**Purpose:** We report an interim analysis from the Balkan-AF Study addressing the stroke and bleeding risk-associated use of oral anticoagulation (OAC) and antiplatelet drug therapies (APT) for stroke prevention in AF in routine clinical practice.

**Methods:** A 12-week prospective “snapshot” survey (December 2014-February 2015) of consecutive non-valvular AF patients seen by internal medicine specialists or cardiologists was conducted in Albania, Bosnia & Herzegovina, Bulgaria, Croatia, Montenegro, Romania and Serbia (a region with ~45 million inhabitants). Each country participated with university/non-university hospitals and outpatient clinics in- and outside the capital cities. Data were collected via an electronic case report form.

**Results:** Of 2080 patients (mean age 69.1±10.8, range 18–96 years), 936 (45.0%) were female. Mean CHADS2-VASc scores were 3.4±1.9 and 3.1±1.7 in all cases and confirmed LA peak emptying velocities [22±10 cm/s]. Mean LAAT width and length of 0.8±0.3 cm and 6.1±5.0 cm. In a first step all patients received antiplatelet therapy with dabigatran (9%), irnabat (11%), or apixaban (10%). FU was performed after at least 6 and 12 weeks after DOAC treatment including transesophageal echocardiography (TEE). Overall VKA showed a poor capability for midterm thrombus resolution after six weeks of intensified anticoagulant treatment. We identified 9 cases (16%) with LAAT disappearance, and one patient experienced a massive LAAT thrombus. After starting anticoagulant treatment to DOAC, LAAT resolution was observed in 18 out of 31 patients (58%), including six patients out of which were treated with rivaroxaban (60%), 7 out of 10 under anticoagulant therapy with dabigatran (70%), and in five out of 10 patients under apixaban (50%). When comparing the absolute LAAT resolution rates of VKA (18%) with DOAC (58%), this difference reached statistical significance (p<0.0005). We observed no major bleeding complication during FU in patients treated with either VKA or DOAC.

**Conclusion:** These preliminary results of a single-centre registry give interesting insights in promising characteristics of all three so far available DOACs. These substances might enable effective anticoagulant therapy of patients with therapeutic failure of VKA therapy.
use of APT was significantly associated with the CHA2DS2-VASc (OR 1.12; 95% CI, 1.05–1.20) compared to placebo (HR 0.86; 95% CI, 0.80–0.93). The risk of major bleeding increased with decreasing CrCl (p < 0.001), but not with the HASBLED (OR 1.07; 95% CI, 0.99–1.16, p = 0.076). With increasing CHA2DS2-VASc score, the odds of major bleeding decreased with increasing CrCl (p < 0.001), but not with the HASBLED (p = 0.076). **Conclusions:** Use of antithrombotic therapies for AF-related stroke prevention in daily clinical practice in the Balkan-AF survey was not based on individual patient stroke and bleeding risk scores. Although internal medicine specialists and cardiologists prescribed OAC to 73% of AF patients, better understanding of treatment principles is necessary to improve the management of AF-related stroke risk.

**Acknowledgement/Funding:** The BALKAN-AF Survey was supported by Pfizer, Bayer and Boehringer Ingelheim.

### P6210 | BEDSIDE

**Predictors of LAA thrombi in patients with atrial fibrillation and low CHA2DS2-VASc score**


**Purpose:** In patients with atrial fibrillation (AF), LAA morphology has been suggested to modify thrombogenesis. We tested the hypothesis that LAA thrombi in low-risk patients are associated with LAA characteristics.

**Methods:** Of 2,069 patients who underwent AF ablation, 25 (1.2%) had a prior LAA thrombus and a low CHA2DS2-VASc score (<1). Those patients were matched for the CHA2DS2-VASc criteria with 94 thrombus free patients and CT data were compared. LAA measurements, morphology (Cactus, Chicken-Wing, Windsock, Cauliflower) and takeoff in relation to the respective takeoff of the adjacent pulmonary vein (PV) were determined. The LAA flow and the heart rate (HR) at the presence of the thrombus and after its resolution was compared.

**Results:** In univariate analysis, patients with prior thrombus had a higher incidence of Non-Chicken-Wing LAA (84% vs. 61%, p < 0.03), a tendency for reduced LAA flow (46±18 vs. 54±17 cm/s, p = 0.08), higher LAA (9±6 vs. 7±3 ml, p = 0.01) and LA volume (138±49 vs. 121±38 ml, p = 0.06), while clinical (HR: 76±25 vs. 82±26 bpm, p = 0.48) or other LAA characteristics were similar between groups. Logistic regression revealed that LAA volume (OR: 1.2/ml, CI: 1.04–1.37, p = 0.01) and Non-Chicken-Wing LAA (OR: 5.9; CI: 1.5–23.3, p = 0.01) were independent predictors of thromb. Intra-group analysis of the study group revealed that in the presence of a thrombus, tachyarrhythmia (89±29 vs. 76±25 bpm, p = 0.03) and reduced LAA flow (34±17 vs. 46±18 cm/s, p = 0.015) were more common than after its resolution.

**Conclusion:** A higher volume and Non-Chicken-Wing LAA predispose to thrombus formation whereas tachyarrhythmia and reduced LAA flow facilitate its perpetuation. These findings may have implications for anticoagulation of AF patients with low CHA2DS2-VASc scores.

### P6211 | BEDSIDE

**Early assessment of bleeding-related hospital readmissions among nonvalvular atrial fibrillation patients treated with the new oral anticoagulants using an electronic medical record database in the US**

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**Background:** Randomized clinical trials have demonstrated that new oral anticoagulants NOACs are efficacious for reducing stroke risk among patients with nonvalvular atrial fibrillation (AF), although the reductions in stroke and bleeding risk vs. warfarin were different.

**Purpose:** To assess bleeding-related hospital readmissions among hospitalized NVAF patients treated with the 3 NOACs, dabigatran, rivaroxaban, and apixaban, in the US.

**Methods:** Patients (≥18 years) with a hospital discharge diagnosis of AF who received apixaban, dabigatran, or rivaroxaban during hospitalization were identified from the Cerner Health Facts hospital database between 1/1/2012 and 8/31/2014. Patients were grouped into 3 cohorts depending on NOAC received. Patient characteristics and hospital resource use associated with the initial hospitalizations and bleeding-related readmissions within 30 days were evaluated and compared among patients treated with the 3 NOACs at the unadjusted and regression-adjusted levels.

**Results:** Among NVAF patients included in the study population, 1,813 were treated with apixaban, 6,637 with rivaroxaban, and 5,751 with dabigatran during hospitalization. Patients who received apixaban were older, had greater severity of comorbidity, and had higher stroke and bleeding risks (Table). After controlling for patient characteristics, including stroke/bleeding risks, in comparison with treatment with apixaban, the odds of bleeding-related 30-day hospital readmissions were estimated at 1.68 (p = 0.03) and 1.33 (p = 0.25) for patients treated with rivaroxaban and dabigatran respectively. In comparison with use of apixaban, the use of rivaroxaban and dabigatran were associated with longer average hospital stay for bleeding-related readmissions (0.07 days, p = 0.07; 0.08, p = 0.03).

**Conclusion:** In this early assessment, after controlling for patient characteristics, treatment with rivaroxaban vs. apixaban was associated with significantly greater risk of bleeding-related 30-day readmissions.

**Acknowledgement/Funding:** Bristol-Myers Squibb and Pfizer

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### Table: Anticoagulation and Atrial Fibrillation III

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>Apixaban</th>
<th>Rivaroxaban</th>
<th>Dabigatran</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean [SD]</td>
<td>74.9 [11.7]</td>
<td>72.1 [12.6]</td>
<td>72.4 [12.2]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Charlson Comorbidity Index (CCI), mean [SD]</td>
<td>2.7 [2.3]</td>
<td>2.4 [2.3]</td>
<td>2.5 [2.2]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CHADS2 score, mean [SD]</td>
<td>2.4 [1.2]</td>
<td>2.1 [1.2]</td>
<td>2.2 [1.1]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAS-BLED score, mean [SD]</td>
<td>2.5 [1.0]</td>
<td>2.3 [1.0]</td>
<td>2.4 [1.0]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**SD, standard deviation.**

**Conclusion:** In this early assessment, after controlling for patient characteristics, treatment with rivaroxaban vs. apixaban was associated with significantly greater risk of bleeding-related 30-day readmissions.

**Acknowledgement/Funding:** Bristol-Myers Squibb and Pfizer

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### Table: P6210 – Table 1

<table>
<thead>
<tr>
<th>Outcome</th>
<th>P*</th>
<th>CrCl 30 to 50*</th>
<th>CrCl ≥ 50 to &lt;80*</th>
<th>CrCl ≥80*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivaroxaban</td>
<td>1.587</td>
<td>1.592</td>
<td>3.113</td>
<td>3.168</td>
</tr>
<tr>
<td>Warfarin</td>
<td>2.868 (78)</td>
<td>3.50 (96)</td>
<td>2.21 (124)</td>
<td>2.46 (138)</td>
</tr>
<tr>
<td>HR (95% CI) for rivaroxaban vs warfarin</td>
<td>0.80 (0.71, 0.90)</td>
<td></td>
<td></td>
<td>1.52 (0.68, 1.87)</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>1.599</td>
<td>1.610</td>
<td>3.128</td>
<td>3.177</td>
</tr>
<tr>
<td>N</td>
<td>4.71 (106)</td>
<td>4.59 (107)</td>
<td>3.48 (170)</td>
<td>3.77 (186)</td>
</tr>
<tr>
<td>HR (95% CI) for rivaroxaban vs warfarin</td>
<td>0.17</td>
<td>1.02 (0.78, 1.34)</td>
<td>0.93 (0.75, 1.14)</td>
<td>1.28 (0.98, 1.68)</td>
</tr>
</tbody>
</table>

*Ccri cut points chosen to coincide with existing FDA analyses.*
Valvular Atrial Fibrillation and the Risk of Hospitalization Due to Bleeding or Thromboembolism


Valvular atrial fibrillation, and this decline was particularly pronounced among patients on warfarin. The relative risks of hospitalization due to bleeding or thromboembolism were younger and had fewer co-morbid conditions at baseline compared to warfarin. If this is related to better drug management needs to be explored in future studies.

Antithrombotic Management in Patients with Atrial Fibrillation Undergoing Stent Implantation: What is the Impact of the ESC Guidelines Adherence?

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Background: Patients with atrial fibrillation (AF) who undergo percutaneous coronary intervention (PCI) and stenting transiently require triple antithrombotic therapy according to current ESC guidelines. The purpose of this study was to assess guidelines implementation and predictive factors of the prognosis related to ESC guidelines adherence.

Methods: Consecutive AF patients referred for PCI with stent were enrolled from 2011 to 2013. Prescription of antithrombotic treatment (ATT), and occurrence of bleeding, myocardial ischemia, stroke and death were obtained by screening hospitalization reports and standardized questions during follow-up.

Results: Among 259 AF patients with PCI and stenting (age 76±10 years), 40% had acute coronary syndrome and 60% had elective PCI. During a follow-up of 633±352 days, there were 53 (34%) undergoing elective PCI who were guidelines adherent, 10 (20%) for non-ST elevation myocardial infarction (NSTEMI) and 8 (15%) for STEMI. Permanent AF (OR 0.46; 95% CI 0.23–0.89; p<0.002), medical history of valvular heart disease (OR 0.51; 95% CI 0.28–0.98; p=0.04), heart failure (OR 0.49; 95% CI 0.25–0.94; p<0.03) and use of OAC before hospitalization (OR 0.48; 95% CI 0.24–0.96; p=0.04) were associated with guideline adherence.

Conclusion: For antithrombotic therapy in patients with AF who undergo PCI and stent implantation are still poorly followed in clinical practice. OAC use increased associated with an increased risk of death in this population.
P6216 | BEDSIDE
Real-life use of non-vitamin K antagonist oral anticoagulants in comparison with vitamin K antagonists for non-valvular atrial fibrillation: data from a prospective cohort

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Current guidelines recommend non-vitamin K antagonist oral anticoagulants (NOACs) or vitamin K antagonists (VKAs) for patients with non-valvular atrial fibrillation (NVAF). Clinical features of patients prescribed with NOACs or VKAs in real-life remain undefined.

Purpose: To evaluate differences between NVAF patients prescribed with NOACs or VKAs in real-life.

Methods: Consecutive patients with NVAF prescribed with NOACs from August 2013 to January 2015 were included in a multicenter prospective cohort and compared with a random sample of patients with NVAF receiving VKAs.

Results: Overall, 1494 patients with NVAF (5.4% new detected, 17.3% paroxysmal, 8.8% persistent, 68.5% permanent) were included: 1021 receiving NOACs (reduced doses in 483 patients) and 473 VKAs. The mean CHA2DS2-VASC score was higher in patients treated with rivaroxaban or apixaban as compared with patients treated with dabigatran (both p<0.001) or VKAs (both p<0.001). Similarly, the mean HASBLED score was higher in patients treated with rivaroxaban or apixaban compared with patients treated with dabigatran (both p<0.001) or VKAs (both p<0.001). These differences were mostly accounted for by a lower mean age in dabigatran patients compared to rivaroxaban, apixaban or VKAs patients and by a higher prevalence of previous stroke, previous major bleeding and labile INR in patients prescribed with NOACs compared with VKAs. Patients prescribed with reduced doses of NOACs have increased CHA2DS2-VASC or HAS-BLED compared to patients treated with VKAs or standard doses of NOACs.

P6217 | BEDSIDE
Real world comparison of major bleeding risk among non-valvular atrial fibrillation patients newly initiated on apixaban, dabigatran, rivaroxaban or warfarin


Background: Limited evidence is available about the real-world safety of apixaban versus other anticoagulants.

Purpose: To compare the major bleeding risk among newly anticoagulated non-valvular atrial fibrillation (NVAF) patients initiating apixaban versus warfarin, dabigatran or rivaroxaban.

Methods: Retrospective cohort from MarketScan® commercial & Medicare supplement US database from 01/01/2013 to 12/31/2013 was used for this comparative assessment. Major bleeding was defined as: (i) bleeding requiring hospitalization (IP) and (ii) inpatient or outpatient bleeding (IP/OP). Cox model estimated Hazard ratios (HR) of major bleeding adjusted for age, gender, baseline comorbidities and comedinations.

Results: Among 29,338 patients, 2402 (8.19%) were on apixaban, 4,173 (14.22%) on dabigatran, 10,050 (34.26%) on rivaroxaban and 12,713 (43.33%) on warfarin. Warfarin (72.5±11.9 yrs) and apixaban (69.3±12.3 yrs) patients were older and sicker versus rivaroxaban (67.3±12.2 yrs) and dabigatran (66.8±12.1 yrs). Patients initiated on warfarin (IP bleeding HR: 1.93, 95% CI: 1.2–3.33, P=0.018; IP/OP bleeding HR: 1.62, 95% CI: 1.2–2.18, P=0.0015) or rivaroxaban (IP bleeding HR: 2.19, 95% CI: 1.26–2.79, P=0.0052; IP/OP bleeding HR: 1.70, 95% CI: 1.26–2.29, P=0.0008) had greater risk of major bleeding versus those on apixaban or dabigatran. Patients initiating dabigatran (IP bleeding HR: 1.71, 95% CI: 0.94–3.1, P=0.079; IP/OP bleeding HR: 1.28, 95% CI: 0.92–1.79, P=0.1441) had numerically greater risk of major bleeding versus those on apixaban (Figure).

Conclusion: Among newly anticoagulated NVAF patients in the real world setting, initiation with rivaroxaban or warfarin was associated with significantly greater risk of major bleeding as compared to initiation on apixaban.

Acknowledgement/Funding: The study is supported by Bristol-Myers Squibb and Pfizer Inc.

P6218 | BEDSIDE
Higher amounts of heparin use with oral factor Xa-Inhibitor compared to oral vitamin K antagonist and thrombin-inhibitor during ablation procedure for atrial fibrillation

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Background: In practice guidelines, an approach of performing catheter ablation for atrial fibrillation (AF) (or either paroxysmal or persistent pattern) Ninety-one patients were under uninterrupted oral VKA (warfarin), 91 under oral direct thrombin-inhibitor (dabigatran), and 91 under direct oral factor Xa-inhibitor (rivaroxaban). We compared amounts of heparin use during the procedure and event rates of bleeding and systemic thromboembolism among three anticoagulants therapy.

Methods: We included 273 consecutive patients who underwent catheter ablation procedure for elimination AF with either paroxysmal or persistent pattern.

Results: Significantly higher amounts of heparin were needed in the rivaroxaban group (252 U/kg ± 91 U/kg) compared to the warfarin group and the dabigatran group (187±59 U/kg and 218±55 U/kg, respectively; p<0.05 with ANOVA analysis). Major or minor bleeding event was seen in one of the rivaroxaban group (1.1%) and none of the other two groups.

Conclusions: This study demonstrates that oral direct factor Xa-Inhibitor rivaroxaban needs significantly higher amounts of heparin use compared to oral VKA warfarin and direct thrombin-inhibitor dabigatran in perioperative management for AF ablation. However, it may not lead to an increase in bleeding complications.

P6219 | BEDSIDE
Management of anticoagulation in patients with non-valvar atrial fibrillation in general practice in UK: Evolution and characteristics of patients treated with antiplatelet therapy alone

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Background: Oral anticoagulation (OAC) therapy for thromboembolic prophylaxis (TEP) is recommended for high-risk patients with non-valvular atrial fibrillation (NVAF), i.e. those with CHA2DS2-VASc ≥ 2. Evidence suggests that aspirin is less effective for TEP, with a risk of major bleeding comparable to OACs. Consequently, recent guidelines (ESC 2012, NICE 2014) recommend limited or no use of antiplatelet therapy for TEP in AF.

Aim: Describe changes over time from 2012 to 2015 in the proportion of NVAF patients treated with aspirin or other antiplatelet agents (APA) for TEP.

Methods: We undertook four cross-sectional analyses on 1 April of each year from 2012–15 (index dates), using the UK Clinical Practice Research Datalink
Conclusions: Coronary computed tomography is a cost-effective alternative for the diagnosis of CAD and should be included in the Brazilian public health system. Stress echocardiography has a similar performance and is an acceptable alternative for most patients, while invasive strategies should be reserved for patients at high risk.

Acknowledgement/Funding: This study was supported by the CNPq (MCT/MS), and the Brazilian National Institute for Science and Technology (INCT)'s HTA Program.
dimensional speckle tracking echocardiography at rest was performed the day before coronary angiography or percutaneous coronary intervention. Apical 3 views were used to examine the duration of ESL. The duration of ESL was defined as time from onset of the Q wave on electrocardiography to maximum myocardial systolic thickening (Figure A).

**Results:** Thirty-five patients, revealed normal coronary angiogram (NCA), and 40 patients, who underwent FFR, had CAD. In patients with significant CAD, 17 patients showed the value of FFR $\geq 0.8$ and 23 patients showed the value of FFR $< 0.8$. The duration of ESL was 39.5±29.5 ms in patients with FFR $< 0.8$, and 29.5±22.3 ms in patients with NCA (P=0.020) (Figure B). However, the duration of LV ESL did not show the significant correlation with the value of FFR (R2 = 0.1, P=0.12).

**Conclusions:** Duration of myocardial ESL was significantly prolonged in patients with significant CAD determined by FFR $< 0.8$ compared with patients with NCA. ESL at rest might be a useful parameter to identify patients with CAD, whereas this new parameter could not predict an FFR in those patients.

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**P6223 | BEDSIDE**

High-frequency QRS analysis compared to conventional ST-segment analysis in a large series of patients with chest pain and normal ECG managed with the propensity score matching for cardiovascular risk

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**Background:** The novel analysis of high-frequency QRS components (HF/QRS) has been proposed in patients with chest pain (CP) and normal ECG referred for emergency coronary angiography (ECA). Aim of the present study was to compare the prognostic value of the ex-ECG to the HF-QRS in the emergency setting.

**Methods:** Patients with CP and normal ECG, normal troponin and normal electrocardiography were considered. All patients underwent ex-ECG for conventional ST-segment analysis and HF-QRS analysis. A decrease $\geq 50$% of the signal of HF/QRS intensity recorded in two contiguous leads, at least, was considered as index of ischemia, as ST-segment depression $\geq 2$ mm or $1$ mm on CP on ex-ECG. Exclusion criteria were QRS duration $> 120$ msec and inability to exercise. Baseline characteristics were adjusted with the propensity score matching for possible confounders. SSFS software allowed estimation of the propensity-score using logistic regression and specifying nearest neighbor matching in cardiovascular risk-factor and TIMI-score, GRACE-score, CHADS2VASc-score. The primary endpoint was the composite of coronary stenosis $\geq 70$% or acute coronary syndrome, revascularization, and cardiac death at the 6-month follow-up.

**Results:** Out of 624 patients (age 61±15 years) considered, 589 were analyzed after matching. The percentage of age-adjusted maximal predicted heart rate was 88±10 and the maximal systolic blood pressure was 169±22 mmHg. Twenty-two patients achieved the end-point. On the univariate-analysis the presence of stenosis $\geq 70$% or acute coronary disease, revascularization, and cardiac death at the 6-month follow-up. Twenty-two patients achieved the end-point. On the univariate-analysis the presence of stenosis $\geq 70$% or acute coronary disease, revascularization, and cardiac death at the 6-month follow-up.

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month 1 (not improving ≥ 1 SAQAF health state) were assumed to discontinue ranolazine and behave like SoC patients.

**Results:** Ranolazine patients accrued a mean of 0.701 QALYs at a cost of £3,502. Those not receiving ranolazine accrued 0.662 QALYs and at a cost of £3,318. The incremental cost-effectiveness ratio (ICER) for the addition of ranolazine was £4,717/QALY. The ICER was most sensitive to ranolazine cost; exceeding £20,000/QALY when the cost of ranolazine increased >53% above base case. The ICER did not change appreciably when indirect costs were included (£3,439/QALY) in the model or mortality rates were assumed to increase with worsening severity of SAQAF health states (£5,171/QALY). Monte Carlo simulation found ranolazine cost-effective in >99% of 10,000 iterations assuming a £20,000/QALY willingness-to-pay threshold.

**Conclusion:** Ranolazine added to SoC in patients with weekly or daily angina appears cost-effective from a UK health-system perspective.

**Acknowledgement/Funding:** The Menarini Group

**P6227 | BEDSIDE**

Four-year clinical outcome of drug-eluting stent following rotational atherectomy for heavily calcified lesions


**Background:** Long term clinical outcomes after drug-eluting stent (DES) following rotational atherectomy (RA) for heavily calcified lesions remains unclear. The aim of this study is to assess long-term clinical outcomes after DES following RA.

**Methods and results:** We enrolled 213 consecutive patients with 245 lesions treated with DES following RA. Clinical follow-up information at 4 years was obtained 98.4%. Angiographic success rate was 98.9%. Mean age was 71.8±11.8 years, 50.2% had diabetes mellitus (DM), 21.8% had hemodialysis, and total stent length was 38.7±21.4 mm. The cumulative 4-year incidence of MACE, defined as cardiac death, myocardial infarction (MI), clinically-driven target lesion revascularization (CD-TLR) was 21.8%. The incidence of cardiac death, MI, and CD-TLR were 6.9%, 6.9%, and 17.8%. Definite stent thrombosis rate was 3.5%. MACE and CD-TLR risk was maximal within 1 year. In a multivariate analysis, significant predictors of MACE were DM (hazard ratio [HR] 1.90; 95% confidential interval [CI] 1.01–3.75; p = 0.049), and ejection fraction <53% (HR 2.89; 95% CI 1.17–6.20; p = 0.02).

The cumulative 4-year incidence of MACE

**Conclusions:** Incidence of MACE and CD-TLR was maximal within 1 year after DES implantation following RA and decreased thereafter. Patients implanting DES following RA with DM or low ejection fraction had poor clinical outcome.

**P6228 | BEDSIDE**

Modifiable risk factors associated with mild cognitive impairment in patients with stable coronary heart disease in the STABILITY trial

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**Background:** Decreased cognitive function is a major cause of disability in the elderly and is more prevalent in patients with cardiovascular disease.

**Purpose:** To evaluate associations between modifiable cardiovascular risk factors and mild cognitive impairment (MCI) in patients with chronic coronary heart disease (CHD) who participated in the global stabilization of Atherosclerotic plaque By Initiation of darapLadIb TherapY (STABILITY) trial.

**Methods:** 10,634 of 15,828 study participants completed the Montreal Cognitive Assessment (MoCA) test a mean of 3.17±0.37 years after randomisation to darapladib or placebo. The odds ratios (OR) for MCI (MoCA score <26 out of 30) versus normal cognitive function (MoCA score ≥26) were determined for clinical and demographic factors assessed at baseline using a multivariable model.

**Results:** The median age was 64 (IQR 59, 70) years and 82% were men. MoCA was <26 in 4,578 (43%) subjects. In the multivariable model older age, lower educational achievement, geographic region and country income level were each associated with MCI (P <0.0001). MCI was also more common in patients with a history of hypertension (OR 1.12, 95% Confidence Interval [CI] 1.02, 1.23), diabetes mellitus (OR 1.11, 95% CI 1.01, 1.21), LDL cholesterol >2.58mmol/L (OR 1.11, 95% CI 1.01, 1.23), HDL cholesterol <1.03mmol/L (OR 1.12, 95% CI 1.02, 1.23), >2.5 hours moderate intensity exercise each week (OR 1.15, 95% CI 1.06, 1.27), renal dysfunction (eGFR <60 mL/min, OR 1.10, 95% CI 1.00, 1.21) and history of stroke (OR 1.42, 95% CI 1.19, 1.70). Randomisation to darapladib or placebo, sex, obesity, current smoking, history of myocardial infarction, coronary artery bypass surgery, multi-vascular coronary artery disease and poly-vascular disease were not independently associated with MCI.

**Conclusion:** MCI is common in patients with stable CHD and associated with several cardiovascular risk factors. Further research is needed of which of these modifiable factors can be modulated. Interventions that suggest that interventions which improve cardiovascular risk factors could, over the long term, decrease the likelihood of developing cognitive impairment.

**Acknowledgement/Funding:** The STABILITY study was funded by GlaxoSmithKline

**P6229 | BEDSIDE**

Effect of ivabradine on heart rate variability in patients with stable coronary artery disease

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**Background:** Ivabradine is a specific heart-rate lowering agent with anti-anginal properties and is commonly used in patients with stable coronary artery disease (CAD). Heart rate variability (HRV) reflects autonomic nervous system activity and predicts outcome. It is not known whether ivabradine modulates HRV in these patients.

**Purpose:** We aimed to evaluate the effect of ivabradine on HRV in patients with stable CAD.

**Methods:** We included 36 patients (61±13 years, 75% women) with stable CAD, on maximal tolerated beta blocker therapy, and in sinus rhythm >65bpm. Ivabradine (5mg bid) was initiated and up titrated to 7.5mg bid, if tolerated. Prior to treatment initiation and after 3 months, a 24h Holter was recorded.

**Results:** Diabetes mellitus, arterial hypertension, and heart failure were known for 58%, 89% and 27% of patients, respectively. All patients were treated with >50% of beta blocker target dose. Ivabradine decreased heart rate in most patients and improved time domain HRV parameters – see table. It increased average 24h high frequency power (p=0.006), but had no significant influence on low frequency power.

**HRV parameters**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR</td>
<td>78±1 bpm</td>
<td>68±1 bpm</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SDNN</td>
<td>125±4 ms</td>
<td>140±5 ms</td>
<td>0.003</td>
</tr>
<tr>
<td>rMSSD</td>
<td>47±3 ms</td>
<td>54±3 ms</td>
<td>0.01</td>
</tr>
<tr>
<td>pNN50</td>
<td>33±3 ms</td>
<td>39±3 ms</td>
<td>0.01</td>
</tr>
<tr>
<td>pNN50</td>
<td>8±1%</td>
<td>10±2%</td>
<td>0.005</td>
</tr>
<tr>
<td>LF</td>
<td>450±48 ms²</td>
<td>463±122 ms²</td>
<td>0.2</td>
</tr>
<tr>
<td>HF</td>
<td>238±41 ms²</td>
<td>382±61 ms²</td>
<td>0.006</td>
</tr>
</tbody>
</table>

All results are presented as mean’s standard error of mean. HR, heart rate; SDNN, standard deviation of all normal-to-normal (NN) intervals; rMSSD, mean of the SD of all NN intervals for all 5-min segments of the entire recording; SDANN, SD of the averages of NN intervals in all 5-min segments of the entire recording; pNN50, the square root of the mean squared differences of successive NN intervals; LF/HF, the proportion of the number of successive interval differences greater than 50 ms to the total number of NN intervals; LF, low frequency power; HF, high frequency power.

**Conclusion:** Ivabradine, on top of maximal tolerated beta blockers, improves HRV in patients with stable CAD.

**Acknowledgement/Funding:** The study was partially funded by Servier.

**P6230 | BEDSIDE**

Circulating high-sensitivity cardiac troponin T is a strong predictor of coronary atherosclerotic burden independently from the presence of inducible ischemia

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**Background:** Circulating levels of high-sensitivity cardiac troponin T (hs-cTnT) are predictors of coronary artery disease (CAD) and long term prognosis in patients with stable angina.

**Purpose:** We aimed to assess whether inducible myocardial ischemia is the major determinant of circulating hs-cTnT levels in these patients.

**Methods:** Hs-cTnT was measured in 378 patients (60±10.5 years, 229 males) with stable angina and unknown CAD enrolled in the Evaluation of Integrated
Cardiac Imaging (EVINCI) European study. All patients underwent stress imaging (nuclear perfusion imaging or echocardiography or cardiac magnetic resonance) to detect inducible myocardial ischemia, and coronary computed tomography angiography (CCTA) to assess the presence of CAD (>50% stenosis of at least one major coronary vessel). Moreover, an individual CTA score, expressing the coronary atherosclerotic burden, was calculated combining extent, severity, composition, and location of plaques.

Results: Patients were subdivided according to the absence/presence of CAD and ischemia. Hs-cTnT concentrations were significantly increased in patients with CAD with or without inducible ischemia (Figure). CTA score progressively increased from the first to the last group (6.3±0.5 to 23.3±1.3, P<0.0001 for trend). In a multivariate model, plasma hs-cTnT was an independent predictor of the CTA score, even after adjustment for age, sex, risk factors and presence of ischemia (coefficient 0.71, SE 0.1, p<0.0001).

Conclusions: Circulating hs-cTnT is a strong predictor of coronary atherosclerotic burden also in the absence of inducible ischemia. These results suggest alternative mechanisms linking coronary atherosclerosis with release of hs-cTnT in patients with stable CAD.

ANGINA PECTORIS STABLE II

P6231 | BEDSIDE
Occurrence and in-hospital mortality of vasospastic angina pectoris in Finland
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Background: Epidemiology of vasospastic angina pectoris (AP) has been studied mainly in Japan while information on western populations is limited.

Purpose: To study occurrence and in-hospital mortality of vasospastic AP in a general population of Finland.

Methods: Occurrence and mortality of admissions caused by vasospastic AP in Finland were studied using a retrospective nationwide, population-based registration (n=39,191,852 person-years) registry of hospital admissions in patients aged ≥18 years. Data were collected from all 22 Finnish hospitals with coronary angiography from May 2000 to October 2009. Incidence was calculated using age and sex matched population data of mainland Finland.

Results: The study period included 1786 vasospastic AP admissions. Vasospastic AP patient was more likely to be male (59.5%; CI 55.9–63.1%) than female (40.5%; CI 37.6–43.6%) with age-adjusted RR of 1.55 (CI 1.03–2.33, p=0.035) for male sex. Female patients were significantly older than male patients (67.6±12.2 vs. 64.9±11.0 years, p<0.0001). Standardized incidence rate for vasospastic AP caused admission was 3.77 (CI 3.58–3.97)/100,000 person-years overall, 5.05 (CI 4.74–5.38)/100,000 among men and 2.74 (CI 2.52–2.98)/100,000 among women. Total incidence increased steadily with age in population aged 40–75 years followed by gradual decrease in population aged older than 85 years. Slope of increase in incidence with aging was steeper among men, while peak in incidence lasted longer in women. Incidence rate ratio for vasospastic AP caused admission was 1.77 (CI 1.41–2.22) among men compared to women (p<0.0001). Vasospastic AP caused 1.3% of all cardiovascular admissions among adults aged 45–60 years, but the proportion decreased gradually to 0.1% among nonagenarians. Total in-hospital mortality for vasospastic AP was 1.6% (CI 1.0–2.3%). Mortality increased with age, but was not associated with sex.

Conclusion: Men have a higher risk for vasospastic AP caused admissions compared to women, but the observed sex-bias was smaller than in previous Japanese reports. Age-distribution of vasospastic AP patients in Finland was similar to that reported previously for Japan. In-hospital mortality for vasospastic AP is low.

Acknowledgement/Funding: Finnish Cardiovascular Society. Clinical Research Foundation of the Turku University Hospital

P6232 | BEDSIDE
Increased level of circulating glutamate and cystine in patients with coronary artery spasm

Background: Glutathione (GSH), an important antioxidant restoring intracellular redox imbalance, is reported to attenuate coronary vasoconstriction to acetylcholine in patients with coronary spasitic angina. GSH synthesis is dependent on the availability of the amino acid precursors such as glutamate, glycine, and cysteine. Because cysteine levels are generally higher than cysteine levels in extracellular fluids, mechanisms for cystine uptake are also crucial for GSH biosynthesis. Cysteine is taken up by the specific cysteine/glutamate transport system (xc-transports), in association with the export of the same amount of glutamate. Extracellular glutamate competitively inhibits import of cystine. This could raise the possibility that potential role of plasma glutamate in coronary vasospasm might be modulated by plasma cysteine level.

Aims: The aim of the study was to examine this possibility in clinical settings.

Methods: We evaluated consecutive 39 patients with chest pain at rest, who had not coronary stenosis nor structure heart disease. Coronary spasm provocation tests were performed by stepwise intracoronary acetylcholine administration (20 to 50 μg for right, 50 to 100 μg for left). Patients were categorized as test-positive if they developed angina with ECG changes accompanied with coronary vasospasm, defined as the transient or near total (>90%) occlusion. Blood samples were collected from aortic root to measure glutamate levels before procedure.

Results: Twenty-five patients were test-positive (spasm group) and 14 were negative (control group). Cystine levels in spasm group (32.5±10.3 mmol/ml) were significantly higher (p=0.018) than control (24.8±5.7 mmol/ml). Glutamate levels in spasm group (61.0±22.0 mmol/ml) were higher than control (48.1±23.1 mmol/ml), but did not reach the statistical significance (p=0.06). To investigate influence of smoking, we divided both groups into current or ex-smokers (n=17) and non-smokers. Glutamate levels in non-smokers of control group (35.8±9.9 mmol/ml) were significantly lower (p<0.05) than other 3 groups (61.4±18.0 mmol/ml for smoker/spasm, 70.2±24.0 mmol/ml for smoker/control, 60.7±26.6 mmol/ml for smoker/spasm). Despite high glutamate levels in smoker of both groups, cystine levels were significantly higher in spasm group than that of control (34.7±12.5 mmol/ml v.s. 22.1±8.3 mmol/ml; p<0.05).

Conclusions: Increased level of plasma glutamate may play an important role in the pathogenesis of coronary artery spasm when associated with high cysteine level.

P6233 | BEDSIDE
The predictive value of stress echocardiography. A real life study from a tertiary center
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Introduction: Stress echocardiography (SE) is a useful tool to diagnose coronary artery disease and guide patient management. In this study we aim to re-assess its predictive value with regard to patient outcomes.

Methods: 912 consecutive patients who underwent SE (dobutamine or exercise) within a calendar year were included in the registry. All demographic data and the result of the SE were collected prospectively in electronic patient records. Follow-up data with regards to MACCE (cardiovascular mortality, cerebrovascular accident, documented myocardial infarction and any repeat revascularization) were recorded for a period of 12 months following the SE.

Results: 27 patients had a non-diagnostic test and 17 did not have full demographic and follow-up data. For the remaining 868, the mean age was 61.07±12.26 years and 49.9% were male. In univariate analysis, male gender (HR: 4.07, 95% CI: 1.72–9.59; p=0.001) and the positive result of the test (HR: 5.15, 95% CI: 1.91–13.86; p=0.001) were correlated to MACCE. Hypertension (HR: 2.03, 95% CI: 0.75–5.47; p=0.161) was close to positive result of the test have a 3.7 -times higher risk of adverse outcome compared to those with a negative SE.

Conclusion: Our study shows that stress echocardiography is not only a useful diagnostic tool but also a strong predictor of patients' outcome. A positive stress echo result was the only predictor of 12-month MACCE. Patients with a positive test have a 3.7 -times higher risk of adverse outcome compared to those with a negative SE.

Fig. 1. MACCE survival curves

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Angina pectoris stable II

P6234 | SPOTLIGHT

Objective:

The purpose of this study was to assess the clinical efficacy of the device to narrow the Coronary Sinus (CS), the Reducer a real world cohort of patients with refractory angina with no option for conventional revascularization methods.

Background:
The CS Reducer is a new method to treat patients with refractory angina pectoris not eligible for conventional revascularization methods. The first-in-man experience with the CS Reducer in 15 un treatable chronic refractory angina patients showed feasibility of this technique and angina improvement in 80% of patients. We investigated 912 consecutive patients referred for CS Reducer procedures in our institute as part of a clinical care.

Methods:

This is a single center retrospective registry to assess outcomes of the CS Reducer in “unselected” patients with refractory angina. Patients were treated if they showed any objective evidence of myocardial ischemia and no option for conventional revascularization. The primary end point of this study was angina improvement according to the Canadian Cardiovascular Society (CCS) classification.

Results:

Twenty-three patients (74% male, mean age 69±9 years) with medically refractory angina (87% previous coronary artery bypass surgery, 48% previous myocardial infarction, 55% previous PCI, 52% diabetes mellitus) and no conventional revascularization options underwent CS Reducer implantation. Procedural success (defined as the successful placement of the device in the CS without any peri-procedural adverse events) was 100%. After a median follow-up of 6 [ICR: 4–11] months there was a significant improvement in CCS class (baseline 3.35±0.49 versus 2.13±0.92 at follow up, P<0.001). The majority of patients (78%) experienced an improvement of clinical symptoms: 9 (39%) by 1 CCS class, 8 (35%) by 2 CCS classes and 1 (4%) by 3 CCS classes. There were 5 (22%) patients with new clinical CCS changes.

Conclusion:

In this single center “real-world” experience, the CS Reducer demonstrated high efficacy in the treatment of refractory angina at mid-term follow-up.

P6237 | BEDSIDE

Angiographic Gensini score predicts coronary plaque burden and components assessed by iMap-intravascular ultrasound in patients with stable angina pectoris


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Background:

Gensini score (GS) is a simple and widely used angiographic tool for evaluating the severity of coronary artery disease (CAD). However, the angiographical assessment of CAD burden is challenged by under- or overestimation mainly due to poor imaging and the threshold disparities between lesion severity determined by angiography and true atherosclerotic burden.

Purpose:

The aim of this study was to determine whether GS can predict coronary plaque burden and its components evaluated by iMap-intravascular ultrasound (iMap-IVUS) system in patients with stable angina pectoris (SAP).

Methods:

We enrolled 154 patients with SAP who underwent percutaneous coronary intervention (PCI) following iMap-IVUS analysis to culprit lesions. GS was calculated based on the coronary angiographic findings before PCI. Patients were divided into the following two groups according to median GS value: low-GS (<78, score <35.4) and high-GS (n=76, score >35.4). Volumetric grayscale- and iMap-IVUS analysis was performed across the entire lesion segment. Plaque components were classified by iMap-IVUS as fibrotic, lipidic, necrotic and calcified components and each volume [fibrotic volume (FV), lipidic volume (LV), necrotic volume (NV) and calcified volume (CV), respectively] was reported as a percentage of the total plaque volume.

Results:

Patients with low-GS, those with high-GS had significantly greater plaque volume (103±52 vs. 66±43 mm³, P=0.025), increased %plaque volume (69±10 vs. 84±10%, P=0.001), higher %NV (36±15 vs. 31±13%, P=0.016), and lower %FV (47±13 vs. 53±15%, P=0.025). The %LV and %CV values did not significantly differ between the groups. The GS correlated positively with plaque volume (r=0.28, p<0.001), %plaque volume (r=0.36, p=0.001), %NV (p=0.21, p=0.01), and inversely with %FV (r=−0.20, p=0.011). In linear regression analysis, the presence of high-GS was significant factor associated with %NV (standardized coefficient β = 0.17, p=0.037) and %FV (β = −0.17, p=0.041) after adjustment for age, hypertension, hypercholesterolemia, diabetes, estimated glomerular filtration rate, and stent number.

Conclusion:

High-GS was associated with increased plaque burden with greater %NV and smaller %FV. These findings suggest that GS can serve as a predictor of coronary plaque burden and its components.
P6238 | BEDSIDE
Impact of moderate vasomotor response to acetylcholine provocation test on long-term prognosis
M. Hoshino, T. Yonetsu, M. Suzuki, A. Matsumura, Y. Hashimoto. Kameda Medical Center, Department of Cardiology, Kamogawa, Japan

Background: Acetylcholine provocation test (Ach-test) has been performed for the diagnosis of vasospastic angina (VSA). However, we experience the cases showing moderate spasm without reaching a definite diagnosis of VSA, whose clinical features are unclear. The aim of this study was to assess the impact of moderate coronary vasomotor responses to Ach-test on long-term prognosis.

Methods: A total of 283 consecutive patients who underwent Ach-test for suspected VSA were retrospectively investigated. The degree of coronary spasm was evaluated by epicardial coronary artery diameter reduction compared with the relaxed state achieved with the intracoronary administration of Isosorbide dinitrate. Patients were divided into 3 groups according to the diameter reduction during Ach-test: severe spasm (SS) showing ≥50% diameter reduction; moderate spasm (MS) showing ≥50% diameter reduction; or the others (N) regardless of the symptoms and ECG changes. Major adverse cardiac events (MACE) included cardiac death, myocardial infarction, coronary revascularization, fatal arrhythmia, and congestive heart failure. MACE rate was compared among the 3 groups.

Results: We excluded the patients with catheter-induced spasm (n=8). Therefore, 277 patients with median follow-up of 4.7 years were investigated: 85 were categorized in SS; 91 were in MS; and 101 were in N. For the treatment of coronary spasm, calcium channel blockers and long acting nitrates were used more frequently in SS and MS compared with N, whereas there was no significant difference in terms of medication between SS and MS. In Kaplan-Meier analysis, the incidences of MACE in the SS, MS, and N were 9.4%, 7.7%, and 1.0% respectively (P=0.028). Cox regression analysis revealed that the degree of spasm by Ach-test remained an independent predictor of MACE even after adjustment for other confounders (HR: 2.32, 95% CI: 1.03–5.30, P=0.043).

Conclusions: Patients with moderate spasm by Ach-test had a comparable cardiac event rate with those with severe spasm, which is significantly worse than those with normal vasomotor response. Moderate spasm should be identified as a risk group requiring an aggressive treatment strategy.

P6239 | BEDSIDE
Ultrasensitive troponin assay predicts cardiac stress and diastolic function
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Aims: Novel ultrasensitive troponin-I assay comprises a feasible alternative approach to monitor cardiac stress. However, physiological and clinical relevance of hs-TNI values in the normal range remains incompletely examined.

Methods: Four hundred patients undergoing myocardial perfusion scintigram were recruited and adenosine-assisted coronary flow reserve (CFR) and cardiac stress-echocardiography test performed. Ultrasensitive Troponin-I assay using microparticle-based immunoassays and single molecule counting technology was used. The troponin-I levels, (LLoQ of 0.4 pg/mL, compared to typical clinical lab tests with a LLoQ at 100pg/mL). Correlation analysis was done among patients with TNI levels below 4.6 pg/ml (normal range).

Results: TNI levels were strongly related to systolic volume (p<0.0001, r=0.4) and ejection fraction (p<0.0001, r=-0.37). Further, TNI levels were correlated to coronary flow reserve (p<0.001, r=-0.19) as well as stress diastolic function (p<0.0001, r=0.27). In a multivariate analysis adjusting for hypertension, age and EF both CFR and hyperemic diastolic relaxation velocity remained independently associated with hs-TNI levels.

Conclusion: TNI as measured using this ultrasensitive assay predicts microvascular function, systolic and diastolic function in CV patients.

ANGINA PECTORIS STABLE III

P6240 | BEDSIDE
Comparison of coronary artery disease consortium consortium 1, 2 and duke clinical score to predict obstructive coronary disease by coronary angiography

Introduction: The first step in evaluating a patient with suspected coronary artery disease (CAD) is the determination of the pretest probability. The European society of cardiology guidelines recommends the use of CAD consortium 1 score (CAD1), that is a modified version of Diamond and Forrester model, which, however, does not include modifiable cardiovascular risk factors. On the contrary, the CAD consortium 2 score (CAD2) and the Duke clinical score (DCS) includes those risk factors.

Purpose: Our aim was to compare the accuracy of those scores in the prediction of CAD in a population referred to invasive coronary angiography.

Methods: We included all patients referred to invasive coronary angiography for suspected CAD between January 2008 and December 2012 (n=2234). The pretest likelihood of CAD was estimated using CAD1, CAD2 and DCS. The presence CAD was defined as stenosis of more than 50% in at least one major epicardial vessel. The performance of those scores was evaluated by the area under the receiver operating characteristic curve.

Results: The observed mean age was 63.7 years and 32.5% were females. The majority (66.9%) was referred for typical angina (13.7% with atypical angina). The prevalence of CAD was 58.5% and the estimated prevalence was 71.1% (DCS), 63.5% (CAD1) and 41.5% (CAD2).

In patients with CAD the pretest likelihood was estimated above 85% in 54.3% using DCS, 21.1% using CAD1 and 1.4% by CAD2. On the other side, in patients without CAD the pretest likelihood was below 15% in 9.9% of cases estimated by DCS, 3.8% using CAD1 and 27.8% by CAD2.

The area under the curve was 0.685 for DCS, 0.664 of CAD1 and 0.683 for CAD2, with a statistical significant difference between CAD1 and the other two (p<0.001). The net reclassification improvement was 20% for DCS, related to adequate reclassification of 38.4% patients with CAD to a higher risk category, and 5% for CAD2, at the cost of adequate reclassification of 89.7% of patients without CAD to a lower risk category.

Conclusion: The estimation of likelihood pretest of CAD using scores that include modifiable cardiovascular risk factors (CAD2 and DCS) seems to improve the accuracy in comparison to CAD1. Our results suggest that, in this population, DCS may better identify patients at higher risk and CAD2 may better predict those at lower risk for CAD.

P6241 | BEDSIDE
Translating clinical trial results into clinical practice for patients with diabetes and multivessel coronary artery disease in British Columbia: A population-based study
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Background: Randomised Clinical Trials are the main tool used by health scientists to test and evaluate interventions. The Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease (FREEDOM) trial, published in Nov/2012 demonstrated superiority of coronary artery bypass grafting (CABG) over percutaneous coronary intervention (PCI) in pts with diabetes (DM) and multivessel coronary artery disease (CAD). We assessed the impact of the FREEDOM trial results in British Columbia, Canada (BC).

Methods: We identified all BC pts with DM in the provincial cardiac registry, from 04/2005 to 03/2014, undergoing PCI or CABG for multivessel CAD at sites capable of performing both PCI & CABG. Patients were selected using the FREEDOM trial inclusion/exclusion criteria. A ratio (PCI:CABG) was calculated with 95% confidence interval (CI) for the time periods pre & post-publication of the FREEDOM trial.

Results: A total of 6008 revascularization procedures made up the final group with 60% undergoing PCI. The PCI & CABG were selected using the FREEDOM trial inclusion/exclusion criteria. A ratio (PCI:CABG) was calculated with 95% confidence interval (CI) for the time periods pre & post-publication of the FREEDOM trial.

Conclusions: In this first "real world" experience of revascularization in DM pts with multivessel CAD post-FREEDOM, there has been a marked increase in the proportion of pts undergoing CABG in BC. The result of the FREEDOM trial has led to significant changes in practice. These findings will have significant resource allocation implications.
P6243 | BEDSIDE
Assessment of the relationship between serum visfatin levels and presence and extension of the coronary slow flow phenomenon

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Background: The coronary slow flow (CSF) phenomenon is a delayed antegrade progression of contrast agent to the distal branch of a coronary artery in the absence of obstructive coronary artery disease (CAD). Levels of visfatin, a novel adipocytokine, are reported to be increased in atherosclerosis, obesity, and type 2 diabetes.

Purpose: The aim of the present study was to investigate the relation between CSF and visfatin in patients who underwent elective coronary angiography for suspected CAD.

Methods: A total of 140 participants were recruited and were divided into two groups according to their coronary flow rates: 90 patients with isolated CSF and 50 control participants with normal coronary flow. Coronary flow was quantified by thrombolysis in myocardial infarction (TIMI) frame count (TFC).

Results: Serum visfatin levels were higher in the CSF group compared with the controls (3.9±1.11 vs. 2.7±0.18 ng/mL, p=0.003). A significant correlation was found between TFC and visfatin (r=0.535,p<0.001). The area under the receiver operating characteristic curve was 0.720 (95% confidence interval, 0.622–0.817,p<0.001) for visfatin in the diagnosis of CSF. If a value of 2.59 ng/mL was used as cutoff, higher levels of visfatin could predict the presence of CSF with 78.9% sensitivity and 64.0% specificity (Figure).

Conclusion: This is the first study to demonstrate the significant association between increased serum visfatin levels and the presence and extent of CSF. We conclude that visfatin levels might be a useful biomarker for predicting CSF in patients who undergo diagnostic coronary angiography.

P6244 | BEDSIDE
Incremental value of B-type natriuretic peptide for detection and risk reclassification of obstructive coronary artery disease on computed tomography angiography

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Background: B-type natriuretic peptide (BNP) is well known to increase as a result of left ventricular systolic dysfunction and is a useful diagnostic marker for heart failure. Whether BNP is associated with obstructive coronary artery disease (CAD) on computed tomography angiography (CTA) is unknown.

Methods and results: A consecutive 884 patients with suspected CAD underwent 64-slice CTA in our institution between 2008 April and 2013 October. Obstructive CAD was defined as ≥50% luminal narrowing. We divided the patients into 4 groups according to BNP quartile (Q1, <10.8 pg/mL; Q2, 10.8–21.8 pg/mL; Q3, 21.8–41.1 pg/mL; Q4, >41.1 pg/mL). The presence of any plaques was detected in 579 patients (61.0%), and obstructive CAD was found in 275 (28.6%) patients. In multivariate logistic analysis, BNP Q3 and Q4 were associated with obstructive CAD, as compared with Q1 (Q3, odds ratio [OR], 2.02; 95% confidence interval [CI], 1.16–3.53; P=0.013 and Q4, OR, 2.66; 95% CI, 1.53–4.63; P<0.001). Analyzing the incremental value of the Morise pre-test score and BNP for predicting obstructive CAD, the predictive value of the Morise pre-test score (area under the curve [AUC], 0.671) could be increased by BNP (AUC 0.694 for the combined model; P=0.006). Analysis of BNP to a model containing the Morise pre-test score resulted in continuous net reclassification improvement of 0.30 (95% CI, 0.17–0.44; P<0.001 for the prediction of obstructive CAD.

P6245 | BEDSIDE
Ivabradine reduces post-ischemic stunning in patients with exercise-inducible ischemia assessed by longitudinal strain

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Background: Ivabradine is an effective treatment for stable coronary artery disease (CAD) and heart failure. Experiments in a canine model have shown that ivabradine reduces both acute left ventricular (LV) dysfunction (DYS) and post-ischemic stunning (PIS). Aim of this study was to investigate the effect of ivabradine on LV-DYS and PIS in patients with CAD.

Methods: We studied 15 patients (66±7 years) with exercise inducible ischemia, ejection fraction >40% and heart rate (HR) >70 bpm. After pharmacologic washout (WO), echocardiography was performed at rest, at peak treadmill exercise and during recovery until return to baseline. After 2 weeks of ivabradine (7.5 mg bid) stress echocardiography was repeated at the same workload achieved during WO. Peak global and segmental (ischemic vs. remote normal segments) LV longitudinal strain (LS) were assessed by 2D speckle tracking analysis.

Results: At WO LS was significantly impaired in ischemic segments compared to remote at peak stress and for several minutes during recovery. In contrast, after ivabradine no significant change in LS was observed in ischemic segments either at peak or during recovery (Figure). Similarly, after treatment global LS at peak

of coronary status. TIMP-1 may, thus reflect a vulnerable plaque situation, and call for more intensive treatment in patients with CAD.

Acknowledgement/Funding: Finnish-Norwegian Medical Foundation
stress was significantly improved (-20% vs. -22%; p=0.03). Blood pressure was unchanged after ivabradine whilst HR was reduced both at rest and at peak stress (both p<0.05).

Conclusion: Ivabradine reduces acute LV-DYS and PIS in patients with exercise-inducible ischemia. We hypothesize that this mechanisms might contribute to reduce chronic LV-DYS in patients with CAD treated with ivabradine. In this setting the drug might limit the development of hibernating myocardium (i.e. chronically dysfunctional, but viable tissue) which is believed to result from repeated episodes of ischemia and stunning.

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P6246 | BEDSIDE
Prevalence and prognostic significance of preprocedural high-sensitivity cardiac troponin elevation among patients with stable coronary artery disease undergoing percutaneous coronary intervention

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Background: High-sensitivity cardiac troponin assays enable the accurate and rapid diagnosis of myocardial infarction (MI) among patients with suspected acute coronary syndromes. The prevalence and prognostic significance of pre-procedural high-sensitivity cTnT elevation among patients with stable coronary artery disease (CAD) scheduled to undergo PCI is unknown.

Purpose: The aim of the present study was to determine the prevalence of pre-procedural hs-cTnT elevation in unselected patients undergoing PCI for stable or silent angina, and to investigate the association between elevated hs-cTnT levels prior to the procedure and one year clinical outcomes.

Methods: Between March 2009 and November 2013, 8605 consecutive patients undergoing PCI were prospectively included in the Bern PCI Registry (NCT02241291) and followed for one year. The Roche hs-cTnT assay was introduced in August 2011. The following 3 inclusion criteria were applied for the present study: 1. Stable CAD or silent ischemia. 2. CKMB level <1 of the upper limit of normal (ULN, 0.014 mcg/L) before PCI. 3. Availability of hs-cTnT levels before PCI. We compared all cause mortality between patients with versus without increase in hs-cTNT (>ULN) before PCI and assessed whether hs-cTNT is a predictor of mortality after correction for age, gender, smoking, diabetes and renal function.

Results: Among 1721 patients fulfilling these criteria, 436 patients (25.3%) had baseline hs-cTnT level >1 ULN and 1285 (74.7%) patients had baseline hs-cTnT level ≤1ULN. Patients presenting with elevated hs-cTnT levels were older, more frequently men, diabetic, and had more often renal failure. At 1 year, patients with preprocedural hs-cTnT >ULN had significantly increased all-cause (7.6% vs. 1.5%, HR 2.8, 95% CI 1.00–4.30, p=0.049) after correction for baseline demographic and cardiovascular risk factors.

Conclusion: Baseline elevation of hs-cTnT concerns 1/4 of patients undergoing PCI for stable CAD and independently predicts all-cause mortality. Routine assessment of hs-cTnT prior to PCI in patients with stable CAD or silent ischemia identifies a population at increased risk for adverse clinical outcomes, which may have important implications for long-term secondary prevention.

P6247 | BEDSIDE
Poor performance of guidelines endorsed CAD prediction tool results in overdiagnosis of CAD risk in patients investigated for chest pain.

A single centre experience in a large cohort of patients

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Background: An optimal investigation strategy for patients with suspected AP relies on the use of clinical risk scores (NICE 2010) use an historical prediction model to estimate the CAD likelihood using symptom characteristics and risk factors profile. The prediction models in use may grossly overestimate CAD prevalence in today patients.

Purpose: Prospective study to assess the actual versus predicted CAD prevalence in CP patients, as documented by either angiographic obstructive CAD or a positive functional test.

Methods: We reviewed 964 consecutive CP clinic patients (age: 57±13 years). Using the NICE model, patients were assigned to an estimated CAD likelihood group: <10% (Gr. A), 10–29% (Gr. B), 30–69% (Gr. C) and >60% (Gr. D). Doing charge or referral to Ca scoring, functional testing or angiography were decided upon based on the expected CAD likelihood, as per a nationally endorsed algorithm.

Results: 515 pts. (53%) had non-anional CP, 239 pts. (25%) had atypical AP and 210 (22%) had typical AP. 208 pts. (21%) were assigned to group A, 202 pts. (21%) to group B, 238 pts. to group C (25%) and 316 pts. (33%) to group D. 324 patients (34%) were discharged and 640 pts. (66%) were further investigated for possible CAD. Investigations results are available for 536/640 patients (84%). The actual prevalence of positive CAD findings as compared with the expected one is detailed in table 1.

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Actual no. of CAD</th>
<th>Predicted CAD prevalence (%)</th>
<th>p</th>
<th>Actual vs. predicted (+/-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A: -10% (n=46)</td>
<td>4</td>
<td>8.6</td>
<td>ns</td>
<td>3.6/0.7</td>
</tr>
<tr>
<td>Group B: 10–29% (n=111)</td>
<td>12</td>
<td>10.8</td>
<td>0.05</td>
<td>-2.8/0.0</td>
</tr>
<tr>
<td>Group C: 30–60% (n=159)</td>
<td>33</td>
<td>20.7</td>
<td>&lt;0.01</td>
<td>-10.7/0.3</td>
</tr>
<tr>
<td>Group D: &gt;60% (n=220)</td>
<td>63</td>
<td>28.6</td>
<td>&lt;0.01</td>
<td>-9.4/1.1</td>
</tr>
</tbody>
</table>

For the whole sample the actual prevalence of CAD was only 112/536 (20.8%) vs. an expected one of 285/536 (53.1%), p<0.01.

Conclusions: 1) The CAD prevalence in patients referred for suspected AP is significantly lower than expected by using accepted historical models.

2) The model is accurate for low risk patients but it increasingly overestimates the actual prevalence as the predicted probability increases.

3) The use of historical CAD prediction models may result in overuse of costly diagnostic strategies in patients perceived to be at ≥ moderate risk of CAD.

4) The results emphasise the need to develop new updated prediction models.

P6248 | BEDSIDE
Soluble vascular endothelial growth factor receptor-1 levels in serum collected from arterial catheter sheath are inversely associated with cardiovascular events in combination with the SYNTAX score


Background: Vascular endothelial growth factor (VEGF) plays a role in endothelial integrity. The soluble VEGF receptor-1 (sVEGFR-1) is an endogenous inhibitor of VEGF. The association between circulating sVEGFR-1 levels and cardiovascular events has been controversial, and it may depend on how to collect blood samples.

Methods and results: We performed a prospective cohort study involving 417 inpatients who attended for elective coronary angiography (CAG) for the first time. Blood samples were collected from the arterial catheter sheath at the beginning of CAG, Serum levels of high-sensitivity C-reactive protein (hsCRP), VEGF, and sVEGFR-1 were measured. The SYNTAX score of angiographic complexity and severity of coronary artery disease was evaluated. Patients were followed up over 1 year. The primary outcome was major adverse cardiac events (MACEs). The median follow-up was 360 (IQR, 28–360) days. During the follow-up period, a total of 120 patients (35.7%) developed MACEs. Patients were divided into two groups based on the median of each biomarker. In Kaplan-Meier analyses, low-sVEGFR-1 (P<0.001 by log-rank test), but not high-hsCRP or high-VEGF, was significantly associated with the risk of MACEs. Multivariate Cox proportional hazard analyses revealed that the SYNTAX score (hazard ratio [HR], 2.1 per 1-SD increase; 95% confidence interval [CI], 1.8–2.3; P<0.0001) was positively, and the sVEGFR-1 (HR, 0.19 per 1-SD increase; 95% CI, 0.05–0.54; P<0.0001), but not high-hsCRP or VEGF, were inversely, and significantly associated with MACEs after adjustment for established risk factors. Finally, we performed multivariate Cox proportional hazard analysis including data on age, gender, systolic blood pressure, low-density-lipoprotein cholesterol, high-density-lipoprotein cholesterol, diabetes, history of smoking, the SYNTAX score, and sVEGFR-1 levels. Notably, the SYNTAX score and sVEGFR-1 were considered to be independent predictors of MACEs. Patients with high-hsCRP or high-VEGF were excluded from this analysis, as we were unable to adjust for the confounding effects of hsCRP and VEGF.

Conclusions: The sVEGFR-1 level in serum, collected from arterial catheter sheath at the beginning of CAG, may serve as an inverse predictor of MACEs in combination with the SYNTAX score.

P6249 | BEDSIDE
Correlation of rise in high sensitive troponins following positive exercise testing with underlying coronary artery disease

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Background: Cardiac troponins are sensitive markers of acute myocardy injury. Recent studies with high sensitive cardiac troponins (hs-TnT) assays have shown prognostic value even in chronic stable angina. It seems plausible that subjects...
with reversible myocardial ischemia during exercise stress testing have a release of hsTnT that is greater than the release seen in subjects with positive stress test but without ischemia.

**Purpose:** The objectives of the study were to correlate the rise of circulating hsTnT post exercise treadmill testing with underlying coronary artery disease (CAD) presence & severity.

**Methods:** 99 subjects of suspected stable angina with positive exercise TMT test were enrolled. Blood samples was obtained before the TMT and again 20 hr after peak exercise and samples were analyzed for troponins using a high sensitive assay. Coronary anatomy was determined by invasive coronary angiography.

**Results:** There was significant increase in mean hsTnT levels following a positive exercise TMT ((0.009±0.012 ng/ml, p=0.0001). The rise in hsTnT levels were significant only in patients obstructive CAD versus those with normal coronaries (p=0.0001). The elevation in hsTnT in subjects with single vessel, double vessel, triple vessel & left main-triple vessel CAD were 0.008±0.007 ng/ml, 0.010±0.012 ng/ml, 0.020±0.015ng/ml, 0.22±0.015 ng/ml respectively. Males had more hsTnT rise (p=0.003). Smoking, diabetes and hypertension did not affect the troponin rise.

**Conclusion:** In patients of stable angina, the rise in hsTnT from baseline after a positive stress test predicts the presence underlying of coronary artery disease and that the degree of rise correlates with the severity of disease conversely. Absence of elevation in hsTnT may indicate a normal anatomy despite a positive stress test.

### INFLAMMATION AND IMMUNITY

**P6250 | BEDSIDE**
Monocyte chemoattractantprotein-1 (MCP-1) as an independent predictor of coronary artery ectasia

**Introduction:** Coronary artery ectasia (CAE) is an infrequent finding that con-
sfers an adverse prognosis. Nonetheless, its pathophysiology is poorly understood, although several theories have been suggested, including inflammation.

**Purpose:** To assess a possible association of several biomarkers related to inflammation, atherothrombosis and myocardial damage with the presence of CAE.

**Methods:** We studied 270 patients with coronary disease that had an acute coro-

nary syndrome (ACS) 6 months before and underwent coronary angiography (CA). Clinical variables were recorded and plasma levels of the following biomark-
ers were determined: monocyte chemoattractantprotein-1 (MCP-1), soluble tumor necrosis factor-like weak inducer of apoptosis (sTWEAK), galectin-3, neutrophil gelatinase-associated lipocalin (NGAL), N-terminal fragment of brain natriuretic peptide (NT-proBNP) and high-sensitivity C-reactive protein. All CA were reviewed by two experienced interventional cardiologists and were diagnosed with CAE or not, according to published criteria. All variables were analyzed by binary logis-
tic regression, taking the presence of CAE as dependent variable. Thereafter, we constructed a multivariate model including all variables with level of significance p<0.2 and then, we removed all variables with p>0.2. The final model included all the significant variables, whose effect is presented as odds ratio (OR) for CAE with its 95% confidence interval (95% CI).

**Results:** Twenty-three (8.5%) patients had CAE. They were more frequently male (91 vs 64%), had more hyperechogenic (83 vs 47%), larger body-mass index (30.8 vs 28.4) and higher triglyceride (155 vs 112 mg/dL), lower density lipoprotein (93 vs 79 mg/dL) and MCP-1 (206 vs 152 pg/mL) plasma levels. We did not find any other significant difference between groups. At multivariate regression analysis, MCP-1 was the strongest predictor of CAE (OR=1.55 for each increase of 50 pg/mL, 95% CI: 1.19–2.00; p=0.001) along with male sex (OR=6.34, 95% CI: 1.31–30.75, p=0.005), hyperlipidemia (OR=6.3, 95% CI: 1.74–22.79; p=0.001) and NT-proBNP (OR=9.0 for each increase of 100 pg/mL, 95% CI: 2.78–30.75, p=0.005), respectively.

**Conclusion:** This is the first report of an independent association between MCP-1 plasma levels and CAE. Further studies are needed to assess a potential role of this pro-inflammatory molecule in the development of CAE.

**P6252 | BEDSIDE**
Functional mannann-binding lectin deficiency is not associated with improved outcome in comatose survivors of out-of-hospital cardiac arrest
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**Introduction:** The mannann-binding lectin (MBL) complement pathway may play a role in the systemic ischemia and reperfusion injury in post-cardiac arrest syn-
drome (PCAS). Functional MBL deficiency has been associated with favorable outcome in stroke patients, however the importance of MBL deficiency in PCAS patients is not known.

**Methods:** In a single center post-hoc analysis of the Target Temperature Man-
agement (TTM) trial, we studied MBL levels in 169 consecutive patients randomly assigned to TTM at 33°C or 36°C for 24 hours. At baseline and 24, 48 and 72 hours we measured MBL concentrations. MBL deficiency was defined as plasma levels ≤100 ng MBL/ml at baseline. Primary outcome was 180 days mortality and secondary outcome was favorable neurological outcome assessed by Cerebral Performance Category (CPC1–2) and modified Rankin Scale (mRS0–3).

**Results:** MBL deficiency was found in 22 (13%) patients. Age, sex, initial rhythm, time to ROSC or lactate levels at admission was not significantly different between MBL sufficient and MBL deficient patients. There was no overall difference in MBL levels between the two temperature groups (p=0.67).

Patients with MBL deficiency carried a 30-day mortality of 41% compared to 32% in MBL sufficient patient, p=0.55 (Figure) with no significant difference in neu-

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**Other references:**

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leukocyte characteristics are routinely analyzed in clinical laboratories and thus readily available. In this study we hypothesized that these characteristics associate with coronary artery disease (CAD) severity and mortality in coronary angiography patients.

**Background:** Leukocyte characteristics are associated with the progression and destabilization of atherosclerotic plaques in both coronary and carotid arteries, leading to cardiovascular events. Microwave radiometry (MWR) allows the rapid, in vivo, noninvasive assessment of the inter nal temperature of carotid arteries, reflecting local inflammation. MWR was used to test the association of leukocyte markers with all-cause and cardiovascular mortality, and non-classical monocytes (CD14+CD16+) with carotid plaque thickness and MACE.

**Methods:** Consecutive patients with significant CAD (≥50% stenosis in at least one major epicardial vessel) were included in the study. Both carotid arteries of patients were evaluated by 1) carotid ultrasound and 2) MWR. MACE was defined as any post-treatment cardiovas cular event. Multivariable Cox regression analysis was used to test the association of leukocyte markers with all-cause and cardiovascular mortality.

**Results:** Monocyte-to-lymphocyte ratio (MLR) showed a stronger predictive value than NRI and integrated discrimination improvement (IDI) analyses were additionally performed.

**Conclusion:** Leukocyte characteristics, especially MLR, are strongly associated with mortality in patients undergoing coronary angiography. Readily available leukocyte characteristics from routine hematology analyzers thus may serve as clinically applicable biomarkers for mortality risk prediction in angiography patients.

**P6256 | BEDSIDE**

Prognostic significance of carotid artery inflammation in patients with coronary artery disease

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**Background:** Previous research about stable coronary artery disease reported that on-treatment CRP level after statin treatment associated with clinical outcomes. However, details of on-treatment CRP level after statin treatment for patients with acute coronary syndrome (ACS) were uncertain. The aim of study was to evaluate efficacy for lipid profiles and inflammation among different statin monotherapies after the first year of treatment.

**Methods and results:** From January 2012 to December 2014, consecutive 352 ACS patients who were admitted to our hospital were enrolled. Excluding patients without statin monotherapies and with data deficiency, 125 patients (male 80.6%, 64.6±10.7 years) were analyzed. Baseline TG, HDL and CRP were significantly lower in patients treated with Rosuvastatin than with other statins.

**Conclusion:** CRP, HDL and LDL were significantly lower in patients treated with Rosuvastatin than with other statins.

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**P6255 | BEDSIDE**

Monocyte subset distribution in patients with stable atherosclerosis and elevated levels of lipoprotein(a)

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**Purpose:** Lipoprotein(a) is a pro-atherogenic plasma lipoprotein currently established as an independent risk factor for the development of atherosclerotic disease and as a predictor for acute thrombotic complications. Today, atherosclerosis is considered to be an inflammatory disease of the vessel wall in which monocytes and monocyte-derived macrophages are crucially involved. Circulating monocytes can be divided according to their surface expression pattern of CD14 and CD16 into at least three subsets with distinct inflammatory and atherogenic potential. Therefore, the aim of this study was to examine whether elevated levels of Lp(a) are associated with changes in monocyte subset distribution.

**Methods:** We included 90 patients with stable coronary artery disease (CAD). Lp(a) was measured and monocyte subsets were identified as classical monocytes (CD14+CD16−/−), intermediate monocytes (CD14+CD16+−/−) and non-classical monocytes (CD14+CD16−+; NCM) by flow cytometry.

**Results:** In patients with elevated levels of Lp(a) (>50mg/dl), monocyte subset distribution was skewed towards an increase in the proportion of IM (70.3±8.9% vs. 52.5±3.5%, p<0.025), while CM (82.6±5.5% vs. 82.0±6.8%, p=0.73) and NCM (10.5±5.3% vs. 12.8±6.0%, p=0.10) remained unchanged. This association was independent of clinical risk factors, choice of statin treatment regime and inflammatory markers.

**Conclusion:** In conclusion, we provide a new link between elevated levels of Lp(a) and a proatherogenic distribution of monocyte subtypes in patients with stable atherosclerotic disease.
monotherapies had a potential to improve inflammation in ACS patients comparing with other statin monotherapies.

**P6257 | BEDSIDE**

**Association of platelet-to-lymphocyte ratio with severity and complexity of coronary artery disease in patients with acute coronary syndromes**

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**Objective:** The Syntax score (SXscore) is an anatomic scoring system based on the coronary angiography (CA), which not only quantifies lesion severity and complexity, but also predicts poor cardiovascular outcomes including mortality in patients with acute coronary syndromes (ACS). Recent studies have shown that platelet-to-lymphocyte ratio (PLR) is associated with worse outcomes in many cardiovascular diseases.

**Purpose:** We sought to investigate the association of PLR with severity and complexity of coronary atherosclerosis as assessed by the SXscore in patients with ACS undergoing urgent CA.

**Methods:** A total of 1016 patients with ACS undergoing urgent CA were included into the study between August 2012 and March 2014. Admission PLR values were calculated before CA. The SXscore was determined from baseline CA. The patients were divided into two groups as low SXscore (<22) and intermediate-high SXscore (≥23).

**Results:** The PLR was significantly higher in patients with intermediate-high SXscore compared with low SXscore (P < 0.001). In hospital mortality was significantly higher in high PLR and intermediate-high SXscore groups. In multivariate analysis, the independent predictors of intermediate-high SXscore were PLR (OR: 1.018, 95% CI: 1.013–1.023, P < 0.001) together with left ventricular ejection fraction (LVEF) (OR: 0.935, 95% CI: 0.910–0.960, P < 0.001), and age (OR: 1.029, 95% CI: 1.029–1.054, P=0.02). An PLR ≥116 had a 71% sensitivity and 66% specificity in predicting intermediate-high SXscore.

**Conclusion:** The PLR at admission is significantly associated with the severity and complexity of coronary atherosclerosis in patients with ACS. Increased PLR is an independent predictor of higher SXscore in patients with ACS undergoing urgent CA.

**P6259 | BEDSIDE**

**Plasma chemerin is elevated in type 2 diabetes, is associated with impaired kidney function and is predictive for cardiovascular events**


**Background and introduction:** Chemerin has been implicated in autocrine/paracrine signaling for adipocyte differentiation and also stimulation of lipolysis. Whether chemerin is predictive for cardiovascular events is still unclear.

**Purpose:** The purpose of our study was to investigate the association of chemerin with cardiovascular event risk.

**Methods:** We measured plasma chemerin levels in 495 patients undergoing coronary angiography for the evaluation of established or suspected stable CAD.

**Results:** Chemerin was higher in patients with type 2 diabetes mellitus (T2DM, n=111) than in non-diabetic subjects (192±73 vs. 170±65 mg/ml, P=0.001). Further, chemerin was significantly and independently associated with the glomerular filtration rate (GFR) in analysis of covariance using age, sex, and BMI as covariates (F=49.6, P=0.001). Prospectively, we recorded 107 cardiovascular events over 3.5 years. Chemerin both univariately and after multivariate adjustment including baseline GFR significantly predicted cardiovascular events, with hazard ratios of 1.63 (95% CI: 1.19–2.23, P=0.006 and 1.67 [1.05–2.67, P=0.030 for the top tertile of chemerin versus the first and second terciles, respectively. A cardiometabo-chip-analysis revealed an association of two nearby located SNPs in TPSBP1 and CAPN3 rs2444030 nominal p-value-=5.2 e-9, and rs3098432 nominal p-value=9.6 e-8) with chemerin concentration. Haplotype analysis for these two SNPs revealed a significantly impaired GFR associated with the fully mutated haplotype compared to all other haplotypes (OR=0.63, P=0.006).

**Conclusion:** We conclude that high chemerin is characteristic of T2DM, is associated with impaired kidney function, and is predictive for cardiovascular events.

**P6260 | BENCH**

**Recombinant human placental growth factor 2 treatment for ischemic cardiomyopathy in atherosclerotic mice**


**Background:** Despite association with elevated troponin and HBA1c levels and reduced LV function, higher levels of the antianti-endothelial antibodies are associ-
Conclusion: An OR of 3.26 (1–30–8.18), with an inverse relationship with CD4 cell count at infection.

Infection, reduced CD4 cell counts and higher prevalence of non-calcific coronary plaques is not clear.

The prevalence of significant coronary stenosis (defined as >90% stenosis) and (15% [9–21] and 14% [8–20]) was 3-fold higher in HIV-positive patients [58% (48–60) and 17% (14–27) with an OR of 3.26 (1.9–5.3)].

Introduction: Asymptomatic patients with human immunodeficiency virus (HIV) infection are at increased risk of vascular disease. Whether asymptomatic HIV patients have increased prevalence or structural differences in coronary artery plaques is not clear.

Methods: Pubmed, Cochrane and Google Scholar were searched for articles evaluating asymptomatic HIV patients evaluated with coronary computed tomography. The prevalence of coronary stenosis (defined as >30% and >50%), of calcified coronary plaques (CCP) viewed as more “stable” plaques, and of non-calcified coronary plaques (NCP) viewed as more “vulnerable” plaques were the end points of interest.

Results: 9 studies with 1229 HIV patients and 1029 controls were included. No end points of interest.

Conclusion: These results provide evidence for cooperative effect of palmitic acid and mmLDL on the macrophage inflammatory response. Our findings suggest how these two, when present simultaneously, escalate the risk of vascular inflammation.

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Conclusion: We hypothesised that inflammatory markers matrix metalloproteinase 8 (MMP-8) and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1) would: 1) discriminate between intracoronary inflammation and non-atherothrombotic induced myocardial injury and 2) show a different concentration profile from the traditional markers troponin T (TnT) and creatine kinase MB mass (CK-MBm) in different types of myocardial injury.

Purpose: To examine whether palmitic acid and minimally oxidized LDL (mmLDL) have cooperative proinflammatory effect and what the mechanism is.

Methods: J774 macrophage cells were exposed to palmitic acid, mmLDL, and lipopolysaccharide alone and in combination. The effect eicosapentaenoic acid (EPA), a polyunsaturated fatty acid, was also evaluated. ELISA assay was performed to check the secretion of chemokines including CXCL2 and TNFalpha. Western blot was used to estimate the effect on the phosphorylation of inflammatory proteins. Microarray result is going to be presented in the congress.
Abstract P6264 — Figure 1

P6265 | BEDSIDE

Similarities in impairment of endothelial glycocalyx between psoriasis and coronary artery disease: the role of oxidative stress and inflammation

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Background: Endothelial glycocalyx is a determinant of vascular integrity, however its relation with inflammation and oxidative stress in psoriasis patients has not been widely validated. We investigated the presence of reduced endothelial glycocalyx thickness in psoriasis, in comparison with coronary artery disease (CAD) patients.

Methods: We compared 114 patients with psoriasis (age: 50±12 yrs, PASI disease activity score: 11±8.3) with 59 patients with angiographically documented CAD and 40 normal controls. We measured a) perfused boundary region (PBR) of the sublingual arterial microvessels (5–25 micron) using Sideview Darkfield imaging. The PBR in microvessels is the cell-poor layer which results from the phase separation between the flowing red blood cells (RBC) and plasma. The PBR includes the most luminal part of glycocalyx that does allow cell penetration. Increased PBR is considered the most accurate index of reduced endothelial glucocalyx thickness because of a deeper RBC penetration in the glycocalyx.

Results: Psoriasis patients had similar PBR. IL-6 and MDA values with CAD patients (p > 0.05) but higher values of these markers than normals (p < 0.05) after adjustment for atherosclerotic risk factors [PBR: 2.05±0.2 vs. 2.01±0.3 vs. 1.77±0.14, IL-6-pg/ml (median values): 2.26 vs. 2.2 vs. 1.7, MDA-nM/L (median values): 1.68 vs. 1.76 vs. 1.01, p < 0.05 for all comparisons]. Increased PBR, indicating reduced endothelial glycocalyx thickness was associated with increased IL-6 (r = 0.36, p < 0.03), IL-10 (r = 0.45, p < 0.03), IL-12 (r = 0.51, p < 0.01), IL-17 (r = 0.36, p < 0.03) and TNFa/IL-10 (r = 0.60, p < 0.005) in psoriasis patients.

Conclusion: Impaired endothelial glycocalyx integrity is associated with increased inflammation and oxidative stress burden in psoriasis patients. Psoriasis and CAD patients present similar impairment of endothelial glycocalyx, possibly because of similar underlying inflammatory and oxidative stress processes.

P6266 | BEDSIDE

Respiratory infection following acute myocardial infarction is an independent predictor of in-hospital cardiovascular mortality


Background: Respiratory infection (RI) has been established as a trigger for the development of acute myocardial infarction (AMI). However, data on prognostic implications of RI complicating hospital admissions for AMI is still scarce.

Purpose: Evaluate the prognostic impact of RI in patients admitted for acute myocardial infarction.

Methods: We retrospectively analyzed 1907 patients who were admitted to our coronary care unit with AMI. Respiratory infection was defined as the presence of clinical, analytical and radiologic data suggestive of respiratory infection. Clinical and laboratory features, treatment and adverse events were compared in each group of patients. The primary endpoint was in-hospital cardiovascular (CV) death.

Results: Patients with RI were older (69±14 vs 64±13 years, p < 0.001) and had increased prevalence of diabetes (37.61 vs 27.21%, p < 0.015). On admission, they more frequently presented with ST-segment elevation myocardial infarction (56.4 vs 45.6%, p < 0.02), Killip class 1–2 (58.12 vs 16.65%, p < 0.001), higher troponin I (35.6 vs 23.2ng/mL, p < 0.001), proBNP (6302 vs 2737pg/mL, p < 0.001), C reactive protein (47.6 vs 14.37mg/L, p < 0.001) and neutrophil count (10683 vs 7816 cells/μL, p < 0.001), lower haemoglobin (13.26 vs 13.87 g/dL, p < 0.05), eGFR MDRD (73.0 vs 84.49mL/min/1.73m², p < 0.001), systolic (121 vs 132mmHg, p < 0.001) and diastolic blood pressure (73 vs 79mmHg, p < 0.001). Individuals with RI required more often ventilation (16.67 vs 9.5%, p < 0.001), aminergic (31.6 vs 4.3%, p < 0.001) and transfusional (14.29 vs 1.3%, p < 0.001) support and intra-aortic balloon pump (15.4 vs 1.79%, p < 0.001). During hospitalization, they had higher values of heart rate (94±18 vs 73±16, p < 0.001), ischemic stroke (3.4 vs 1.2 vs 0.7%, p < 0.002), reinfection (5.1 vs 2.1%, p < 0.036), heart failure symptoms (81.2 vs 25.1%, p < 0.001), and IR was also associated with an increased incidence of major adverse cardiovascular events at follow-up (stroke, acute coronary syndrome, death) (43.3 vs 29.8%, p < 0.005). Compared with non-infected patients, RI had 6.12 times higher inhospital CV mortality [OR 6.12; 95% CI (3.34–11.21); p < 0.001]. In multivariate analysis, adjusting for significant predictors of CV mortality (age, gender, SBP, eGFR, proBNP, Killip class and haemoglobin), RI remained as an independent predictor of in-hospital CV mortality [infected vs non-infected, OR adjusted 3.93; 95% CI (1.704–9.074); p < 0.001].

Conclusion: Respiratory infection is an independent predictor of in-hospital CV mortality in patients admitted for AMI.
Role of macrophage migration inhibitory factor (MIF) and its endogenous inhibitor Gremlin-1 in intracoronary thrombosis of patients with acute myocardial infarction


Background: Macrophage migration inhibitory factor (MIF) is involved in atherothrombosis progression and instability leading to intracoronary thrombosis. Gremlin-1 (Grem1), a member of the DAN/Cerberus-protein family, has been recently identified as endogenous inhibitor of MIF. Intracoronary thrombi are a main cause of acute myocardial infarction in patients with coronary artery disease. The thrombus leading to an acute vessel occlusion consists of platelets and other blood cells, such as monocytes, macrophages, and CD34+ peripheral stem cells. There is evidence that arterial thrombi may influence the development of neointima after coronary stenting. However, the underlying pathophysiological role of arterial thrombi during and after acute myocardial infarction remains unclear. Therefore we analyzed the histology of and the expression of MIF and Grem1 in intracoronary thrombi.

Methods and results: We analysed the cellular constituents of 25 thrombi aspirated from coronary lesions with a thrombectomy device in 25 patients who underwent emergent coronary intervention for the treatment of acute (<24 h) or recent (24 to 72 h) ST-segment elevation myocardial infarction. Immunohistological analysis of aspirated thrombotic materials revealed a high expression amount of Grem1 and MIF in the platelet rich areas of the thrombi, as determined by immunohistological staining and in regions with a high amount of inflammatory cells such as monocytes and macrophages, as determined by immunostaining for CD14 and CD68. Grem1 was also expressed in fibroblasts within the arterial thromb, as determined with S100B immunostaining.

Parts of intracoronary thrombi were brought in tissue culture and grown over 15 days. Between day 4 and day 7 cells grew from the main thrombus and formed colonies of fibroblasts and cells positive for endothelial cell markers. Expression of Grem1 and MIF could be detected within these colonies on day 15 of tissue culture, analyzed by FACS.

Conclusion: These findings suggest a potential role of Grem1 and MIF during intracoronary thrombus formation. Grem1 and MIF might furthermore be involved in processes of regeneration after acute plaque rupture. However, the underlying pathophysiological role of arterial thrombi during and after acute myocardial infarction remains unclear. Therefore we analyzed the histology of and the expression of MIF and Grem1 in intracoronary thrombi.

Three-year results of stenting of bifurcation stenoses of the left main coronary artery: data of intravascular ultrasound study

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Aim: Using objective methods of intravascular imaging to evaluate the results of bifurcation stenting stenosis of the left main coronary artery.

Methods: Three-years results of endovascular treatment of patients with true bifurcation stenosis of the left main coronary artery were evaluated in 94 patients, of whom 48 patients were using one stent technology “provisional-1”, and 46 were stented “two stent” techniques. All interventions were constricted by final dilation by “kissing-balloon” high pressure balloons and under IVUS guidance. Long-term results were assessed by following criteria: frequency of cardiovascular complications (death, myocardial infarction, re-intervention), IVUS data (residual area of vessel lumen in the proximal segment of left main, zone of bifurcation, the ostia of anterior descending artery and circumflex artery). Decrease in diameter in remaining lumen >70% was considered as criteria for restenosis.

Results: Survival amongst patients in late period was 97.9%, 2 patients died from non-cardiac causes. The frequency of cardiac events in both groups was not detected in either group. The average residual area of the lumen of the left main coronary artery in the proximal part, after “two stent” treatment was stenting 7.89±0.03, and after a full bifurcation stenting of 8.0±0.02 mm² (p<0.05), at the ostia of the circumflex artery 5.62±0.12 and 5.98±0.01 mm² (p<0.05), at the ostia of the anterior descending artery 6.62±0.03 and 6.78±0.04 mm². These results did not significantly differ compared to the same 12 months of observation.

Conclusion: This study demonstrates that the use of objective methods of visualization of coronary arteries in patients with bifurcation stenosis of left coronary artery as a method of monitoring the results of stenting, as well as adequate final dilation “kissing balloons” high pressure leads to low frequency of cardiovascular complications and restenosis in long-term period that have a positive impact on the prognosis of such patients.
P6273 | BEDSIDE
Associations of ankle-brachial index with the severity and characteristics of coronary atherosclerosis in patients with stable angina pectoris: assessment by Gensini score, IVUS, and OCT

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Background: Ankle-brachial index (ABI) is a non-invasive method to assess the patency of the lower extremity artery and to screen for the presence of peripheral arterial disease (PAD). Low ABI levels have been reported to be associated with cardiovascular mortality. However, the relationship between ABI and severity of coronary artery disease has not been sufficiently elucidated.

Purpose: The aim of this study was to investigate the association of ABI with the severity and characteristics of coronary atherosclerosis as assessed by Gensini score, iMap-intravascular ultrasound (iMap-IVUS), and optical coherence tomography (OCT) in patients with stable angina pectoris (SAP).

Methods: We enrolled 130 patients with SAP who underwent percutaneous coronary intervention following iMap-IVUS and OCT to culprit lesions. The ABI of bilateral lower extremities were measured, and their mean values were calculated in each patient. The PAD was defined as the ABI value <0.90. Gensini score was used as the parameter of angiographic severity of coronary atherosclerosis. Culprit plaque components were classified by iMap-IVUS as fibrotic, lipidic, necrotic and calcified, and each area (FA, LA, NA, and CA, respectively) was reported as a percentage of the total plaque area. Thickness of fibrous cap overlying a lipid core in culprit plaque was measured in its thinnest part by OCT. Associations of ankle-brachial index with the severity and characteristics of coronary atherosclerosis were evaluated.

Results: We identified 22 and 108 patients with and without PAD, respectively. Patients with PAD had significantly higher prevalence of multivessel diseases (64 vs. 36%, p=0.016) and higher Gensini scores than those without PAD (61.7±45.2 vs. 38.3±17.9, p=0.016), smaller %FA (32±9% vs. 46±18%, p=0.007), and thinner fibrous cap thickness (91.7±1.2 vs. 166±151 μm, p=0.007) than in those without PAD. In linear regression analysis, a mean ABI was significantly correlated with Gensini score (standardized coefficient β =−0.31, p=0.008), %NA (β =−0.37, p=0.018), and %FA (β =−0.38, p=0.013) after adjustment for age, hypertension, hypercholesterolemia, diabetes, cigarette smoking, estimated glomerular filtration rate, and statin use.

Conclusions: The lower ABI value was related to higher Gensini score and plaque components with greater %NA, smaller %FA, and thinner fibrous cap. These findings suggest that ABI can serve as a predictor of the severity and characteristics of coronary atherosclerosis.

P6274 | BEDSIDE
Association of platelet to lymphocyte ratio with inflammation and severity of coronary atherosclerosis in patients with stable coronary artery disease: a single center large scale study

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Objective: Atherosclerotic coronary artery disease (CAD) is known as a complex and chronic inflammatory disease. The platelet to lymphocyte ratio (PLR) has recently been emerged as a new potential inflammatory biomarker. Hence, we aimed to assess the relationship between PLR and the extent/severity of CAD by using Gensini score in association with the inflammatory marker including C-reactive protein in patients with stable CAD.

Methods: Angiographic data of 1615 patients were analyzed retrospectively in this study. Patients were categorized according to Gensini scores as no CAD (control), mild CAD and severe CAD groups. Independent predictors of the severe CAD were determined by logistic regression analysis.

Results: PLR in the control group were significantly lower than those of the other groups (Figure). After multivariate logistic regression analysis PLR (Odds ratio: 1.228 [1.106–1.362], p<0.001) was found as independent predictor for the severity of CAD. Furthermore, there was a significant positive correlation between PLR and the severity of CAD determined by Gensini score (r=0.260, p<0.001) and inflammatory marker like CRP (r=0.162, p<0.001).

Conclusion: PLR is independently and positively associated with the severity of coronary atherosclerosis in patients with stable CAD. In addition, PLR was positively correlated with CRP as a reliable indicator of inflammation. These results suggest that PLR is an easily available and cheap inflammatory indicator, so that PLR can be used in prediction of the severity of coronary atherosclerosis.

P6275 | BEDSIDE
The acute and chronic effects of ivabradine on the parameters of central aortic pressure in patients with stable coronary artery disease

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Background: Data from small studies in healthy humans show that heart rate (HR) increase induced by vasoactive drugs or pacing is associated with a reduction in augmentation index (AIx) and even central diastolic pressure. However, it remains unclear if parameters of central aortic pressure (CAP) such as AIx, AIx normalization for HR of 75 bpm (AIx75), and augmented pressure (AP) increases during HR-lowering therapy in patients (pts) with coronary artery disease (CAD). The aim of our study was to investigate the acute and chronic effects of HR inhibitor ivabradine on the parameters of CAP in pts with CAD.

Methods: 30 pts with proven CAD, stable angina (3.0±0.4 CCS), mean baseline HR of 76±12.4 bpm and peripheral systolic/diastolic blood pressure (SBP/DBP) of 111.9±1.2/70.3±1.1 mm Hg were enrolled in this study. The parameters of CAP were quantified noninvasively using applanation tonometry of the radial artery. Measurements were made at baseline, 3 hours after the intake of 5 mg ivabradine and then after 1 and 2 months of ivabradine therapy (mean dose 11.5±0.7 mg/day). All pts received guideline-based therapy (including beta-blocker bisoprolol 5 mg/day), which remained unchanged.

Results: A single dose of ivabradine and then 1 and 2 months treatment with ivabradine resulted in a pronounced HR reduction (~10.8%, p<0.01; ~17.5%, p<0.001; and ~22.1%, p<0.001, respectively). No significant changes in aortic SBP and AP were noted during the acute test: 103.9±1.2 mm Hg vs. 101.8±1.2 mm Hg and 7.6±0.9 mm Hg vs. 7.4±0.9 mm Hg, respectively. After 1 and 2 months of treatment, the pronounced HR reduction was sustained (~10.8%, p<0.01; ~17.5%, p<0.001; and ~22.1%, p<0.001, respectively). No significant changes in central aortic systolic blood pressure (AP) and augmentation index (AIx) were noted. However, all parameters of central aortic pressure significantly reduced (~10.8%, p<0.01; ~17.5%, p<0.001; and ~22.1%, p<0.001, respectively). These results suggest that ivabradine can have a positive effect on the parameters of central aortic pressure in patients with stable coronary artery disease.
months of Ivabradine therapy these parameters remained unchanged: aortic SBP (102.1±1.1 mm Hg and 101.6±1.1 mm Hg) and AP (7.8±0.9 mm Hg and 7.9±0.7 mm Hg). Afx did not significantly change: 22.7±2.4% at baseline vs. 21.8±2.6%, 23.4±2.6%, and 23.9±2.1% after the acute test, and 1 and 2 months of therapy, respectively. But Afx@75 decreased significantly from 23.4±2.1% (baseline) to 19.1±2.4% (acute test, p<0.05), 17.6±2.6% (1 month, p<0.02) and 16.7±2.1% (2 months, p<0.01).

Conclusion: HR reduction with Ivabradine does not worsen the parameters of CAP in pts with CAD. It may be considered as a positive characteristic of this agent. Further studies are needed to investigate long-term effects of Ivabradine on the parameters of CAP.

P6276 | BEDSIDE
Efficacy of everolimus-eluting stent implantation in patients with small coronary (<2.5 mm) arteries: outcomes of 4-year clinical follow-up

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Background: Previous studies have demonstrated that patients with small coronary artery lesions (SCAL) are at increased risk for late cardiac events after percutaneous coronary intervention (PCI). It remains uncertain whether second-generation drug-eluting stents have an advantage first-generation drug-eluting stents (DES) in patients with SCAL. This study aimed to evaluate the long-term efficacy of everolimus-eluting stent (EES) and sirolimus-eluting stents (SES) on SCAL.

Methods and results: Consecutive 390 patients with 432 SCAL, who were treated with EES (187patients, 212 lesions) and SES (203 patients, 220 lesions) were enrolled. SCAL was defined as lesions with reference vessel diameter (RVD) <2.5 mm. Within ten months angiographic follow-up results and 4-year clinical outcomes were compared between EES and SES groups. The prevalence of diabetes was higher and the stent length was longer (23.0±7.0 vs. 20.1±6.8, p<0.05) in EES group than in SES group. Initial success rate was similar in both groups. There was no difference in 4-year %binary restenosis, TLR (3.1±5.1%), and MACE (4.0%vs 8.9%) rates between 2 groups. This similar major adverse cardiovascular events rate remained after adjustment. However, the rate of stent thrombosis was 0% in the EES group and 3.2% in the SES group (p<0.10).

Conclusions: EES demonstrated comparable clinical outcomes to those of SES in SCAL. The absence of stent thrombosis among patients treated with EES suggests a good safety profile for this second-generation drug-eluting stent, which is indicated in SCAL. The absence of stent thrombosis among patients treated with EES sug-

P6277 | BEDSIDE
Ivabradine reduces symptoms and improves quality of life in patients with stable angina and diabetes mellitus

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Introduction: Diabetic patients present extensive and rapidly progressive coronary artery disease (CAD), as well as a propensity to higher angina burden. Purpose: To evaluate the antianginal efficacy of ivabradine co-administered with a β-blocker and its impact on quality of life (QOL). To record compliance with treatment, during 4-months’ therapy in patients with CAD and a history of diabetes mellitus (DM).

Methods: This is a post hoc analysis (739 patients with DM) of a Pan-Hellenic, prospective, non-interventional study including 2403 patients with CAD and stable angina. Patient follow-up was performed at baseline, at 1 and 4 months after inclusion. Patients’ QOL was assessed by means of the EQ-5D questionnaire.

Results: Of 739 CAD patients, 19 (2.6%) prematurely discontinued treatment. Addition of ivabradine decreased the % of patients with heart rate (HR) - 80 bpm from 47% (1st visit) to 1% (3rd visit) (mean decrease -17.8 bpm). Patients with ≥2 angina attacks decreased from 57.6% at baseline to 14.1% (2nd visit) and 5.5% at study completion (P<0.001). Consumption of nitroglycerin decreased from 1.72±2.2 times/week (1st visit) to 0.4±0.9 (2nd visit) and 0.2±0.5 times/week (3rd visit) (P<0.001). 2.1% of patients presented angina Canadian Cardiovascular Society class III-IV at study completion vs. 21.7% at baseline (P<0.001). QOL was improved; 25% more patients reported being autonomous in self-care, 73% and 53% more patients had no difficulties in their usual activities or mobili-

P6278 | BEDSIDE
Percutaneous coronary intervention for restenosis with stent fracture after drug-eluting stent implantation compared between first and new drug-eluting stents


Background: Stent fracture (SF) is related to restenosis after drug-eluting stent (DES) implantation. Although SF is a rare complication in the era of new gener-

P6279 | BEDSIDE
Blood bioactive sphingolipids and activity of sphingomyelinases in patients with multivessel coronary artery disease

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Introduction: Measuring the sphingolipid and sphingomyelinase activity in biofluids can be useful for the diagnostics of arteriosclerosis. The aim of the present study was to investigate the level of different bioactive sphingolipids in plasma, erythrocytes and platelets in patients with multivessel coronary artery disease. 20 healthy control subjects (C) – mean age 58±4 years, and 32 patients (P) – mean age 65 y, with multivessel coronary artery disease (confirmed angiographically) participated in the study. Blood samples were taken from the antecubital vein and separated in three fractions: plasma, erythrocytes and platelets. The following sphingolipids were quantified in each blood fraction by means of high pressure gas-liquid chromatography: Cer, S1P, sphingosine (SO), sphinganine (SA) and sphinganine-1-phosphate (SA1P). Plasma, the activity of ASmase was measured by isotopic method.

Results: The plasma concentration of S1P (P=1.46±4.28 pmol/l, C-197.1±58.3, p=0.002) and SA1P (P=20.8±6.6 pmol/l, C-28.0±6.7, p=0.001) was reduced in the group of patients. The concentration of other sphingolipids was stable. The content of the of examined sphingolipids in erythrocytes was simi-
was a significant decrease in ADP Agg (%) from 76.89±15.98 to 38.43±23.87 (p=0.0009), in collagen Agg (%) from 87.02±14.49 to 71.27±20.82 (p=0.0002) and in SUA level (p=0.22), PLT count (p=0.10) and PLT Agg to ADP, PLT rich plasma, SUA level and PLT count at baseline and after one month of treatment. Statistical analysis was performed.

Results: At baseline SUA level (p=0.22), PLT count (p=0.10) and PLT Agg to ADP (p=0.19) and collagen (p=0.23) were similar in both groups. In ALLO+ there was a significant decrease in ADP Agg (%) from 76.89±15.98 to 38.43±23.87 (p=0.0009), in collagen Agg (%) from 87.02±14.49 to 71.27±20.82 (p=0.0002) and in SUA level (p=0.0003) compared to the respective values at baseline. No significant difference of dROMs levels was observed between baseline and after ACh administration in the ACh provocation positive group. The dROMs levels after ACh administration might be affected by the antioxidant activity of the released NO from the endothelial cells.

Conclusion: The changes of dROMs levels in the coronary sinus vein during the intracoronary ergonovine spasm provocation test in patients with rest angina were quite different from the ACh provocation test.

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Impact of diabetes mellitus for angiological mid-term outcome in new generation drug eluting stent
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Background: New generation drug eluting stent (DES) showed better outcomes compared to 1st generation DES. However, it is not clear about the relationship between angiographical outcomes and diabetes mellitus (DM) in new generation DES.

Purpose: We performed this study to investigate the association between angiographical mid-term outcomes after new generation DES implantation and lesions in patients with DM/non-DM.

Methods: We compared the mid-term (9–12 months) angiographical outcomes among 4 new generation DES (Nobori; Biolimus-eluting stent: BES, Promus: Everolimus-eluting stent: EES-P, Resolute: Zotarolimus-eluting stent: ZES). In addition, we compared the angiographical outcomes of each DESs between DM and non-DM.

Results: We treated 3745 lesions in 2027 patients between February 2010 and April 2014 with new generation DES in our centers. Hybrid stenting lesions were not included. Within them, angiographic follow up was performed 2680 lesions (BES: 215 lesions, EES-P: 1136 lesions, EES-V: 1087 lesions, ZES: 242 lesions) in 1595 patients. Lesion characteristics were not well matched among those 4 groups. In DM patients, lesions with DM were revealed significantly higher restenosis rate compared to other kinds of DES. However, target lesion revascularization (TLR) rate were similar among 4 groups. Although restenosis rate was higher in BES, EES-P and EES-V in lesions with DM patients compared to non-DM patients, that in ZES was similar. Similarly, TLR rate in ZES was similar between lesions with DM and non-DM (Figure).

Conclusion: ZES showed similar restenosis and TLR rate compare to EES-P and EES-V in lesions with DM patients. And there was no significant difference about restenosis and TLR rate between DM and non-DM patients.

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The Difference between Ergonovine and Acetylcholine in the Changes of Reactive Oxygen Metabolites during Intracoronary Spasm Provocation Test in Patients with Vasospassic Angina
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Background: We reported that direct measurement of diacron reactive oxygen metabolites (dROMs) levels in the coronary sinus during the acetylcholine (ACH) provocation negative group. However, it is not clear about the relationship between angiographical outcomes and diabetes mellitus (DM) in new generation DES.

Purpose: We compared the mid-term (9–12 months) angiographical outcomes after new generation DES implantation and lesions in patients with DM/non-DM.

Methods: We compared the mid-term (9–12 months) angiographical outcomes among 4 new generation DES (Nobori; Biolimus-eluting stent: BES, Promus: Everolimus-eluting stent: EES-P, Resolute: Zotarolimus-eluting stent: ZES). In addition, we compared the angiographical outcomes of each DESs between DM and non-DM.

Results: We treated 3745 lesions in 2027 patients between February 2010 and April 2014 with new generation DES in our centers. Hybrid stenting lesions were not included. Within them, angiographic follow up was performed 2680 lesions (BES: 215 lesions, EES-P: 1136 lesions, EES-V: 1087 lesions, ZES: 242 lesions) in 1595 patients. Lesion characteristics were not well matched among those 4 groups. In DM patients, lesions with DM were revealed significantly higher restenosis rate compared to other kinds of DES. However, target lesion revascularization (TLR) rate were similar among 4 groups. Although restenosis rate was higher in BES, EES-P and EES-V in lesions with DM patients compared to non-DM patients, that in ZES was similar. Similarly, TLR rate in ZES was similar between lesions with DM and non-DM (Figure).
Mechanisms of ischemic preconditioning in coronary artery disease by arterial compliance and heart rate variability

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Background: Ischemic preconditioning (IP) seems to be universal protective mechanism for patients with cardiovascular diseases. We propose that the effects of IP could be based positive effect on arterial compliance and heart rate variability (HRV).

Aim: Study of IP impact on pulse wave amplitude (PWA) and velocity (PWV), pulse pressure and heart rate variability (HRV) in CHD patients.

Methods: The randomized controlled crossover design study with active control in 25 stable patients with CHD and in control group (n=11) was performed. The PWA, PWV and HRV (AlCor, Australia) were estimated before and after IP (blood pressure 50 mm Hg) versus sham IP (diastolic IP) according to randomization. The next day the same patients were investigated before and after the on the contrast from the former test sham IP/IP.

Results: IP did not change heart rate in both groups (Table); peripheral and central systolic and diastolic blood pressure decreased (p<0.01) but not in control (p=0.89); IP in compare to sham significantly improved some HRV parameters (Triangular index, SDNN) and had the same tendency in rest of them but not in control.

In patients with CHD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CHD group (n=25)</th>
<th>Control group (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, beat/min</td>
<td>74.5 ± 7.2</td>
<td>72.7 ± 7.4</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>165.7 ± 15.2</td>
<td>129.9 ± 12.9</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>3.98 ± 3.3</td>
<td>3.3 ± 1.4</td>
</tr>
<tr>
<td>Aortic syst BP mm Hg</td>
<td>15.6 ± 12.1</td>
<td>2.9 ± 1.9</td>
</tr>
<tr>
<td>Aortic syst pulse pressure, mm Hg</td>
<td>13.6 ± 3.2</td>
<td>3.2 ± 0.3</td>
</tr>
<tr>
<td>Augmentation pressure, mm Hg</td>
<td>3.07 ± 1.59</td>
<td>1.59 ± 1.5</td>
</tr>
<tr>
<td>PWV, m/sec</td>
<td>0.34 ± 0.69</td>
<td>0.63 ± 0.2</td>
</tr>
<tr>
<td>Triangular index</td>
<td>−3.38 ± 1.06</td>
<td>−1.06 ± 0.37</td>
</tr>
<tr>
<td>SDNN index</td>
<td>−14.99 ± 30.1</td>
<td>−23.2 ± 30.1</td>
</tr>
</tbody>
</table>
| RR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; FEV, forced expiratory volume; AR, augmentation pressure; PWV, pulse wave velocity. *p<0.05.

Conclusions: IP showed positive effect on cardiovascular system decreased permanently high systolic and pulse pressure also in aorta and increased triangular index and some HRV parameters that may partly explain its positive effect in CHD patients.

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Prolonged chest symptoms in patients with vasospastic angina: what do they mean?

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Background: Clinicians often encounter patients with vasospastic angina (VSA) who have chest symptoms for a prolonged duration. However, the characteristics of such patients remain unclear. Therefore, we analysed the clinical characteristics of such patients.

Methods: We enrolled 122 patients with VSA, which was diagnosed by the spasm provocation test using acetylecholine (ACh). Medical interviews of all patients were conducted, and the maximum duration of chest symptoms and the presence of cold sweats were checked. In addition, we analysed the incidence of variant angiopathy (VA), which was defined as angiina with ST-segment elevation on electrocardiography during the attacks. The patients were divided into the two groups according to the duration of maximal chest symptoms: normal group (N, <15 min) and prolonged group (P, >15 min). During the spasm provocation test, the incidence of multi-vessel spasm, the findings induced by a low dose of ACh, total occlusion due to spasm, use of nitroglycerine (NTG) for relief of spasm during the provocation test, were investigated in the two groups.

Results: There were 96 patients in Group N and 26 patients in Group P (21%). The patients’ characteristics did not differ between the two groups. The presence of cold sweats was more frequently observed in Group P (15% vs. 1% in Group N, p<0.001), and VA tended to be more frequently observed in Group P (4% vs. 0% in Group N, p=0.0537). NTG use for relieving severe spasm during the provocation test was more frequently observed in Group P (56% vs. 37% in Group N, p=0.04). The incidence of multi-vessel spasm (P: 70% vs. N: 69%), positive provocation by a low dose of ACh (P: 32% vs. N: 20%) and total occlusion due to spasm (P: 12% vs. N: 11%) were not different in the two groups.

Conclusions: These findings suggest that VSA patients with prolonged chest symptoms may comprise one-fifth of all VSA patients. Such patients may have more severe characteristics of VSA.

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Comparison between plain old balloon angioplasty and drug-eluting stent implantation for the treatment of stent fracture

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Objective: The aim of this study was to evaluate clinical outcomes after percutaneous coronary intervention (PCI) for stent fracture (SF).

Background: SF has been reported as a predictor of in-stent restenosis (ISR) and stent thrombosis (ST).

Methods: Between January 2009 and December 2012, consecutive SF cases treated with either drug-eluting stent (DES) or plain old balloon angioplasty (POBA) were retrospectively enrolled in this study. The study endpoints were all-cause death, cardiac death, myocardial infarction (MI), target vessel revascularization (TVR), target lesion revascularization (TLR), ST, re-stent fracture (re-SF) and major adverse cardiac events (MACE) defined as the composite of cardiac death, MI and TLR.

Results: 135 SF cases, 67 (49.6%) cases were treated with DES, whereas 68 (50.4%) cases with POBA. Median follow-up period was 1401 (IQR: 967 to 1771) days. The estimated MACE rate at 3 years was significantly lower in the DES group as compared with the POBA group largely driven by less TLR (25.7% vs. 55.8%, p<0.001). Moreover, 1-year landmark analysis after PCI for SF revealed that MACE continued to occur even after 1 year irrespective of the treatment option (p<0.47). On multivariable Cox regression analysis, POBA and large post-procedural angle (Δ) defined as the degree difference between the end systolic and diastolic angle were identified as independent predictors for TLR.

Conclusion: DES implantation for SF is associated with lower TLR as compared with POBA possibly due to a smaller post-procedural angle (Δ). MACE, mainly driven by TLR, continued to increase even after 1 year irrespective of treatment option.

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Long-term clinical outcome of angiotensin-converting enzyme inhibitor versus angiotensin II receptor blocker use in patients with acute myocardial infarction undergoing percutaneous coronary intervention

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Background: Current guidelines recommend that angiotensin-converting enzyme inhibitor (ACEI) should be used as the first choice for post myocardial infarction (MI) treatment and angiotensin II receptor blocker (ARB) should be considered in patients who are intolerant to ACEI. Although 2 large randomized clinical trials were published at the early 2000s, there have been little data about head-to-head comparisons at percutaneous coronary intervention (PCI) era.

Methods: We consecutively enrolled AMI patients who underwent PCI in the COREA-AMI (COnvergent REgistry of cAtholic and chonnAm university for AMI) from January 2004 to December 2009. Of 4,748 AMI patients, 2,332 and 1,245 patients were treated with ACEI and ARB at discharge, respectively. The primary exclusion was the incidence of post-AMI death.

Results: Median follow-up duration was 43.8 months. In overall population, long-term survival was superior in ACEI group (201 death, 10.1%) as compared with ARB group (150 death, 15.2%) (p<0.01). In multivariable Cox regression, adjusted HR is 1.37 (95% CI 1.10 to 1.70, p<0.01). Overall findings were consistent in propensity matched population. In subgroup analyses, there were significant interaction between preserved (HR 1.07, 95% CI 0.81 to 1.46, p=0.69) and de

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of treatment in AMI patients andARB might be used as alternative with careful consideration of renal function or clinical diagnosis.

Methods: Consecutive cardiac patients (coronary artery disease and/or heart failure) with documented moderate to severe SDB (full overnight polysomnography, PSG), were treated by PAP (continuous positive airway pressure, CPAP or adaptive servoventilation, ASV). Markers reflecting heart failure/structural heart disease (BNP, CK, CKMB, myoglobin), liver disease (ALT, AST), inflammation (high sensitive CRP, Fibronectin, IL-6, lactate) and renal failure (creatinine) were taken the morning after diagnostic PSG and the morning after PAP therapy initiation.

Results: In 39 patients (77% male, 65±10 years, BMI 31±6 kg/m², 69% si-nous rhythm, 62% Diabetes, 82% CAD, 10% NYHA III/IV) SDB was successfully treated by PAP, with a decrease in apnoea-hypopnoea index from 36±19 to 11±10/h (p<0.001). This was associated with a significant decrease in CK (126±98 U/l vs 111±87 U/l, p=0.001) and high sensitive CRP (0.48±0.70 mg/l vs. 0.34±0.57 mg/l, p=0.001) and a decrease in BNP (181±213 pg/ml vs. 170±208 pg/ml, p=0.08) and troponin (0.24±0.075 pg/ml vs. 0.18±0.04 pg/ml, p<0.09)

Conclusion: Treatment of moderate to severe SDB with PAP therapy in cardiac patients results in a decrease of inflammatory markers and markers representing cardiac damage. This might be responsible for beneficial effects with long-term PAP therapy in such patients.

ADJUNCTIVE MEDICAL THERAPY

P6289 | BEDSIDE

Association of neutrophils to lymphocytes ratio, carotid atherosclerosis, and coronary artery disease in patients with chest pain

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Background: Inflammation plays a role in the pathogenesis of systemic atherosclerosis, and neutrophils and lymphocytes ratio (NLR) has been studied as new predictors of cardiovascular risk. This study aimed to investigate the relationships between NLR and the parameters of carotid atherosclerosis in the common carotid artery (CCA) in patients with suspected coronary artery disease (CAD).

Methods: Carotid artery US was performed in 839 patients with suspected CAD, and mean IMT, total plaque area (TPA), and inflammatory markers including NLR, platelet to lymphocyte ratio (PLR), and high-sensitive C-reactive protein (hs-CRP) were measured. Inflammatory parameters were analyzed according to the presence of CAD (>50% in diameter stenosis) and the carotid atherosclerosis (defined as an increased IMT ≥0.9 mm or with a plaque).

Results: Compared to patients without CAD (n=592), patients with CAD (n=247) showed significantly higher NLR (2.19±1.94 vs. 2.79±2.96, p=0.003), PLR (104.1±44.5 vs. 117.7±91.8, p=0.027), mean CCA IMT (0.66±0.15 mm vs. 0.73±0.20 mm, p<0.001) and TPA (0.13±0.24 vs. 0.29±0.62 cm², p<0.001). NLR showed significantly correlated with the presence of CAD (r=0.120, p=0.001) and carotid atherosclerosis (r=0.138, p<0.001). When the patients were classified into four groups based on the presence of CAD and carotid atherosclerosis, patients with CAD and carotid atherosclerosis showed the highest NLR (no CAD without carotid atherosclerosis; 1.82±0.91 vs. no CAD with carotid atherosclero-sis; 2.63±2.62, vs. CAD without carotid atherosclerosis; 2.78±2.95 vs. CAD with carotid atherosclerosis; 2.84±3.03, p=0.001). On receiver operating characteristic analysis, NLR was found to have the largest area under the curve (AUC = 0.590, p<0.001 and AUC = 0.605, p=0.001, respectively) with an optimal NLR cut-off value of 1.98 (sensitivity 49%, specificity 65%) and 1.77 (sensitivity 62%, specificity 57%) for predicting the presence of carotid atherosclerosis and significant CAD.

Conclusion: In patients with chest pain, high NLR was significantly associated with the carotid atherosclerosis and CAD. These findings support the role of NLR as a simple inexpensive and readily available marker an index of atherosclerosis and serves as a predictor of significant coronary and carotid atherosclerosis.

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Single-night ventilation therapy for sleep disordered breathing is associated with a decrease in inflammatory markers in patients with heart diseases

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Purpose: Inflammatory markers (IM) have been shown to be higher in patients with heart failure (HF) and sleep disordered breathing (SDB) compared to HF patients without SDB. We investigated whether positive airway pressure (PAP) ventilation therapy reduces IM within one night of therapy.

Results: In 39 patients (77% male, 65±10 years, BMI 31±6 kg/m², 69% si-nous rhythm, 62% Diabetes, 82% CAD, 10% NYHA III/IV) SDB was successfully treated by PAP, with a decrease in apnoea-hypopnoea index from 36±19 to 11±10/h (p<0.001). This was associated with a significant decrease in CK (126±98 U/l vs. 111±87 U/l, p=0.001) and high sensitive CRP (0.48±0.70 mg/l vs. 0.34±0.57 mg/l, p=0.001) and a decrease in BNP (181±213 pg/ml vs. 170±208 pg/ml, p=0.08) and troponin (0.24±0.075 pg/ml vs. 0.18±0.04 pg/ml, p<0.09)

Conclusion: Treatment of moderate to severe SDB with PAP therapy in cardiac patients results in a decrease of inflammatory markers and markers representing cardiac damage. This might be responsible for beneficial effects with long-term PAP therapy in such patients.
Conclusion: ECG prediction of LVMI may be improved by using a more complicated model, and the use of such an approach is warranted to ensure further improvements in LVH detection.

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Left atrial ejection force as a quantitative measure of left ventricular diastolic dysfunction measured by Doppler echocardiography
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Background: The value and clinical importance of Left atrial ejection force.

Aim: To assess the left atrial ejection force as a quantitative measure of left ventricular diastolic function compared to traditional Doppler measurements of diastolic function. Furthermore, the relationship between left atrial ejection force and LV end diastolic pressure was studied.

Patients and methods: We enrolled 120 patients presenting with different grades of LV Diastolic dysfunction (Grades I, II, and III); allocating 30 patients to each group and 30 healthy subjects as a control group. A detailed transthoracic echocardiogram, including mitral flow velocities, tissue Doppler mitral annular velocities, and left atrial (LA) volume, was performed in both groups. LAEF was calculated using formula postulated by Manning et al. (LAEF = 1/3 x MVA x A').

Results: In the test group, we found that Left atrial ejection force is a statistically significant quantitative measure of LV diastolic dysfunction. The %LAEF increases from Grade I (average 188.93% ± 40.12%) to become 239.70% ± 74.25% in grade Ia, then increasing further to 256.57% ± 45.92% in grade II and dramatically falling to 57.88% ± 32.49% in grade III Diastolic dysfunction. LAEF was increased in elderly patients, with a weak positive correlation between age and LAEF (r=0.27, p<0.003). A moderate negative correlation existed between different LV dimensions and %LAEF. Similarly, a moderate negative correlation existed between %LAEF and LAVI. (r=−0.342, p<0.0001). A good positive correlation existed between LAEF and IVRT. DT. A wave velocity and septal E' with a p value 0.0001 and r=0.449, 0.425, 0.53 and 0.457 respectively (p<0.0001).

Conclusion: Impaired diastolic function affects LA and increased LAEF is one of its manifestations. The initial rise in LAEF in the degree of diastolic dysfunction is due to the increase in LVDEVP and thus a greater left atrial systolic force is necessary while the tail in LAEF in grade III may be explained by LA dilatation and failure. LAEF may also have diagnostic importance in diastolic-dimension, but these findings should be confirmed by further studies.

P6294 | BEDSIDE
The association between semi-quantitative microalbuminuria, altered cardiac geometry, diastology and contractile mechanics in asymptomatic individuals
K.T. Sung, Y.H. Lai, C.I. Lo, W.R. Lan, T.C. Hung, J.Y. Kuo, J.Y. Hou, H.I. Yeh, C.L. Hung, Mackay Memorial Hospital, Cardiovascular, Taipei, Taiwan, ROC

Background: Microalbuminuria as an early sign of renal impairment may occur before overt reduction in filtration rate. The impact of proteinuria on cardiac geometry and associated cardiac mechanical changes remain largely unknown.

Methods: We consecutively examined 2D speckle tracking in an asymptomatic group of cardiac geometry, diastology, myocardial (LV) Doppler, strain and twist/torsion analysis. We further categorized the study population into four groups based on urine dipstick results: ordered proteinuria amount: 0, 0.5, 1, 2 or >3+.

Results: Totally 3,787 subjects had both urine dipstick and speckle-tracking results available (mean age 50.16±11.07 years, 67.7% female) with preserved LV ejection fraction. A trend toward greater LV wall thickness, higher LV mass index, impaired mitral annulus relaxation E, and larger LA volume index across 4 groups were observed (Table1, all trend p<0.001). We also noticed graded reduction of longitudinal (−20.29, −20.01, −19.91, −18.37%, adjusted p<0.04, p<0.05) and circumferential strains (−24.12, −23.80, −23.82, −23.10%, trend p<0.0001 and r=0.449, 0.425, 0.53 and 0.457 respectively (p<0.0001).

Conclusion: Microalbuminuria in asymptomatic population is associated with altered cardiac geometry accompanied by subclinical LV contractile disturbances.
in terms of all strains. Our data suggested that proteinuria, even as minor degree, may be associated with detrimental effects on systolic function.

P6296 | BEDSIDE
Tissue mitral annular displacement - a novel technique for rapid quantitative assessment of global left ventricular systolic function based on speckle tracking algorithm
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Background: TMAD (tissue mitral annular displacement) is a new technique for rapid quantitative assessment of global left ventricular function based on tracking of acoustic markers. It allows for the assessment of mitral annulus displacement relative to the apex, based on standard apical views.

Objective: To assess the feasibility and accuracy of measurements obtained with TMAD technique for the analysis of global left ventricular function using 3D ejection fraction (LVEF) measurements as a reference technique.

Methods: The study included 49 patients (33 men, mean age 65±10 years) with coronary artery disease, who underwent 2D and 3D transhoracic echocardiography with off-line measurement of LVEF using 3D datasets. Furthermore a TMAD algorithm was performed in all patients.

Results: TMAD analysis of one apical view took 10±4 seconds. Mean LVEF was 47.8±12.2%. Due to the suboptimal quality of the data, insufficient for tracking the acoustic markers by the TMAD algorithm, 5 patients were excluded. In the remaining 44 patients there was a statistically significant correlation between LVEF and the midpoint mitral annulus displacement towards the apex in the apical four chamber view (r=0.57, p<0.0001) and the percentage of the midpoint mitral annulus displacement (r=0.63, p<0.0001). A similar correlation was observed between midpoint mitral annulus displacement in the apical two chamber view (r=0.56, p<0.0001) and the percentage of the midpoint mitral annulus displacement (r=0.65, p<0.0001).

Conclusion: Measurement of midpoint mitral annulus displacement by TMAD technique is very rapid and provides satisfactory correlation with 3D LVEF measurements. This technique, however, requires echocardiographic recording of good quality.

P6297 | BEDSIDE
Wasted myocardial work in left ventricular dyssynchrony: a preliminary report of a novel principle to predict response to cardiac resynchronisation therapy
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Background and aim: Cardiac resynchronisation therapy (CRT) in heart failure is limited by a large fraction of non-responders. We explore if degree of left ventricular (LV) work identifies responders to CRT.

Methods: Twenty one patients who received CRT according to current guidelines were studied before and after an average of 8±2 months. By definition, segments which shorten in systole perform positive work, whereas segments which lengthen do negative work. Work was calculated from non-invasive LV pressure and strain by speckle tracking echocardiography. For each myocardial segment and for the entire LV wasted work fraction (WWF) was calculated as negative work in percentage of positive work. LV wall motion score index (WMSI) was assessed by echocardiography. Response to CRT was defined as ≥15% reduction in LV end-systolic volume (ESV).

Results: Responder rate to CRT was 71%. In responders WWF for septum was 117±102%, indicating more negative than positive work, and decreased to 14±12% (p<0.01) with CRT. In the LV free wall WWF was 19±16% and showed no significant change. Global WWF decreased from 36±21 to 19±10% (p<0.01) with CRT. In multiple linear regression analysis septal WWF and WMSI were the only significant predictors of ESV reduction (septal WWF: β=0.14, p<0.01; WMSI: β=1.25, p=0.03). Septal WWF together with WMSI showed AUC=0.86 (CI 0.71–1.0) for CRT response prediction.

Conclusions: In this pilot study septal WWF together with WMSI was a strong predictor of response to CRT. This novel principle should be studied in future larger studies.

Acknowledgement/Funding: This study was funded by a grant from the Norwegian Research Council to Oslo University Hospital’s Center for Cardiological Innovation (CCI).

P6298 | BENCH
Myocardial stiffness as an important determinant of early systolic lengthening and post-systolic shortening
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Background: Although early systolic lengthening (ESL) and post-systolic shortening (PSS) observed in the ischemic segment could be affected by the myocardial stiffness, there have been no reports to directly prove it.

Methods: In 6 open-chest dogs, left ventricular short-axis images were acquired at baseline, during left anterior descending coronary artery (LAD) occlusion and after intramyocardial injection of ethanol into the LAD territory to stiffen the myocardium in addition to ischemia. Circumferential strains were analyzed and the amplitude of ESL (βESL) and PSS (βPSS) were measured in each stage. To correct the effect of tension from the nonischemic segment, βESL was divided by the peak systolic strain (∝peak) in the nonischemic segment and PSS was divided by the difference of strains at end systole between ischemic and nonischemic segments (ΔxESL). The Young’s modulus was measured at the ischemic and non-ischemic myocardium from the excised heart with a digital force gauge.

Results: ∝peak were almost similar during LAD occlusion and after ethanol injec-
tion. However, ESL and PSS significantly decreased after ethanol injection compared to during LAD occlusion (ESL: 6.8±2.7% vs. 0.28±0.30%, p < 0.05; PSS, −8.2±1.3% vs. −1.8±1.1%, p < 0.05; corrected +ESL, −0.54±0.37 vs. −0.24±0.11; corrected +PSS, 0.49±0.08 vs. 0.15±0.10, p < 0.05) (Figure). The Young’s modulus of the myocardium in the LAD territory was higher than that of the nonischemic myocardium indicating that the myocardium became stiff by ethanol injection (0.07±0.02 vs. 0.28±0.13 N/cm², p < 0.05).

Conclusion: ESL and PSS are affected not only by myocardial ischemia but also by myoccardial stiffness. The feasibility of noninvasive assessment of myocardial stiffness in the ischemic segment using ESL and PSS should be investigated.

ECHO-IMAGING EVALUATION OF THE RIGHT VENTRICLE

P6299 | BEDSIDE
Validation of right ventricular volume derived from 3-dimensional speckle tracking echocardiography: application for adult congenital heart disease
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Newly developed 3D speckle tracking imaging (STI) system specialized for the right ventricle has been validated using sonomicrometry in experimental animal model, recently. Accordingly, the purpose of this study was to investigate the accuracy of the newly developed RV 3D echo STI in evaluating the chamber volume and ejection fraction (EF) in which cardiac magnetic resonance (cMR) was performed as the gold standard in various heart disease patients including adult congenital heart disease (ACHD).

Methods: Sixteen ACHD (7 ventricular septal defect, 6 tetralogy of Fallot, 2 pulmonic stenosis, 1 Ebstein) and 53 patients with other cardiovascular disease were included. In RV 3D echo STI, end-diastolic RV inlet, apex, and outlet endocardial borders were manually traced, then, end systolic volume (ESV) and EF were automatically calculated (Figure).

Results: Among total of 69 patients, 22 (32%) were excluded because of the inadequate echo image quality. In ACHD group, only 2 (12%) patients were excluded. Among remaining 47 patients, all RV subendocardial contour could be visualized in 22 (48%) patients. In remaining 25 patients, RV end diastolic volume, ESV, EF derived by 3D echo STI showed close relations with these by cMR (R2=0.91, 0.91, 0.67, all p < 0.001, respectively), however, the bias and limits of agreement between two procedure −6ml (−43 to 30) in EDV, −2ml (−32 to 28) in ESV, and −3% (−15 to 10) in EF. Intra- and inter-analyzer reproducibility was 4.9±6.1% and 7.1±9.2% in RV EF for ACHD subgroup.

Conclusion: While further technical progress should be required to overcome the limitation of the RV outlet asessment, RV 3D speckle tracking is the promising imaging modality in assessing RV volume and function with significant but small systemic underestimation.

P6300 | BEDSIDE
Pseudonormal right ventricular filling pattern reflects left ventricular systolic dysfunction and remodeling
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Background: Transtricuspid flow pattern is used to estimate right ventricular (RV) filling pressure, and high ratio of tricuspid inflow E velocity to tissue Doppler e’ (E/e’) is implicated as increased right atrial pressure. Left ventricular (LV) function may affect right heart function, but the relationship between LV function and RV filling pattern is not fully understood.

Methods: We retrospectively analyzed 915 patients who underwent echocardiography to assess cardiac function between January 2013 to March 2014 in our hospital. Transtricuspid early (E) and late (A) diastolic filling velocity ratio (E/A) and tricuspid E/e’ ratio were measured. Patients were divided into two groups: non-pseudonormal (low tricuspid E/e’ (<6), n=658) and pseudonormal (high tricuspid E/A (<0.8) and high tricuspid E/e’ (>28), n=257) RV filling groups.

Results: The pseudonormal RV filling group displayed lower LV ejection fraction (61 [52–65%] vs. 63 [57–68%], p < 0.01), lower LV systolic velocity (6.9 [5.7–8.2] cm/sec vs. 7.9 [6.4–9.5] cm/sec, p < 0.01), and larger LV end-diastolic volume (89 [79–102] mL vs. 84 [69–101] mL, p < 0.05) than non-pseudonormal RV filling group, suggesting that pseudonormal RV filling pattern reflected LV systolic dysfunction and remodeling. We next assessed the patients in the setting of elevated LV filling pressure. Out of 915 patients, 79 patients presented increased LV filling pressure pattern (mitral E/A:0.8 with mitral E/e’<15), Pseudonormal RV filling group (n=25) showed lower LV ejection fraction (52 [32–63%] vs. 63 [53–68%], P < 0.01) and larger LV end-diastolic diameter (51 [47–60] mm vs. 47 [45–55] mm, P < 0.01) than non-pseudonormal RV filling group (n=54), indicating that RV filling pattern may straticfy the category of the patients with elevated LV filling pressure pattern.

Conclusions: The transtricuspid flow pattern reflects LV condition, and useful for rigorous risk stratification of the patients with increased LV filling pressure.

P6301 | SPOTLIGHT
Impact of an expedition to 8000m peak on the right heart - the echocardiographic assessment of right ventricle structure, performance and mechanics in the setting of extreme altitude
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Introduction: Extreme mountaineering has aroused in a popularity last years. The chronic and acute exposure to altitude, even in healthy, prone individuals has an impact on the right heart but still little is known what happens after return from hypoxic condition. Therefore, we intended to evaluate right ventricle in alpinists after climbing eight thousands peak.

Methods: The echocardiographic examination was performed according to protocol, including 2D echocardiography, Doppler echocardiography, pulsed tissue Doppler imaging, and 2D speckle tracking echocardiography near the sea level in 11 subjects participating in an expedition to K2 or Broad Peak (BP) before and after altitude exposure.

Results: After the 6–8 weeks of residence above 2500 meters (m) aimed to climb K2 (8611m) or BP (8515m) right ventricle (RV), Tei index increased (0.5±0.1 after vs. 0.4±0.1 before; p=0.028) and RV free wall (RV FW) longitudinal systolic strain decreased (−23.1±2.7% after vs. −25.9±2.4% before; p=0.043). It was observed the decrease in peak systolic strain and strain rate in the basal (−24.4±4.4% after vs. −30.9±3.5% before; p=0.017 and −1.4±0.3 s−1 after vs. −1.8±0.3 s−1 before; p=0.017) and mid (−28.7±3.9% after vs. −34±3.3% before; p=0.028 and −1.5±0.2 s−1 after vs. −1.9±0.3 s−1 before; p=0.028) segments of the RV FW. A trend toward lower tricuspid annular plane systolic excursion, RV systolic excursion velocity, right ventricle ejection fraction and right ventricle fractional area change after expedition was found. The linear RV dimensions such as RV outflow tract proximal and RV outflow tract distal increased (accordingly; 31.3±4mm after vs. 29.2±3mm before; p=0.025 and 27±2.7mm after vs. 24±3mm before; p=0.012) and the ratio RV/LV was higher (0.8±0.1 after vs. 0.7±0.1 before; p=0.046). None of the subjects have high altitude pulmonary edema (HAPE) episode and pulmonary artery systolic pressure (PASP) remained unchanged.

Conclusions: In short time after return from exposure to extreme altitude such as climbing 8000m peak, in HAPE resistant individuals, RV dilatation and change in RV performance is observed, whereas PASP is normal. The Tei index and RV free wall longitudinal systolic strain are superior to other RV performance indices to detect changes in RV function after exposure to extreme hypoxic stress. Observed alterations in cardiac morphology and function seem to be the persistence of physiological adaptation to high altitude condition in healthy individuals. RV performance evaluation should be a part of the sport qualification to altitude activities.

P6302 | BEDSIDE
Pre-operative right ventricular function predicts clinical outcome after prophylactic tricuspid ring implantation
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Background: Symptomatic patients with organic mitral regurgitation respond to mitral valve repair surgery which results in reduced left atrial pressure and pulmonary venous congestion, hence symptomatic improvement. However, the nature of the required open heart surgery is known to be associated with reduced right ventricular (RV) function and potential worsening of tricuspid regurgitation.
TAPSE and FAC measurement were feasible in 90 patients (100%) and of RV systolic function and CMR-derived measurement of RVEF and RV volume were evaluated. 

Results: Both A-FAC and F-FAC were measurable in 90 patients (100%) and M-FAC measurement was feasible in 84 patients (93%). End diastolic area (Area ED) (cm²) of A-FAC and F-FAC showed correlation with CMR-derived end diastolic volume, respectively (p < 0.001, r = 0.768 vs P = 0.0001, r = 0.784). End systolic area (area ES) (cm²) of A-FAC and F-FAC showed correlation with CMR-derived end systolic volume, respectively (p < 0.001, r = 0.791 vs P < 0.0001, r = 0.820).

A-FAC and F-FAC has good correlation with CMR-derived RVEF (p < 0.0001, r = 0.638 vs P = 0.0001, r = 0.663), respectively. M-FAC has no correlation with CMR-derived RVEF (p = N.S., r = 0.438). There were no significant agreement between TAPSE, s′ and CMR-derived RVEF in this study.
P6306 | BEDSIDE
Right ventricular regional and systolic function in patients before and after percutaneous closure of atrial septal defect assessed by three-dimensional echocardiography

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Objective: To evaluate right ventricular (RV) regional volume and systolic function in patients with atrial septal defect (ASD) before and after percutaneous closure using real-time three-dimensional echocardiography (RT3DE).

Methods: RT3DE was performed in 86 patients with ASD the day before closure and within 24 hours afterwards to obtain RV regional end-diastolic volume (EDV), end-systolic volume ( ESV), systolic volume (SV) and ejection fraction (EF) in three compartments (inflow, body and outflow). Two-dimensional and Doppler parameters including RV fractional area change (FAC), tricuspid annular plane systolic excursion (TAPSE), pulmonary vascular resistance (PVR) and maximum diameter of ASD (ASD-D) were analyzed. Forty age and gender matched normal adults were included as controls.

Results: RT3DE images were successfully acquired and analyzed in 94% of all the subjects. When compared with controls, RV global and regional EDV, ESV and SV were significantly enlarged (all P<0.001) and EF was significantly decreased (all P<0.001) in pre-closure patients. Pre-closure TAPSE was higher while pre-closure FAC was lower in post-closure patients than in controls (all P<0.05). RV global and regional EDV, ESV and SV in pre-closure patients were significantly correlated with ASD-D (r=0.487–0.695, all P<0.001). RV global EF, regional EF in the inflow compartment, TAPSE and FAC were negatively correlated with PVR in patients before closure (r=−0.228 to −0.302, all P<0.05).

Conclusions: RV regional volume and systolic function decrease rapidly during the first 24 hours after percutaneous closure, but RV volume was still larger and systolic function was still lower than normal subjects. RV volume was positively correlated with RV pre-load, and RV regional systolic function in the inflow compartment was negatively correlated with RV after-load in patients with ASD.

P6307 | BEDSIDE
Differentiation of early arrhythmic right ventricular cardiomyopathy from right ventricular outflow tract ventricular tachycardia

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Methods: We included 44 consecutive RVOT-VT patients (age 47±14 years) and compared to RVOT-VT subjects, but RVOT diameters did not differ (33±5mm vs. 32±5mm, P=0.06).

Results: By echocardiography, we assessed RVOT and RV basal diameter (RVD), fractional area change (RVFAC) and LV ejection fraction (EF). By 2D speckle tracking strain echocardiography we assessed RV mechanical dispersion as standard deviation of time to peak longitudinal strain rate (Δ1 T′) and radial strain rate (Δ1 R′).

Conclusion: Increased RVD, pronounced RV mechanical dispersion by echocardiography and reduced RV function by CMR discriminated early ARVC from RVOT-VT patients and may help correct diagnosis and treatment decisions.

P6308 | BEDSIDE
Assessment of right atrial and ventricular function by strain and strain rate imaging in patients with single ventricular physiology after cardiac progenitor cell therapy

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Background: The staged palliations for single ventricle lesions are not associated with cardiac function improvements directly in short-term. Recent clinical trials have suggested that cardiogenic-derived cell (CDC) infusion may enhance regional cardiac function in patients with heart diseases. Purpose: By using speckle-tracking echocardiography (UCG) and feature-tracking cardiac magnetic resonance imaging (dMRI), we sought to determine whether CDC therapy may improve myocardial strain and strain rate in patients with univentricular heart disease.

Methods: A total of 29 consecutive patients aged 2.7±1.4 years have enrolled the PERSEUS phase 2 randomized trial (NCT: NCT01829750) to receive intracoronary injection of CDCs after staged palliations in our institution. Twelve patients have received CDC infusion 1 month after surgery and 17 patients were assigned as controls with standard shunt procedure alone. Global and regional cardiac function were assessed by UCG and cMRI during follow-up of staged palliations and compared between 2 groups.

Results: CDC-treated patients showed significant increase in EF (44.8±8.7% at baseline vs. 50.3±9.0% at 3m, P=0.003), whereas control patients had no changes during the same follow-up period. Compared with controls, CDC-treated patients showed reduced Tei index at 3 months follow-up (P=0.03). To validate these observations, right ventricular strain and strain rate were assessed by UCG and cMRI. We found that global longitudinal strain, circumferential strain, and radial strain were all significantly improved in CDC-treated group compared with baseline (Long: −18.8±5.6% at baseline vs. −22.1±4.5% at 3m, P=0.01; Circ: −4.7±1.8% at baseline vs. −6.7±2.5% at 3m, P=0.02; Rad: 3.8±1.4% at baseline vs. 4.8±1.4% at 3m, P=0.03). Increased right ventricular strain was closely associated with reduced circumferential strain rate in CDC-treated patients (−0.4±0.1/s at baseline vs. −0.5±0.1/s at 3m, P=0.005). In addition, CDC infusion significantly improved atrial strain that was addressed by greater early diastolic strain rate (1.6±0.6/s at baseline vs. 2.0±0.6/s at 3m, P=0.03), increase in atrial fractional area change (29.7±9.0 at baseline vs. 35.0±6.7 at 3m, P=0.04), and reduced mitral infow velocity modified by early diastolic strain rate (P=0.005).

Conclusions: There is a significant favor of CDC therapy in patients with univentricular heart disease. Our results suggest that strain and strain rate parameters measured by UCG and cMRI closely reflect the regional improvements in both atrial and ventricular function after CDC infusion.

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P6309 | BEDSIDE
Pressure-volume relationship in the stress-echo lab: does (left ventricular end-diastolic) size matter?

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Background: The ESPVR is calculated as the variation between rest and peak stress End-Systolic Pressure-Volume Relation (ESPVR). The ESPVR is an afterload independent index of left ventricular (LV) contractility which allows a more accurate prognostic stratification than ejection fraction in patients without inducible wall motion abnormalities. Whether and to what extent it depends upon LV end-diastolic volume (EDV) remains unclear.

 Aim: To assess the dependence of ESPVR upon LVEDV during physical or pharmacological stress in patients with negative stress echo (SE) and all ranges of resting LV function.

Methods: We analyzed interpretable data obtained in 891 patients, (593 men, age 62±11 years) with ejection fraction 47-12%. We used correlations of near-normal or hypertensive; 229 were coronary artery disease; 324 were ischemic or non-ischemic dilated cardiomyopathy. They were studied with SE during exercise (n=172), dipyridamole (n=482) or dobutamine (n=237). The ESPVR was evaluated at rest and peak stress from raw measurement of systolic arterial pressure by cuff sphygmonanometer and EDV and ESV by biplane Simpson rule from 2D-echo.

Results: In the overall population, the relationship between ESPVR and LVEDV was linear at rest (r2 = 0.5, p=0.00; Fig. left panel), at peak stress (r2 = 0.4, p=0.00; Fig. middle panel), but absent if only the ESPVR (Delta rest-stress ESPVR) was considered (r2 = 0.1, p = ns; Fig. right panel). The ESPVR value was
highest for normals or near-normals and hypertensives, and lowest for ischemic or non-ischemic dilated cardiomyopathy patients.

Conclusion: LV end-diastolic volume does not affect the rest-stress changes in ESPVR in either normal or abnormal left ventricles, during physical or pharmacological stress. The JESPVR is independent from the EDV.

P6310 | BEDSIDE
New echocardiographic parameters in the diagnosis of heart failure with preserved ejection fraction
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Background: Heart failure with preserved ejection fraction (HFpEF) is a serious clinical disease. Non-invasive diagnostics of this condition is still unsatisfactory. The aim of this work is to find new echocardiographic parameters, which could improve the current non-invasive diagnostics of HFpEF. The parameters are the diastolic wall strain of posterior wall (DWS PW) and the vortex formation time (VFT).

Methods: The study includes 76 patients with exertional dyspnea having normal left ventricular ejection fraction and 19 healthy volunteers. All subjects underwent a spirometry examination, determination of plasma levels of NT-proBNP and transthoracic echocardiography. In addition to the standard parameters used in the diagnosis of HF, DWS PW and VFT were assessed in all patients. The DWS PW is based on the linear elastic theory. The VFT is based on the parameters from transmittal Doppler left ventricular filling, end-diastolic left and end-systolic ventricular volumes and diameter of the mitral annulus in early diastole.

Results: HFpEF has been proved in 27 patients with dyspnea. Patients with HFpEF were compared to other subjects with dyspnea, where significantly different values were found: DWS PW (0.25±0.065 vs. 0.340±0.066, p<0.001), E/E′ (10.9±2.5 vs. 8.5±1.9, p<0.001), LV mass index (110.4±27.9 g/m² vs. 82.3±16.0 g/m², p<0.001), NT-proBNP (366.3±301.3 pg/ml vs. 115.8±82.4 pg/ml, p<0.001) and VFT (2.80±0.93 vs. 4.1±1.4, p<0.001). There were no significant differences in the parameters among patients with noncardiac dyspnea and the control group

Conclusions: Improvements in ventriculo-arterial coupling and myocardial energetics under dobutamine stress were independent determinants of cardiovascular outcome in patients with DCM.

P6312 | BEDSIDE
Association of periodontitis with subclinical myocardial dysfunction in patients with diabetes
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Introduction: In patients with type 2 diabetes mellitus (T2DM), the association between periodontitis and cardiovascular disease (CVD) is established recently. However, the association between periodontitis and subclinical cardiac dysfunction, especially exercise induced cardiac alterations in T2DM patients are not clear. In the present study, our goal was to investigate the relationship between periodontitis and subclinical cardiac dysfunction by 1) basic dental examination and 2) detailed cardiac assessment using resting and exercise echocardiography.

Methods: Fifty-two T2DM patients without histories of CVD were enrolled, and all received dental examination, resting and exercise transthoracic echocardiography. Echocardiographic images were analyzed in detail with the following parameters i) Left ventricular function evaluated (LVEF) by Simpson’s method derived global longitudinal strain (GLS), ii) diastolic function was assessed by tissue Doppler derived E’ and E/E’ ratio. Dental measurement parameters include tooth loss number (TL) and probing depth (PD).

Results: The mean age of the recruited participant are 64.8±8.7, 50% of them are men. Male even though LVEF didn’t have significant relationship with dental parameters, TL was significantly correlated with resting (r=0.40, P<0.01) and exercise (r=0.46, P<0.01) E’ and E/E’ ratio. Multivariate analysis demonstrated TL and PD were independent predictors of impaired resting GLS (B=−0.03, CI: −0.06 to −0.001, P<0.01) and exercise (B=−0.04, CI: −0.06 to −0.01, P<0.01) GLS, resting (r=−0.33, p=0.03) and exercise (r=−0.46, p<0.01) E’. Further, multivariate analysis demonstrated TL and PD were independent predictors of impaired resting GLS (B=−0.09, CI: −0.18, P<0.04) and exercise (B=−0.18, CI: 0.05 to 0.20, P<0.04 respectively). In addition PD were independent related with exercise E’ (B=−0.01, CI: −0.02 to −0.001, p<0.03) and exercise E/E’ ratio (B=−1.28, CI: 0.14 to 2.42, P=0.03) after multivariate analysis.

Conclusion: The present study demonstrated an independent relationship between the severity of periodontitis and myocardial systolic and diastolic dysfunction both at rest and exercise status. The finding suggested patients with periodontitis thus required detailed clinical assessment to detect subclinical myocardial dysfunction in order to prevent adverse cardiac outcome.

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P6313 | BEDSIDE
Subclinical myocardial dysfunction detected by two-dimensional and three-dimensional speckle tracking echocardiography in asymptomatic type 1 diabetic patients
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Background: We sought to assess left ventricular (LV) function using two-dimensional (2D) and three-dimensional (3D) speckle tracking echocardiography...
(STE) for the detection of preclinical diabetic cardiomyopathy, in asymptomatic type 1 diabetic patients, and to evaluate potential progression over a 6-year follow-up.

Methods and results: Sixty-six asymptomatic type 1 diabetic patients with no cardiovascular risk factors were compared to 26 matched healthy controls. Ventricular, 2D and 3D STE were performed at baseline. A subgroup of 14 patients underwent a 6-year follow-up evaluation. At baseline, diabetic patients had similar LV ejection fraction (60 vs. 61%; p=NS), but impaired longitudinal function, as assessed by 2D global longitudinal strain (GLS) (−18.9±2 vs. −20.5±2, p=0.002) and 3D GLS (−20.5±2 vs. −19.2±1, p=0.03). At follow-up, diabetic patients had worsened longitudinal function compared to baseline (2D GLS: −18.4±1 vs. −19.2±1, p=0.03). Global circumferential (GCS) and radial (GRS) strains were unchanged at baseline and during follow-up. Metabolic status did not correlate with GCS, whereas GCS and GRS showed a good correlation, suggestive of a compensatory increase of circumferential and radial function in advanced stages of the disease - long-term diabetes (GCS: −26±3 vs. −23.3±3, p=0.008) and in the presence of microvascular complications (GRS: 38.8±9 vs. 34.3±8, p=0.04).

Conclusion: Subclinical myocardial dysfunction can be detected by 2D and 3D STE in type 1 diabetic patients, independent of any other cardiovascular risk factors. Diabetic cardiomyopathy progression was demonstrated by a decrease in longitudinal function at follow-up, but did not extend to a clinical expression of the disease.

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P6314 | BEDSIDE
The superior value of quadriolar versus bipolar left ventricular leads for cardiac resynchronisation therapy: a cost effective analysis in a UK registry
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Background: Healthcare systems require evidence of value for money and clinical effectiveness of medical technology in real-world practice. We recently reported improved clinical outcomes in quadriolar (Q) left ventricular (LV) leads compared with bipolar (B) leads for CRTD delivery. We evaluated whether Q-based systems are cost effective given their £1200 higher purchase price.

Methods: Rehospitalisation episodes and intervention rates were coded over a mean follow up 879 days amongst 330 patients. 2014/15 NHS tariffs were applied to estimate the cost of each lead to service commissioners. EQ-5D questionnaire values were applied to mortality and heart failure events to estimate quality-adjusted life year (QALY) differences. A 3-year time horizon was adopted; effects beyond 1 year were subject to a 3.5% annual discount.

Results: Groups were age and sex matched. A lower proportion of patients implanted with a quadriolar lead were hospitalised (Q:117 (51%) vs. B:72 (71%), p=0.001) and 107 consecutive patients (72 males; 35 females), referred for a CCTA were prospectively included using a dual-source CT system in a high pitch (n=51) or a sequential mode (n=56) according to heart rate (mean DLP = 204.6 mGy.cm).

P6315 | BEDSIDE
Reduced-dose dual-source coronary computed tomography angiography (CCTA): is raw-data-based iterative reconstruction able to maintain diagnostic confidence?
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Introduction: The assessment of coronary artery disease with CCTA requires a good image quality and can be easily hampered by the noise generated in a reduced-dose acquisition. When faced with the challenge of providing diagnostic quality at the lowest possible radiation dose, the medical community demonstrated the usefulness of iterative reconstruction (IR) algorithms, which reduce the level of noise. However IR algorithms are also known to change the texture of CT images and could lead to misdiagnosis by making the sharpness of the coronary borders.

Purpose: To evaluate image quality and diagnostic confidence of a raw-data-based iterative reconstruction technique (IR) in reduced-dose CCTA images in comparison with standard-dose filtered back projection (FBP) images.

Methods: 107 consecutive patients (72 males; 35 females), referred for a CCTA were prospectively included using a dual-source CT system in a high pitch (n=51) or a sequential mode (n=56) according to heart rate (mean DLP = 204.6 mGy.cm).

Results: In Group 1, there was a significant increase in noise compared to Group 2 (36.8 HU 67.7±3 vs. 30.4 HU ±25; p<0.0001) and a CNR impairment (15.6±3.4 vs. 18.7±4.5; p<0.0001). In Group 3, despite the 30% dose reduction, IR was able to maintain the objective image quality: mean noise 31.1 HU ±5.4 (p<0.8) and CNR=18.5±5.0 (p=0.7). However the diagnostic confidence was altered when compared with Group 1 (p<0.0001), mainly rated as moderate with a blurred aspect of the coronary borders (81/107 [75.7%], p<0.0001) and a significant number of potentially non-discriminant plaques described in vessels considered as normal in Group 1 (105/428 [24.5%], p<0.0001).

Conclusions: Raw-data-based iterative reconstruction allowed significant noise reduction but may be associated with blurring of the coronary luminal borders, which can decrease diagnostic confidence. When reporting reduced-dose CCTA with iterative reconstruction, false smooth plaque artifacts must be considered in diagnostic assessment and subsequent patient management.

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P6316 | BEDSIDE
Submillisecond computed tomography with model-based iterative reconstruction before pulmonary veins radiofrequency catheter ablation of atrial fibrillation: impact on radiation exposure and outcome

Background: The outcome of radiofrequency catheter ablation (RFA) of atrial fibrillation (AF) has improved thanks to left atrium (LA) anatomy reconstruction by computed tomography with adaptive statistical iterative reconstruction algorithm (CT-ASIR) before the procedure. However, CT-ASIR strategy is associated to an increase of cumulative effective radiation dose (ED) in these patients. Recently, a model-based iterative reconstruction algorithm (MBIR, GE Healthcare, Waukesha, Wisconsin) has been developed (CT-MBIR) for image noise reduction. However, ED close to chest X-ray exposure. The aim of this study is to compare the CT and RFCA characteristics, AF recurrence after procedure and radiation exposure of IRCA and MBIR guided CT-ASIR versus CT-MBIR.

Methods and materials: One hundred twenty consecutive patients with drug-refractory paroxysmal or persistent AF were addressed to CT-ASIR (Group 1: N: 60; mean age 60±10.1 yo; male: 46) or CT-MBIR protocol (Group 2: N: 60; mean age 59.7±11.3 yo; male:45) for evaluation of LA before RFCA. All patients were subsequently treated by image integration-supported RFCA. Image noise, signal to noise ratio (SNR), contrast to noise ratio (CNR), RFCA procedural characteristics, rate of AF recurrence and radiation exposure were measured and compared between the two groups.

Results: The two groups were homogeneous in terms of demographic characteristics, cardiovascular risk factors, prevalence of persistent AF, medical therapy and echocardiographic characteristics. The mean follow-up was similar (578±284 vs. 591±278 days, respectively, p=NS). Group 2 showed a higher signal to noise ratio (25.6±5.1 vs. 13.8±5.1) and contrast to noise ratio (22.7±4.5 vs. 14.0±4.1) of left atrium as compared to Group 1 (p<0.001). No differences were found in terms of RFCA parameter (procedural duration (130.9±130.6 vs. 143.8±80.4 min); fluoroscopy time (27.9±14.1 vs. 32.0±16.4 min); pulmonary

Conclusion: Implantation of quadriolar CRTD systems present a cost saving to the UK healthcare system compared with bipolar systems. With improved clinical outcomes and reduced overall costs, this data suggests quadriolar leads should become the gold standard for CRT delivery.

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Do not hallucinate. 

31 cases (91%) were available for prognostic inquiry over 1 year after CCTA underwent coronary intervention immediately after CCTA. Of residual 34 cases, (6.6%) showed vulnerable features of both of LDP and PR. proximal RCA (12.1%) and mid LAD (12.4%). Of 531 single-plaques, 35 plaques

Background: As previously reported coronary CT angiography (CCTA) verified features of vulnerable plaque are low-density plaque (LDP) and positive vessel remodeling (PR). However, there is no available evidence whether only these 2 features positive plaque is really prone to rupture.

Methods: CCTA was carried out in 5267 consecutive patients (Nov/2006-July/2009) for suspected coronary artery disease. Of 5267 patients, 531 patients showed only an atherosclerotic lesion in their coronary tree, namely single plaque. The excluded patients mostly in minimal LAD (52.7%), followed by proximal RCA (12.1%) and mid LAD (12.4%). Of 531 single-plaques, 35 plaques (6.6%) showed vulnerable features of both of LDP and PR.

Results: Of 35 single plaques with features of both of LDP and PR, one case showed only an atherosclerotic lesion in their coronary tree, namely single plaque. The excluded patients mostly in minimal LAD (52.7%), followed by proximal RCA (12.1%) and mid LAD (12.4%). Of 531 single-plaques, 35 plaques (6.6%) showed vulnerable features of both of LDP and PR.

Conclusions: Although previous studies revealed that LDP with PR was vulnerable feature of a coronary plaque in patients with advanced coronary artery disease (CAD), in the present study, our data suggests that CCTA verified vulnerable features of coronary plaque, LDP and PR, do not provide predictive value of plaque rupture in patients with quite early CAD.

P6318 | BEDSIDE

Diagnostic performance of combined computed tomography perfusion in coronary artery disease

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Background: Computed tomography perfusion (CTP) combined with computed tomography angiography (CTA) is an emerging methods that can provide anatomical and physiological information by one time examination. However, appropriate patient selection criteria of CTP is not well known.

Purpose: To assess the clinical implication of CTA+CTP over CTA.

Methods: We prospectively enrolled 19 coronary artery disease patients (67.0±9.8 years, male 73.7%) who were referred for clinically indicated CTA+CTP. The accuracy of CTA alone and CTA+CTP for diagnosis of ischemia was compared with SPECT or FFR as reference. We also compared the accuracy of SPECT and CTA+CTP for diagnosis of significant stenosis with quantitative coronary angiography as reference.

Results: For diagnosis of ischemia, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy were 100%, 6.8%, 31.3%, 100%, and 42.1%, respectively in CTA, and were 80.0%, 92.9%, 80.0%, 92.9%, and 89.5%, respectively in CTA+CTP. For diagnosis of significant stenosis, sensitivity, specificity, PPV, NPV, and accuracy were 66.7%, 87.5%, 85.7%, 70.0%, and 68.4%, respectively in SPECT, and were 88.9%, 87.5%, 89.9%, 87.5%, and 88.2%, respectively in CTA+CTP.

Conclusions: CTA+CTP improved specificity and PPV for diagnosis of ischemia compared with CTA by decreasing false positive especially in calcified lesion. CTA+CTP also improved sensitivity and NPV for diagnosis of significant stenosis compared with SPECT by decreasing false negative especially in multi vessel or small vessel lesion due to the superior spacial resolution.

P6319 | BEDSIDE

New algorithm for real time cardiac computed tomography and coronary angiography image registration as a tool for chronic total occlusion intervention

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Background: Chronic total occlusions (CTO) guide software (prototype, SIEMENS) provides online navigational guidance in the CTO percutaneous coronary intervention (PCI) through the display of computed tomography angiography (CTA) image information as a 3D roadmap side-by-side with live angiography images. The CTA image orientation is synchronized with the C-arm, which also allows the selection of the ideal treatment projection angle without additional contrast medium or radiation exposure.

Objective: The aim of this study is to evaluate the benefit of the use of this novel system for CTO PCI.

Methods: A total of 258 patients, who underwent PCI for CTO lesions from September 2010 to December 2013, were included in this study. We divided two groups, Group A: 30 patients with and Group B: 228 patients without CT guidance. We compared procedural success rate, the amount of contrast media and the consumption of radiation exposure between two groups.

Results: There were not significant differences of baseline patient characteristics between group A and B: the prevalence of diabetes mellitus (43.3% vs. 41.2%, P=0.845), hypertension (80.0% vs. 74.0%, P=0.655) and chronic kidney disease (16.7% vs. 29.5%, P=0.194). Success rate of CTO coronary interventions (78% vs. 75%, P=0.55) and the amount of contrast media (183±63 vs. 189±84, P=0.705) did not differ between two groups, whereas radiation exposure was significantly reduced in CT-guided PCI group (1033.7±188.7 vs. 1904.3±126.1, P=0.006).

Conclusions: CT-guided PCI using CTO guide software significantly reduced the total consumption of radiation exposure while maintaining the success rate. Further studies are warranted.

P6320 | BEDSIDE

Distribution and predictors of direct costs of acute heart failure in Greece: a social security system perspective

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Introduction: Heart failure management constitutes a significant economic burden for the health care systems across Europe, accounting for 1% to 3% of total health care expenditures. Usually, this cost is covered mainly by the social security systems as it is true for Greece.

Purpose: The objective of this study was to estimate the total direct cost and the distribution of costs for the management of acute heart failure (AHF) from the Greek social security system perspective, as well as to identify which factors increase these costs.

Methods: Economic and outcomes data were extracted from the ESC Heart Failure Pilot Survey. Eight different secondary and tertiary cardiology departments across Greece have participated in this registry and recruited 177 patients hospitalized for AHF. The analysis was conducted from the Greek social security system perspective with 2014 as reference year. Only direct costs have been estimated including costs of hospitalisations, medications, other relevant cardiovascular interventions, clinical and laboratory follow-up, for up to one year after the index hospitalisation.

Results: The mean annual economic burden of the social security system per patient was estimated at €4,755±3,921, which accounts for more than a 25% of the national gross domestic product per capita. The mean costs of the index hospitalisation with a median 7-day length of stay was €2,292±3,092 and the mean annual costs after the index hospitalization was €3,067±5,271. About 67.5% of the latter was associated with in-patient care, 16.1% with drug treatment and 12.5% with laboratory monitoring. Physicians’ costs accounted for only 3.9% of
the AHF outpatient management costs. Hospitalisation and total costs were significantly higher in male patients with reduced ejection fraction, renal dysfunction and atrial fibrillation \((p<0.05)\). Other significant independent predictors of the total cost were anaemia, uncontrolled hypertension and increasing levels of TSH.

### Conclusion
AHF imposes a significant economic burden for the Greek social security system and national economy, mainly because of the often, long and costly hospitalisations. It is particularly important for the decision makers to have an estimate of the costs attributed to AHF, as they will have to plan and finance the care of the aging population.

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### P6321 | BEDSIDE
Growth and geographical variation in the use of cardiac imaging in Australia may reflect ineffective utilisation

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**Background:** Growth rates and regional differences in the use of cardiac imaging are potential metrics of quality of care. The medical, social and service delivery correlates of high and low use may identify clues to an equitable provision of services. This study sought to define growth and regional variation in outpatient cardiac imaging in Australia.

### Methods: Analyses
Based on the rate of outpatient transthoracic (TTE), transesophageal (TEE) and stress echocardiography (SE) and single-photon emission computed tomography (SPECT) per 100,000 people in each Medicare Local (ML) in Australia. Numbers of tests from 2002–13 were obtained from Medicare Australia; number of doctors was obtained from the Health Workforce data and demographic data (total population, rural areas, and quintiles of disadvantage) were obtained from census data. Statistical analysis was performed using negative binomial regression.

### Results:
Over the last eleven years, TTE reimbursements/100,000 people rose from 1,780 to 3,497 (a 96% increase, 8.8% annualized growth per year), TEE from 33 per 1,000 (2002) to 99 (2013) and SPECT from 287 to 337. SE has the biggest increment (from 181 to 947), a total growth of 423% with an average growth rate of 38.5% per year. The relationships between the use of each cardiac imaging and demographics (mean age, gender, proximity to big cities, socio-economic level) and medical factors (cases per patient, outpatient tests reimbursed in 2012). The rate of TTE (age corrected) per 100,000 people varied from 382.8 to 7,184; TEE from 0 to 242; SE from 0 to 2,991 and SPECT from 0 to 955.8 tests per 100,000 people. The main correlate of TTE and TEE use per capita appears to be the number of doctors per 1,000 people \((B=1.23 \ [97.5\% CI 1.16–1.31] \ p<0.01; B=1.14 \ [97.5\% CI 1.13–1.15] \ p<0.01\); respectively), independent of regional burden of cardiovascular disease and social determinants. However, women were additionally associated with the use of TTE \((B=1.13 \ [97.5\% CI 1.01–1.26] \ p<0.03)\). The use of TEE seems to be less frequent when people with cardiovascular disease should be tested in outpatient environments \((B=0.98 \ [97.5\% CI 0.97–0.98] \ p<0.01)\). For SPECT, women, living in regional areas and doctors are the main drivers for testing \((B=2.24 \ [97.5\% CI 1.69–2.98] \ p<0.01; B=6.14 \ [97.5\% CI 3.06–12.32] \ p<0.01; B=1.13 \ [97.5\% CI 1.02–1.25] \ p<0.02\). Interestingly, SPECT was negatively associated with increasing age in 2013 \((B=0.74 \ [97.5\% CI 0.64–0.87] \ p<0.001)\). The Conclusion: Variation in the use of TTE in Australia is not illness-related and may be evidence of under- and over-utilization. An appropriate use process may be tested in outpatient environments \((B=0.98 \ [97.5\% CI 0.97–0.98] \ p<0.01)\). This study sought to define growth and regional variation in outpatient cardiac imaging in Australia.

### P6322 | BEDSIDE
Coronary artery calcification, left atrial, and left ventricular size measured from non-contrast cardiac CT predict incident heart failure hospitalization in the general population

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### Background:
Non-contrast cardiac computed tomography (CT) is increasingly used to assess risk of future cardiovascular events by detecting atherosclerotic disease and the presence of coronary artery calcifications (CAC).

### Methods:
Analyses were based on the rate of cardiac CT imaging in Australia. Numbers of tests from 2002–13 were obtained from Medicare Australia; number of doctors was obtained from the Health Workforce data and demographic data (total population, rural areas, and quintiles of disadvantage) were obtained from census data. Statistical analysis was performed using negative binomial regression.

### Results:
Over the last eleven years, CAC, LA and LV area were measured from axial images and CAC was quantified by the Agatston score. We describe means of LA and LV size as median (IQR) and CAC score for subjects with and without incident hospitalization. Cox-regression analysis determined the association of each CT-measure with incident HF hospitalization in unadjusted and HEART-score adjusted analysis. Hazard ratios (HR) and 95% confidence intervals are shown per standard deviation of LA/LV area and increase in log (CAC+1) by 1.

### Conclusion:
LA size, LV size, and CAC-score as measured from non-contrast cardiac CT are associated with incident HF hospitalization in the general population. Once cardiac CT is performed, quantification of LA and LV size in addition to CAC-score may identify subjects at early and subclinical stages of HF that qualify for further cardiac workup.

### P6323 | BEDSIDE
Cost evaluation and comparison of three decision strategies for cardiac revascularization: results of the suspected CAD protocol of the European CMR registry

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### Background:
The public health burden of coronary artery disease (CAD) is important. Perfusion cardiac magnetic resonance (CMR) is generally accepted to detect and monitor CAD. Few studies have so far addressed its costs and cost-effectiveness.

### Objectives:
In a large CMR registry the costs of a CMR-guided strategy vs two hypothetical invasive strategies for the diagnosis and the treatment of patients with suspected CAD.

### Methods:
In 3'647 patients with suspected CAD included prospectively in the EuroCMR Registry (59 centers; 18 countries) costs were calculated for diagnostic examinations, revascularizations as well as for complication management over a 1-year follow-up. Patients with ischemia-positive CMR underwent an invasive CMR, cardiac death and non-fatal myocardial infarctions occurred in 0.38%/y. In a hypothetical arm, the same proportion of ischemic patients and outcome was assumed as for the CMR+CXA strategy. The coronary stenosis - FFR Registry relationship in the literature was used to derive the proportion of patients with ≥50% diameter stenoses (=CXA+FFR strategy). To model this hypothetical arm, the same proportion of ischemic patients and outcome was assumed as for the CMR+CXA strategy. The coronary stenosis - FFR relationship reported in the literature was used to derive the proportion of patients with ≥50% diameter stenoses (Psten) in the study cohort. The costs of a CXA-only strategy were also calculated. Calculations were performed from a third party perspective for the German, UK, Swiss, and US healthcare systems.

### Results:
The CMR+CXA strategy reduced costs vs the CXA+FFR strategy by 14%, 34%, 27%, and 24% in the German, UK, Swiss, and US context, respectively. In contrast vs the CMR-CXA strategy, ischemia-negative patients by CMR, cardiac death and non-fatal myocardial infarctions occurred in 0.38%/y. In a hypothetical invasive arm the costs were calculated for an initial FCA followed by FFR testing in vessels with ≥50% diameter stenoses (=CXA+FFR strategy). This modelled this hypothetical arm, the same proportion of ischemic patients and outcome was assumed as for the CMR+CXA strategy. The coronary stenosis - FFR relationship reported in the literature was used to derive the proportion of patients with ≥50% diameter stenoses (Psten) in the study cohort. The costs of a CXA-only strategy were also calculated. Calculations were performed from a third party perspective for the German, UK, Swiss, and US healthcare systems.

### Conclusions:
A CMR+CXA strategy to manage patients with suspected CAD is less costly than a hypothetical invasive CXA+FFR strategy when applied 1) in a real-world registry with a low to intermediate prevalence of disease, and 2) for diagnostic work-up, treatment, and complication management are taken into account. These findings warrant further confirmation in prospective cost-effectiveness trials.
P6324 | BEDSIDE
Long-term clinical impact of coronary CT angiography in patients with recent acute-onset chest pain
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Background: The prognostic implications of a coronary computed tomographic angiography (CCTA)-guided treatment strategy has not been compared in a randomized fashion to standard care in patients with chest pain.

Purpose: To investigate the long-term clinical impact of a CCTA-guided treatment strategy in patients with recent acute-onset chest pain, as compared to standard care.

Methods: Patients referred with acute chest pain but normal electrocardiogram and troponins were randomized to treatment guided by either CCTA or standard care (bicycle exercise echocardiography or myocardial perfusion imaging). The primary endpoint was a composite of cardiac death, myocardial infarction (MI), hospitalization for unstable angina pectoris (UAP), elective revascularizations and readmission for chest pain.

Results: We randomized 299 patients to the CCTA-guided strategy and 301 to standard care. After inclusion 24 patients withdrew their consent. The median (interquartile range) follow-up duration was 18.7 (16.8–20.1) months. In the CCTA-guided group 30 patients (11%) suffered a primary endpoint versus 47 patients (16%) in the standard care group; p=0.04, hazard ratio (95% confidence interval) 0.62 (0.40–0.98). A major adverse cardiac event (cardiac death, MI, hospitalization for UAP and elective revascularization) was observed in 5 patients in the CCTA-guided group versus 14 patients in the standard care group, p=0.04, hazard ratio =0.36 (0.16–0.95). Events over time are illustrated in Figure 1.

Conclusion: A CCTA-guided treatment strategy appears to improve clinical outcome in patients with recent acute-onset chest pain and normal electrocardiogram and troponins, as compared to standard care with a functional test.

P6325 | BEDSIDE
Is there a structural basis for vasovagal syncope? Cardiac functions in patients with vasovagal syncope
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Introduction: The pathophysiology of vasovagal syncope is not completely understood. In this study we aimed to evaluate the baseline echocardiographic parameters in patients with vasovagal syncope with special focus on RV and RA functions.

Materials and methods: We evaluated 42 patients with vasovagal syncope (VVS) and 41 age and sex matched healthy subjects. Patients with at least two syncopal attack and positive head-up tilt test were enrolled in the study. All of the study participants undergone comprehensive echocardiographic examination early in the morning in fasting state.

Results: Among left ventricular function parameters, there were no significant differences between groups. Right ventricular functional parameters also did not significantly differ between groups except for the maximal pulmonary systolic flow (PVmax). PVmax was significantly lower in VVS group compared to control group. Right atrial area (RAA) was significantly higher and ratio of tricuspid filling velocities (E/At) was significantly lower in VVS group. On multivariate analysis the independent predictors of vvs were found as PVmax (OR: 0.05, 95% CI: 0.004–0.751 p: 0.03) and E/At (OR: 0.238, 95% CI: 0.065–0.874, p: 0.03).

Conclusion: The findings of this study indicate a subtle right atrial diastolic dysfunction in patients with VVS. Decreased right atrial contribution to RV filling may cause, a lower RV stroke volume which explains the lower PVmax values in our VVS group. All together, these findings may serve for a tendency to low output states and hypotension as in VVS.

P6326 | BEDSIDE
Improvement of ventricular contraction and dyssynchrony in patients with idiopathic ventricular arrhythmias undergoing catheter ablation
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Background: Idiopathic ventricular arrhythmias (VA) possess the risk of VA-related cardiomyopathy and catheter ablation offers beneficial effect. Three-dimensional echocardiography (3DE) has been used for evaluation of mechanical contraction and dyssynchrony in cardiac resynchronization therapy but rarely in patients with VA. We postulated that 3DE could demonstrate improved mechanical contraction and dyssynchrony in VA after ablation.

Methods: A total of 20 patients with VA and normal LVEF underwent ablation were enrolled after excluding structural heart disease, and received 3DE before and 6 months after ablation. The speckle tracking analysis was performed offline with commercial software provided with the Artida Echocardigraphy.

Results: There was no difference of ejection fraction (EF) before and after ablation, while significantly increased circumferential strain (−22.8±6% vs. −17.1±4.8%, p<0.001) and longitudinal strain (−11.7±4.8% vs. −6.2±3.0%, p<0.001) were found after ablation. Dyssynchrony of ventricular contraction also improved after ablation, reflecting by lower standard deviation of time to peak radial and circumferential strain.

Table 1. Echocardiographic parameters before and after ablation

Variable | Before ablation | After ablation | P value
--- | --- | --- | ---
Ejection fraction, % | 57.8±6.5 | 60.0±3.9 | 0.080
Radial strain (RS), % | 21.6±11.6 | 27.4±7.6 | 0.029
Radial dyssynchrony index, sec | 125.7±44.8 | 80.5±32.0 | 0.026
Circumferential strain (CS), % | −22.8±8.3 | −28.2±4.5 | 0.015
CS dyssynchrony index, sec | 78.8±32.8 | 50.9±20.1 | 0.025
Longitudinal strain (LS), % | −11.7±4.8 | −16.2±3.0 | 0.001
LS dyssynchrony index, sec | 111.7±65.0 | 84.7±33.0 | 0.147
Torsion, % | 1.3±1.1 | 1.1±1.0 | 0.278
Torsion dyssynchrony index, sec | 131.3±84.7 | 138.1±81.6 | 0.877
Twist, degrees | 5.3±3.1 | 4.4±3.2 | 0.425
Twist dyssynchrony index, sec | 120.8±74.5 | 163.7±101.4 | 0.262

Conclusion: Despite comparable ejection fraction before and after ablation, significant improvement of mechanical contraction and dyssynchrony was noted by 3DE analysis.

P6327 | BEDSIDE
The role of quality improvement approach on reducing systematic errors in echocardiographic hemodynamic parameters assessment
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Background: Accurate assessment of cardiac structures, ventricular function, and hemodynamics are the primary goal of any echocardiographic laboratory. Quality Improvement (QI) processes described by the American Society of Echocardiography (ASE) and the Intersocietal Accreditation Commission (IAC) should be instrumental in reaching this goal. However no studies so far validated this approach to show the expected impact on echocardiography interpretation.

Purpose: To determine whether a QI process following the IAC and ASE guidelines will have an impact on the quality of echocardiography interpretation in a busy community hospital.

Methods: All patients undergoing transthoracic echocardiogram (TTE) followed by cardiac catheterization within 24 hours at Christiana Care Health System in 2011 and 2012 were identified, with 126 and 133 cases respectively. Hemodynamics parameters of left Ventricular Systolic Pressure (LVSP), Pulmonary Artery Systolic Pressure (PASP), average E/E' and RA pressures on TTE correlated poorly with catheterization in 2011. An educational process developed on the basis of ASE and IAC recommendations was institutionalized to identify frequently encountered errors and to provide methods for improved performance at quarterly QI meetings. The process included binominal lectures for technologists, fellows and attendings concentrating on the common errors encountered as well as personalized feedback. The hemodynamic parameters were then re-examined in 2012 post-intervention.

Results: Following a teaching intervention in 2012, there was noted improvement amongst the following parameters on TTE and their catheterization correlates in 2012 vs. 2011. There was significant improvement in the correlation between invasive and echocardiographic hemodynamic measurements in both diastology (68% vs 95% (p<0.001)), and RA pressures (33% vs 21% (p<0.04) respectively. Similarly there was a significant improvement in correlations between echo and cath LVEF (R2=0.77 vs R2=0.71; p<0.001) as well as average E/E' and LVEDP (R2=0.39 vs R2=0.20, p=0.006) in 2012 compared to 2011 and a trend to
These findings suggest that TNF produced by the cardiomyocyte

**Conclusion:**

size of cmTNF−/− hearts (56±1%) compared to I/R (55±1%, p=ns). In isolated
diomyocyte is required to mediate the beneficial effect of IPost.

Results:

Body weight (32.8±0.8 versus 32.6±0.7 g) and heart weight-to-tibia

**Acknowledgement/Funding:** Department’s sources

**Methods and results:** Cardiomyocytes derived from neonatal SD rats were subjected to 35 min global ischemia/45

methods were such as hypoxia or no reperfusion (NP). Expression of

P6331 | BENCH

Hypoxia/reoxygenation could shift microRNA-150 from inhibition to

Methods:

**Conclusion:**

In the present study, the effects of miR-19a on cardiac autophagy were evaluated by treatment of H9c2 cardiomyocytes with a hypoxic environment. The results demonstrated that miR-19a significantly inhibited the expression of Bim, a key pro-apoptotic protein, and promoted autophagy markers such as LC3-II and Beclin-1. These findings imply a potential role of miR-19a in modulating cardiac autophagy and apoptosis.

H9c2 cells were treated with hypoxia for 24 hours followed by a 48-hour reoxygenation period. The expression levels of Bim and autophagy markers were assessed using qRT-PCR and Western blotting. The results showed that miR-19a mimic significantly reduced the expression of Bim and increased the levels of autophagy markers, while the expression of miR-19a inhibitor had the opposite effects.

Furthermore, the apoptosis assay revealed that miR-19a mimic decreased the percentage of apoptotic cells, whereas the miR-19a inhibitor increased the apoptosis rate. These results suggest that miR-19a plays a crucial role in regulating cardiac autophagy and apoptosis through modulating the expression of Bim.

In conclusion, our findings indicate that miR-19a could be a potential therapeutic target for cardiac protection against hypoxia-induced apoptosis by promoting autophagy.

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**References:**


P6332 | BEDSIDE
Effect of remote ischemic preconditioning on extracellular vesicles in patients with acute ST-elevation myocardial infarction
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Background: Remote ischemic preconditioning (RIPC) before primary percutaneous coronary intervention (PCI) reduces myocardial injury and adverse cardiac events. Endothelial cell-derived extracellular vesicles (EVs) are associated with inflammation, coagulation, and the development of vascular disease. We hypothesized that the mechanisms of RIPC are associated with changes in the levels of EVs.
Purpose: The aim of the current study was to assess the effect of RIPC on the numbers of EVs in the blood of patients with ST-elevation myocardial infarction (STEMI).
Methods: Forty-eight patients with STEMI were randomly divided into two groups: those who would receive RIPC and those who would not receive RIPC. Intermittent arm ischemia-reperfusion through four 5-minute cycles of inflation/deflation with a blood-pressure cuff to 200 mm Hg prior to primary PCI. Blood samples were collected from some of the patients before and after PCI. EVs were captured with 15-nm magnetic nanoparticles coupled with antibodies specific for different membrane antigens. We evaluated in patients’ blood platelet-derived EVs (CD31-captured CD42+CD123-CD42-MHC class-I+), and endothelial-derived EVs (CD31-captured CD42-MHC class-I+) using an original nanotechnology-based assay for analysis of the antigenic composition of individual EVs.
Results: There was no significant difference in the number of EVs at admission between the two groups. In patients who had received RIPC, there was a significant decrease, by 37.8% and 30.0%, respectively, in the numbers of platelet-derived EVs (CD31-captured CD42+MHC class-I+) and endothelial-derived EVs (CD31-captured CD42-MHC class-I+) in comparison with a significant increase in the numbers of EVs (p<0.01 and p<0.05, respectively, in patients without RIPC).
Conclusion: Remote ischemic preconditioning prior to primary PCI decreases the numbers of both platelet-derived and endothelial-derived EVs in STEMI patients. This decrease in the numbers of EVs can have an important bearing on the effects of RIPC.
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P6333 | BENCH
Mechanical stretch induces apoptosis regulator trb3 in cultured cardiomyocytes and volume-overloaded heart
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Aims: The expression of TRB3 (tribles 3), an apoptosis regulated gene, increases during endoplasmic reticulum (ER) stress. How mechanical stretch affects the regulation of TRB3 in cardiomyocytes during apoptosis is not fully understood. We hypothesized that cardiomyocytes apoptosis induced by cyclic stretch is TRB3 dependent.
Methods and results: neonatal rat cardiomyocytes grown on a flexible membrane base were stretched by vacuum to 20% of maximum elongation at 60 cycles/min. In an in vivo model of aorta-caval shunt in adult rats was used to investigate TRB3 expression. Cyclic stretch significantly increased TRB3 protein and mRNA expression. Addition of c-jun N-terminal kinase (JNK) inhibitor SP600125, JNK siRNA and TNF-alpha antibodies reduced the induction of TRB3 protein induced by stretch. Cyclic stretch induced the DNA-binding activity of growth arrest and DNA damaged inducible gene-153 (GADD153) by electrophoretic mobility shift assay. SP600125, JNK and siRNA, TRB3 protein expression was enhanced by stretch was inhibited by the addition of TRB3 siRNA. An in vivo model of aorta-caval shunt in adult rats also demonstrated the increased TRB3 protein expression in the myocardium.
Conclusion: Cyclic stretch-induced TRB3 expression in cultured rat cardiomyocytes. The stretch-induced TRB3 is mediated by TNF-alpha, JNK and GADD153 pathway. These results indicate that TRB3 plays an important role in stretch-induced cardiomyocyte apoptosis. TRB3 is also enhanced by volume overload in rat myocardium.

P6334 | BENCH
Role of Two-pore channels in cardiac autophagy
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Introduction: Two-pore channels (TPCs) were initially identified as a novel family of nicotinic acid adenine dinucleotide phosphate (NAADP)Ps. It has been recently demonstrated that TPCs can couple the cell’s metabolic state to endolysosomal function, and some authors have suggested that they can regulate autophagy processes in several tissues. Autophagy has been implicated in the pathogenesis of a wide range of cardiovascular pathologies, including heart failure. In previous studies, we found that blocking human left-ventricular mycardium, we have found correlated alterations in gene expression of TPC1 and TPC2 and markers of metabolism and cell viability.
Purpose: Since metabolic remodeling in heart failure is also associated with changes in autophagy, our aim was to clarify if TPCs play a role in cardiac autophagy regulation.
Methods: Neonatal rat cardiomyocytes were knockdown using a small interfering siRNA for TPC1, TPC2 and TPC1/2. 24 hours after transfection, cells were infected with adenovirus expressing GFP-LC3 and subsequently starved. Confocal microscopy was used to study LC3 puncta. Western blot was carried out to identify possible changes in LC3II/I and p62 accumulation by these conditions. Electron microscopy was used to determine the lysosome number and diameter in cardiac tissue of TPC1/2 knockout vs. wt mice.
Results: TPC1 and TPC2 but not TPC1 knockdowns induced an increase in LC3-puncta (p<0.001, n=4) and LC3II/I basal protein levels (p<0.01, n=5), while only TPC1 knockdown provoked statistically significant changes in starvation-induced LC3-puncta (p<0.05, n=4) and LC3II/I protein levels (p<0.05, n=5). Importantly, a significant increase in p62 levels was caused by the knockdown of TPC2 (p<0.01, n=5) and TPC1/2 (p<0.05, n=5) under basal conditions, and by TPC1 (p<0.05, n=5), TPC2 (p<0.05, n=5) and TPC1/2 (p<0.05, n=5) knockdown in starvation-induced conditions. Finally, an increase in the lysosome number and diameter was observed in cardiac tissue of TPC1/2 knockout (n=3) vs. wild type (n=3) mice.
Conclusion: TPCs seems to have a key role not only in autophagy initiation but also in autophagy progression as it was shown by the accumulation of p62. All these results point to a crucial role of TPCs in cardiomyocyte autophagy regulation, a mechanism that is involved in the pathophysiology of some cardiovascular diseases.

P6335 | BENCH
Biological pacemaker created by HCN4-overexpressing mouse embryonic stem Cell-derived cardiomyocytes
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Background: To establish a biological pacemaker, enhancement of the funny current (I(f)) flowing through hyperpolarization-activated cyclic nucleotide-gated (HCN) channels and attenuation of the inward rectifier current (I(K1)) flowing through inward rectifier potassium (Kir) channels are needed. Therefore, we generated HCN4-overexpressing mouse embryonic stem cells (mESCs) and induced cardiomyocytes that originally show poor I(f). We investigated whether HCN4-overexpressing mESC-derived cardiomyocytes (mESC-CMs) function as a biological pacemaker.
Methods and results: The rabbit Hcn4 gene was transcribed into mESCs, and stable clones were selected. The mESC-CMs were generated via embryoid body (EB) formation under serum-free and lactate-supplemented conditions. Approximately 90% of the purified cells were troponin-I-positive by immunostaining. In mESC-CMs, the expression level of Kcnj2, which encodes Kir2.1 current (I(K1)) and the density of HCN4-overexpressing mESC-CMs demonstrated that HCN4 functions are increased. We established HCN4-overexpressing mESC-CMs that show phenotypical characteristics of cellular pacemakers. HCN4-overexpressing mESC-CMs showed a greater firing rate than HCN4-overexpressing mESC-CMs. The beating rate of HCN4-overexpressing mESC-CMs responded to ivabradine and isoproterenol.
Conclusions: We established HCN4-overexpressing mESC-CMs that show spontaneous beating and responses to drugs. The results show the positive
sibility of application of HCN4-overexpressing stem cell-derived cardiomyocytes as a biological pacemaker.

P6336 | BENCH

Relationship of cardiac IL33/ST2 system with natriuretic peptide system and inflammation in an experimental model of obesity

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Background: Obesity is a well-known risk factor of cardiovascular disease (CVD). Interleukin (IL)-33 acts via its receptor ST2 and is involved in the pathogenesis of inflammatory disorders including CVD. Recently there was also talk of its involvement in obesity.

Purpose: The aim of this study was to investigate cardiac alterations of IL33/ST2 system in obesity and its relationship with natriuretic peptides (NP) system as well as inflammatory mediators.

Methods: Cardiac mRNA expression of IL-33/ST2 system was evaluated by Real-Time PCR in cardiac biopsies from n=27 obese Zucker rats (O) and n=20 controls (CO). In the same sample groups, NPs and receptors were considered to assess cardiac function and IL-6 together with TNF-alpha to evaluate inflammatory process.

Results: Significantly lower mRNA levels of the soluble ST2 (sST2) were observed in O compared to CO [O: 0.990±0.685 (mean±standard deviation); CO: 3.29±3.23; p=0.034], while no significant difference for ST2L (transmembrane isoform), IL-33 and IL-1TRACP was detected. Correlations between IL-33/ST2 system and NP systems and inflammatory mediators is reported in table 1.

Conclusions: Expression of sST2 in cardiac tissue decreased by obesity. The strong relationships with NP systems and inflammatory mediators could suggest a role for IL33/ST2 system in cardiac mechanisms associated to obesity.

P6337 | BENCH

IL-33/ST2 in angiogenesis and limb ischemia in mice

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Aim: Interleukin (IL)-33 is a cytokine that reportedly acts as danger signal released from cells after injury. Once released, IL-33 binds to the ST2 receptor present on the plasmaeema. The IL-33/ST2 signalling has been shown to induce angiogenesis, but the signaling of inflammatory disorders. However, the role of IL-33/ST2 in post-ischemic angiogenesis is still unexplored. IL33 availability can be compromised by a soluble form of ST2 (sST2) that act as a decoy receptor. We previously showed that high plasmatic levels of sST2 are correlated with severity of critical limb ischemia (LI) in diabetic patients. Here, we have studied the effect of secreted IL-33 on cardiac endothelial cells (ECs) and the impact of ST2 gene therapy and IL-33 gene therapy in post-LI blood flow recovery and angiogenesis in mice.

Methods: We have developed an adenovirus (Ad.) that allows production of a secretable form of mouse IL-33 (Ad:IL-33) and tested its effect on human umbilical vein ECs (HUVECs) seeded on Matrigel to study their angiogenic responses. Unilateral Li was induced by left femoral artery occlusion in ST2 gene knockout mice and wild-type (WT) mice. The IL-33 gene therapy was performed by in-jecting either Ad:IL-33 or an Ad Null (control) into the ipsilateral adductor muscle. Ischemic and non-ischemic limb muscles were harvested from terminally anaesthetized mice at 3 days post-surgery (n=3 per group). In different mice (n=10–13 per group), post-ischemic Blood Flow (BF) recovery was measured over time by colour Doppler (Doppler-Moore) for up to 3 (gene therapy protocol) or 5 weeks.

Results: HUVECs infected with Ad:IL-33 secrete high levels of IL-33 and showed improved angiogenesis capacities. Expression of IL-33, ST2 and sST2 were increased in ischemic muscles 3 days after Li. In ST2−/− mice, the BF recovery was impaired compared to WT mice (p<0.05 vs. WT controls at 5 weeks). IL-33 gene therapy significantly improved the BF recovery in WT mice (p<0.05, vs. Ad.Null control at 3 weeks), but not in ST2−/− mice (p=NS vs Ad.Null in WT; p<0.05, vs. Ad:IL33 in WT).

Conclusions: The IL-33/ST2 system contributes to post-LI BF recovery. We successfully developed an Ad. for secreted IL-33 that produced angiogenic responses in cultured ECs. IL-33 gene therapy improved post-ischemic functional recovery in the model of Li, dependently of the presence of ST2 receptor in mice.
Results: MiR-223 was downregulated in ET-1 induced hypertrophic CMs and in hypertrophic myocardium compared with respective controls. MiR-223 overexpression in CMs alleviated ET-1 induced hypertrophy, evidenced by smaller cell surface area and downregulated ANP, α-actinin, Myh6 and Myh7 expression. Luciferase reporter gene assay showed that TNNI3K serves as a direct target gene for miR-223. Intracellular calcium was measured by sensitive fluorscent indicator (Fura-2). Video-based edge detection system was employed to measure cardiomyocyte contractility. 

Conclusion: MiR-223 secreted from cardiomyocytes acts as an inhibitor of excess myocardial fibrosis through a paracrine action, negatively correlated with the signature myofibroblast gene, α-SMA. Thus, ARVC5 might result from disrupted mechanotransduction through interactions between S358L-TMEM43 and EMD and SUN2. 

Excessive myocardial fibrosis is a main pathological process in the development of cardiac remodeling and heart failure, it is therefore important to prevent the excessive myocardial fibrosis. By using a microRNA array, we identified miR-378 which was cardia enriched and deeply repressed gene in the early stage of mechanical stress. 

To examine the effects of miR-378 on cardiac fibrosis following mechanical stress, 

Methods and results: Mechanistic stress, which imposed respectively to mice by transverse aortic constriction (TAC) procedure and to cardiac fibroblasts by stretching of the silicon dishes induced significant increases in fibrotic responses including myocardial fibrosis, fibroblasts hyperplasia and proteins and genes expression of collagens and matrix metalloproteinases (MMPs). All these fibrotic responses were attenuated by a chemically modified miR-378 mimic (Agomir) but exaggerated by the inhibitor (Antagomir) which was given to mice for three consecutive days after TAC by intravenous injections and to cells by direct addition to culture medium, respectively. Endogenous miR-378, which was specifically expressed in IHH-myocytes but not in cardiac fibroblasts, could be released from cardiomyocytes during early stage of mechanical stress in an exosome dependent secretory machinery and inhibit fibrotic responses of cardiac fibroblasts. Mechanistically, miR-378-exerted anti-fibrotic effects were partially through suppression of p38 MAP kinase phosphorylation and activation of signal transducers and activators of transcription 3 in cardiac fibroblasts. 

Conclusion: miR-378 secreted from cardiomyocytes acts as an inhibitor of excessive cardiac fibrosis through paracrine mechanism.
P6346 | BEDSIDE
Pre-operative growth differentiation factor 15 (GDF-15) as a novel biomarker of acute kidney injury after cardiac bypass surgery
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Objective: Previously, we demonstrated that preoperative plasma GDF15 levels significantly improved the prognostic value of the EuroSCORE for mortality after cardiac surgery. Despite the strong correlation between GDF15 and renal function, no data are available regarding the potential interest of preoperative GDF15 levels to improve the prediction of acute kidney injury (AKI) after coronary artery bypass grafting (CABG).

Design: 134 patients operated on for CABG of whom 50 underwent off-pump surgery at our university hospital were included in this prospective, observational study. Exclusion criteria were age < 18 years or > 80 years, previous atrial fibrillation/flutter, previous severe renal failure (estimated glomerular filtration rate (eGFR) < 30 ml/min), previous cardiac surgery, and emergency surgery. AKI was defined according to AKIN network criteria. GDF15 levels in plasma were measured at the time of anesthesia and 12 hours after surgery.

Results: 42 and 2 patients were involved in postsoperative AKI which had significantly higher preoperative plasma GDF15 levels (OR=2.85; 95% CI: 1.32–6.13, p=0.008), higher preoperative serum creatinine levels (OR=1.025; 95% CI: 1.003–1.05; p=0.026), and most often underwent cardiopulmonary bypass (CPB) surgery (OR=3.67; 95% CI: 1.11–11.44, p=0.020). On ROC curves, GDF15 was found to be the best preoperative biomarker to predict AKI (AUC 0.83; CI 0.75–0.89, compared with eGFR (AUC 0.67; 95% CI 0.59–0.75 p=0.003) and NT-proBNP (AUC 0.62; CI 0.51–0.72 p<0.001). GDF15 level was also significantly better than the EuroSCORE in predicting AKI (AUC 0.75; CI 0.65–0.84, p<0.001). Our predictive model including high blood pressure, diabetes, preoperative eGFR and CPB surgery was significantly improved when preoperative GDF15 was added.

Conclusion: Preoperative GDF15 plasma levels are associated with postsoperative AKI in patients undergoing CABG. Preoperative GDF15 may improve preoperative risk stratification and discrimination among candidates for surgery.

P6345 | BENCH
Cardiac Ampk alpha 1 promotes Ap-1 activity via Pkc-zea
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Question: AMP-activated protein kinase (Ampk) regulates myocardial energy metabolism and is involved in the response to increased cellular stress. In failing hearts, an isoform shift of the predominant α2 isoform to the α1 isoform was observed.

Purpose: To identify possible isoform specific effects of Ampk1 in cardiomyocyte models.

Methods: Experiments were performed in Ampk1-deficient and corresponding wild-type mice following pressure overload by transverse aortic constriction (TAC) or Angiotensin II infusion and in HL-1 cardiomyocytes. Overexpression of constitutively active Ampk1 increased the phosphorylation of protein kinase C (Pkcζ) constitutively active Ampk1 further increased Ap-1 dependent transcriptional activity and mRNA expression of Ap-1 target genes: c-Fos, Il6 and Ncx1, effects blunted by Pkcζ protein abundance as well as the increase of Ap-1 activity, subunits might therefore modulate cardiac stress signaling.

Conclusion: Preoperative GDF15 plasma levels are associated with postsoperative AKI in patients undergoing CABG. Preoperative GDF15 may improve preoperative risk stratification and discrimination among candidates for surgery.

P6344 | BEDSIDE
Pathological hypertrophy stimulation generates mitochondrial dysfunction and induces the expression of the mitochondrial motor protein KiSIS

Purpose: Mitochondrial dysfunction is observed in many diseases, including cardiovascular syndromes. In late stage heart failure mitochondrial dysfunction has been reported, but it is unclear whether this arises already during cardiac hypertrophy development. We therefore investigated whether a single pathological or physiological hypertrophy stimulus would be able to affect mitochondrial function in vitro and investigate the involved factors.

Methods: Mitochondrial OXPHOS activities were investigated in primary neonatal rat cardiomyocytes (NRVCs) treated with pathological (phenylephrine; PE) and physiological (and insulin growth factor-1, IGF-1) stimuli. Mitochondrial oxidative consumption rate (OCR) was determined with a Seahorse flux analyzer mitochondrial biogenesis and gene expression profiling was performed and KiSIS investigated.

Results: Cardiomyocytes were stimulated with PE and IGF-1, resulting in hypertrophy development as determined by cell size and protein synthesis measurements. In PE treated cells this was accompanied by pathological gene expression (a.o. ANP). OXPHOS measurements revealed that complex II state 3 activity was diminished after PE stimulation only. In contrast, IGF-1 strongly stimulated complex I state 3 activity. The observed changes were not rapid, but developed during 24 hours stimulation. In this time frame no mitochondrial biogenesis was observed and levels of OXPHOS complexes did not alter. Gene array analysis did show minor changes in mitochondrial metabolic gene expression in IGF-1 stimulated cells, whereas in PE treated cells, no obvious changes in metabolic routes were observed. Interestingly, KiSIS a gene reported to control mitochondrial function, was upregulated in PE treated only. Increased expression was confirmed in pathological hypertrophy animal models (TAC, MI), but not in physiological hypertrophy (exercise). Interestingly, in PE treated cells mitochondria were also more dispersed than could be reverted by silencing of KiSIS. This silencing did not improve complex II activity in PE treated cells, but did further diminish it. This indicates that increased KiSIS expression is not responsible for decreased complex II activity, but is rather a compensatory mechanism.

Conclusion: Pathological hypertrophy, induced by a single neurohumoral stimulus is accompanied by mitochondrial dysfunction, whereas physiological stimulation improves mitochondrial function. Increased expression of KiSIS under pathological conditions affects mitochondrial localization and may have a compensatory function.
P6348 | BENCH
Adiponectin attenuates adverse cardiac remodeling following cardiac injury by up-regulating matrix metalloproteinase 9 expression
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Background: Adiponectin (APN) is a multifunctional immunomodulatory adipocytokine that inhibits left ventricular hypertrophy induced by pressure overload as well as hypertension and attenuates fibrosis after myocardial infarction. Coxsackievirus B3 (CVB3) causes severe myocarditis associated with intense extracellular matrix remodeling and susceptibility to atrial and ventricular arrhythmia. Here, we investigate whether APN inhibits adverse ECM remodeling in vitro and in cardiac injury models by affecting matrix metalloproteinase (MMP) expression.

Methods: Cardiac cells were cultured in vitro. Cardiac injury was induced by experimental autoimmune myocarditis, CVB3 infection or myocardial infarction in APN-KO and WT mice. Gene expression and gelatinolytic activity/protein expression of MMPs was quantified by qRT-PCR and zymography, respectively. Activation status of protein kinases was determined by immunoblot. Collagen 1 turnover was assessed by CTXI ELISA.

Results: In cultured cardiac myocytes (CM) and fibroblasts (CF) APN up-regulates MMP-9 gene and protein expression through activation of AMPK and ERK1/2 without affecting MMP-2, MMP-3 and MMP-13 expression levels. Both AMPK and MEK1 control the up-regulation of MMP-9 expression by pro-inflammatory stimuli in cardiac fibroblasts. Accordingly, APN further-enhanced the up-regulation of MMP-9 expression triggered by TNFa, LPS and R848 in CF. Conversely, cardiac fibroblasts from APN-KO mice displayed reduced expression of MMP-9 after stimulation with TNFa, LPS and R848 ex vivo. In line with these observations we also detected attenuated MMP-9 activity in subacute CVB3 myocarditis at day 7 post infection and myocardial infarction. Moreover, splenic MMP-9 expression was also diminished in APN-KO mice at day 7 post-infection correlating with diminished immune cell infiltration in hearts of APN-KO mice. Accordingly, cardiac collagen split product (CTXI) accumulation was significantly reduced in hearts of APN deficient mice in CVB3 myocarditis and following myocardial infarction indicating attenuated collagen turnover 1

Conclusions: Our observations indicate that APN inhibits adverse cardiac remodeling following cardiac injury by inducing MMP-9 expression in resident cardiac and infiltrated immune cells. Persistently enhanced cardiac MMP-9 activity results in increased cleavage of accumulating collagens and augmented ECM turnover that might result in inhibition of fibrosis and cardiac dysfunction.

ION CHANNELS AND ELECTROPHYSIOLOGY

P6349 | BENCH
Nos1AP alters QTc intervals upon overexpression in mice
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Background: Cardiac cells are cultured in vitro. Cardiac injury was induced by experimental autoimmune myocarditis, CVB3 infection or myocardial infarction in APN-KO and WT mice. Gene expression and gelatinolytic activity/protein expression of MMPs was quantified by qRT-PCR and zymography, respectively. Activation status of protein kinases was determined by immunoblot. Collagen 1 turnover was assessed by CTXI ELISA.

RESULTS: In cultured cardiac myocytes (CM) and fibroblasts (CF) APN up-regulates MMP-9 gene and protein expression through activation of AMPK and ERK1/2 without affecting MMP-2, MMP-3 and MMP-13 expression levels. Both AMPK and MEK1 control the up-regulation of MMP-9 expression by pro-inflammatory stimuli in cardiac fibroblasts. Accordingly, APN further-enhanced the up-regulation of MMP-9 expression triggered by TNFa, LPS and R848 in CF. Conversely, cardiac fibroblasts from APN-KO mice displayed reduced expression of MMP-9 after stimulation with TNFa, LPS and R848 ex vivo. In line with these observations we also detected attenuated MMP-9 activity in subacute CVB3 myocarditis at day 7 post infection and myocardial infarction. Moreover, splenic MMP-9 expression was also diminished in APN-KO mice at day 7 post-infection correlating with diminished immune cell infiltration in hearts of APN-KO mice. Accordingly, cardiac collagen split product (CTXI) accumulation was significantly reduced in hearts of APN deficient mice in CVB3 myocarditis and following myocardial infarction indicating attenuated collagen turnover 1

CONCLUSIONS: Our observations indicate that APN inhibits adverse cardiac remodeling following cardiac injury by inducing MMP-9 expression in resident cardiac and infiltrated immune cells. Persistently enhanced cardiac MMP-9 activity results in increased cleavage of accumulating collagens and augmented ECM turnover that might result in inhibition of fibrosis and cardiac dysfunction.

P6350 | BENCH
Cardiac sodium channel mutation associated with epinephrine-induced QT prolongation and sinus node dysfunction
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Background: Long-QT syndrome (LQT) is an inherited arrhythmia characterized by prolonged ventricular repolarization and malignant tacharyrhythmias, LQT1–3 caused by mutations in KCNQ1 (LQT1), KCNH2 (LQT2), and SCN5A (LQT3) accounted for approximately 90% of genotyped LQT patients. Most of the cardiac events in LQT1 occur during exercise, while patients with LQT3 tend to have arrhythmic events during rest or sleep.

Objectives: The purpose of this study is to identify a genetic mutation in a Japanese male who presented sinus node dysfunction and prolonged QT interval during an epinephrine stress test, and also clarify the electrophysiological properties of the mutant channel.

Methods and results: As a result of comprehensive genetic analyses, we identified a heterozygous missense CSN5A mutation, V2016M, which changed the last amino acid of the cardiac sodium channel. Electrophysiological analyses revealed that the mutant channels exhibited a loss-of-function feature, decreased peak sodium current density (WT, 175 ± 17.6 pA/pF; V2016M, 97 ± 16.0 pA/pF, p < 0.01, Figure A). In addition, the mutant channels showed gain-of-function features: increased late sodium currents by protein kinase A activation (WT, 0.07±0.01%; VM, 0.17±0.03%; p=0.05, Figure B), and impaired inactivation of sodium channels by protein kinase A or C activation.

Conclusions: We identified an SCN5A mutation in a patient with sinus node dysfunction and epinephrine-induced QT which was an atypical phenotype for LQT3. Electrophysiological analyses indicated that this mutation presented both loss-of-function and gain-of-function features. The latter was observed by adrenergic stimulation. The electrophysiological properties of the mutant channels might be associated with the overlapping clinical features of the patient.

P6351 | BENCH
Abnormal expression of cardiac ion channels-associated genes in lamin A/C-related cardiomyopathy-specific induced pluripotent stem cell derived cardiomyocytes
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Lamin A/C gene, LMNA, encodes nuclear membrane proteins, lamin A and C, and laminas interact with numerous gene regulators and modulate gene expression levels. The mutations in LMNA are associated with familial dilated cardiomyopathy (DCM) with cardiac conduction system disease (CCD) and malignant ventricular arrhythmias, but causal mechanisms is still unclear. Induced pluripotent stem cells (iPSC) offer an opportunity to model human diseases in relevant cell types, and it is useful to reveal mechanisms of genetic disease development.

We generated iPSCs from fibroblasts obtained from a 52-year-old Japanese male with lamin A/C cardiomyopathy and CCD carrying a deletion mutation (p.S363S365del) in LMNA. iPSCs were differentiated into cardiomyocytes and analyzed at 40 days after cardiac differentiation. Gene expression analysis showed decreased LMNA mRNA levels in the patient-specific iPSCs-derived cardiomyocytes (LMNA-iPSC-CMs) by half compared to control-iPSC-CMs, suggesting that haploinsufficiency due to nonsense-mediated mRNA decay was the underlying cause. With regard to the cardiac ion channels-related genes, the expression of HCN4, that is required for the generation of pacemaker potentials (If current), was down-regulated in LMNA-iPSC-CMs compared to control-iPSC-CMs (0.51±0.14; p=0.0017, Figure 1). The spontaneous beating rate in LMNA-iPSC-CMs was significantly slower than that of control-iPSC-CMs (23.1±8.7 vs 61.9±31.2; p<0.001, Figure 2).

Human iPSC-based model of LMNA-related cardiomyopathy showed the low ex-
**P6352 | BENCH**

** PITX2c deficiency augments anti-arrhythmic effects of sodium channel blockers: results in a mouse model and validation in a simulation study of the human atrium**

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**Background and objectives:** Polymorphisms close to the PITX2 gene on chromosome 4q25 are associated with incident and recurrent atrial fibrillation (AF). Carriers of variant rs10033464 respond relatively well to antiarrhythmic therapy with sodium channel blockers. To test whether reduced atrial PITX2 mRNA expression alters the electrophysiological effect of sodium channel blockers, we studied the effect of flecainide (Flec) in mice with heterozygous PITX2c gene deletion, a model for reduced Pitx2 mRNA expression and AF susceptibility.

**Methods:** We assessed the effect of 1 μM Flec on left atrial (LA) monophasic, transmembrane and optical action potentials in Pitx2c−/− mice and their wild-type (WT) littermates. We measured conduction velocity (CV), action potential duration (APD), AP amplitude (APA), maximum upstroke velocity (dV/dtmax) and resting membrane potential (RMP) during atrial pacing at 80–120ms fixed-rate cycle lengths (CL); and effective refractory periods (ERP) with arrhythmia inducibility during programmed (S2) stimulation. Post-repolarisation refractoriness (PRR) was defined as the difference between ERP and APD90. Using simulations of conduction with the Courtemanche human atrial model, we assessed whether the electrophysiological changes associated with reduced Pitx2 mRNA expression altered the response to sodium current (INa) block.

**Results:** Flec abolished arrhythmias in Pitx2c−/− (8/18 base vs 0/15 Flec, p < 0.05) but less so in WT atria (3/35 base vs 3/12 Flec). Pitx2c−/− atria had a higher resting membrane potential (WT −70±1.7mV, n = 30 cells vs Pitx2c−/− −68±1.3mV, n = 23 cells, p < 0.05) and lower APA (WT 78±1.2±1.3, n = 30; Pitx2c−/− 71±1.3, n = 32). Flec had no effect on the RMP and reduced CV, APA and Vmax in both genotypes. Flec doubled the ERP increase in Pitx2c−/− atria compared to that for WT (V1/2 for Pitx2c−/−: 47±1.3, n = 32 vs 14±2ms, n = 13 vs WT 7±2ms, n = 10; p < 0.05). However, no significant changes were observed in the recovery from fast inactivation and fast inactivation rate. Steady-state inactivation curve, assessed after 500ms depolarizing pulses, for Pitx2c−/− was remarkably delayed compared to that for WT (V1/2 for Pitx2c−/−: −110.7±0.8mV, n = 16; WT: −85.0±5.2mV, n = 17, p < 0.01). Steady-state fast inactivation curve, assessed after 20ms depolarizing pulses, for Pitx2c−/− was also shifted to the same degree. Recovery from fast inactivation after 20ms depolarizing pulses for Pitx2c−/− was remarkably delayed compared to that for WT (tau for Pitx2c−/−: 246.7±14.3ms, n = 8; WT: 3.7±0.3ms, n = 8, p < 0.01). To assess activity-dependent loss of INa availability, twenty times repetitive depolarizing potentials for 20ms at cycle lengths of 0.1, 0.5 or 2s were applied. WT INa remained constant during successive stimuli at all cycle lengths. However, at cycle lengths of 0.5 and 0.1s, Pitx2c−/− INa at the second pulses decreased to 79% and 26% of initial currents amplitudes, respectively, but remained almost constant throughout the following train of stimuli.

**Conclusions:** SCNSA R1632C showed a loss-of-function of INa by an enhanced fast-inactivated state stability with pronounced impairment of recovery from fast inactivation and severe activity-dependent loss of INa availability, which may explain the arrhythmic phenotype in humans. Our findings might be helpful to clarify the causal mechanism of CCD phenotype in human LMNA-related cardiomyopathy.

**P6354 | BENCH**

**Do major ion channels of pacemaker cell also play a role in atrioventricular nodal conduction in young and aged rats?**

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**Purpose:** Cellular mechanisms that influence atrioventricular (AV) nodal conduction are complex. Multiple studies have been performed to explain such phenomena but none can fully explain the "riddle" of the AV node. The role of pacemaking channels on the AV nodal conduction has not been previously studied. Also with ageing there is an increase in the incidence of AV nodal dysfunction leading to AV block. We have studied the role of pacemaking ion channels and gap junctions on the AV nodal conduction with ageing.

**Methods:** Electrophysiological (EP) and immunohistochemistry experiments are performed on male rats aged 3 months (equivalent to 20 year old humans; n=24) and 2 years (equivalent to 70 year old humans; n=15). In the electrophysiology experiments, Atrio-nasian (AH) interval, Wenkebach cycle length (WCL) and AV node effective refractory period (AVNERP) was measured. We have used caesium (Cs+) (2 mM) to block HCN channels responsible for the funny current (If), and ryanodine (2 μM) to block RyR2 channels responsible for Ca2+- release from the sarcoplasmic reticulum. This disease-specific model was studied using immunofluorescence and confocal microscopy on sections from each group (n=8 young and n=9 old rats) from different regions of the AV conduction axis: inferior nodal extension (INE), compact node (CN) and penetrating bundle (PB). We used t-test for statistical analysis.

**Results:** Without drugs to block the HCN and RyR2 channels, there was a significant prolongation of the AH interval (P<0.005), WCL (P<0.005) and AVNERP (P<0.001) with ageing. In young rats (but not old rats), Cs+ prolonged the AH interval (0.001<P<0.005), WCL (P<0.001) and AVNERP (P<0.001) with ageing. Cs+ decreased the AH interval (P<0.01) and WCL (P<0.01) in young and old rats. Immunofluorescence revealed that with ageing: Cx43 (a gap junctional protein) is downregulated in the INE and CN (P<0.05); In terms of calcium handling proteins: RyR2 is downregulated in the CN and PB (P<0.05); SERCA2a is upregulated in the PB (P<0.05). A trend of down regulation was observed in HCN4 expression in the PB (P<0.051).

**Conclusion:** For the first time, we have shown that both HCN and RyR2 channels play a role in AV nodal conduction. With ageing the effect of If-current in the AV nodal conduction decreases. The change in RyR2 and SERCA2a reduces the calcium concentration in the AV node with ageing. Both these effects are likely to decrease conduction across the AV node with ageing that can results in higher incidence of AV block.

**P6355 | BENCH**

**Nitratred fatty acids suppress fibrilbolization and oxidative stress in a murine model of AngII-induced atrial fibrillation**

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**Background:** Atrial fibrillation is one of the most striking features in the pathology of heart failure which is largely driven by local generation of free radicals. We have shown previously that nitrated fatty acids – potent endogenously occurring anti-inflammatory lipid mediators – significantly attenuate the vulnerability for AF. Herein, we elucidated the underlying molecular mechanism.

**Methods:** Wild-type (WT) or R1632C SCNSA were coexpressed with hSA subunit in tsA201 cells, and whole cell sodium currents (INa) were recorded using patch-clamp methods.

**Results:** INa density, measured at −20mV, for R1632C was significantly smaller compared to that for WT (R1632C: −43±5±3mV, n=14; WT: −67±9±3mV, n=15; P<0.05). However, no significant changes were observed in the recovery from fast inactivation and fast inactivation rate. Steady-state inactivation curve, assessed after 500ms depolarizing pulses, for R1632C was remarkably shifted to hyperpolarizing potentials compared to that for WT (V1/2 for R1632C: −110.7±0.8mV, n=16; WT: −85.0±5.2mV, n=17, p<0.01). Steady-state fast inactivation curve, assessed after 20ms depolarizing pulses, for R1632C was also shifted to the same degree. Recovery from fast inactivation after 20ms depolarizing pulses for R1632C was remarkably delayed compared to that for WT (tau for R1632C: 246.7±14.3ms, n=8; WT: 3.7±0.3ms, n=8, p<0.01). To assess activity-dependent loss of INa availability, twenty times repetitive depolarizing potentials for 20ms at cycle lengths of 0.1, 0.5 or 2s were applied. WT INa remained constant during successive stimuli at all cycle lengths. However, at cycle lengths of 0.5 and 0.1s, R1632C INa at the second pulses decreased to 79% and 26% of initial current amplitudes, respectively, but remained almost constant throughout the following train of stimuli.

**Conclusions:** SCNSA R1632C showed a loss-of-function of INa by an enhanced fast-inactivated state stability with pronounced impairment of recovery from fast inactivation and severe activity-dependent loss of INa availability, which may explain the arrhythmic phenotype in humans. Our findings might be helpful to clarify the causal mechanism of CCD phenotype in human LMNA-related cardiomyopathy.
Methods and results: In angiotensin II (AngII) treated wild-type mice niche nitric-oxide acid (OA-NO2) strikingly attenuated vulnerability for atrial fibrillation. Picrasimix red staining revealed that AF inducibility correlated with the degree of atrial fibrosis (amount of fibrinous areas/atrium, vector vs AngII + OA-NO2 vs AngII + vehicle: 1.0±0.2 vs. 2.7±1.0 vs. 0.7±0.2, p<0.05). In this regard, OA-NO2 reduced transforming growth factor β (TGF-β) induced smooth muscle actin (α-SMA) expression in 3T3 fibroblasts mediated by decreasing Smad2 activation suggesting that the protection from fibromod coling was mediated by inhibition of myofibroblast transdifferentiation (Ctnr vs TGF-β vs TGF-β/OA-NO2 vs OA-NO2: 0.6±0.3 vs. 0.8±0.3 vs. 0.5±0.3 vs. 0.3±1.0, p<0.05; (ii) TGF-β induced smooth muscle actin (α-SMA) expression in 3T3 fibroblasts mediated by decreasing Smad2 activation suggesting that the protection from fibromod coling was mediated by inhibition of myofibroblast transdifferentiation (Ctnr vs TGF-β vs TGF-β/OA-NO2 vs OA-NO2: 0.6±0.3 vs. 0.8±0.3 vs. 0.5±0.3 vs. 0.3±1.0, p<0.05; (iii) oxidative burst (PMA) 320±30 vs. 270±21 CL (RLU×1000), p<0.05). In this context, LPS-induced expression of NOX2 and activation of p38 MAPK in isolated macrophages was diminished (NOX2 and activation of p38 MAPK phosphorylation, vehicle vs. LPS: 0.95±0.7 vs. 0.89±0.102, p<0.05; LPS vs. PAF: 0.98±0.102 vs. 0.86±0.024, p<0.05; p38 MAPK phosphorylation, vehicle vs. LPS: 0.89±0.008 vs. 0.95±0.075, p<0.05; LPS vs. OA-NO2: 0.95±0.075 vs. 0.62±0.071, p<0.05). Nothoedrothelium staining of atrial sections strongly corroborates reduction of elevated ROS production in OA-NO2 (exposure, vehicle vs. LPS: 0.10±0.01 vs. 0.89±0.102, p<0.05; LPS vs. OA-NO2: 0.98±0.102 vs. 0.86±0.024, p<0.05; p38 MAPK phosphorylation, vehicle vs. LPS: 0.89±0.008 vs. 0.95±0.075, p<0.05; LPS vs. OA-NO2: 0.95±0.075 vs. 0.62±0.071, p<0.05). The heart has been suggested not to be a uniform entity but rather a heterogenic electromechanical organ.

Purpose: Electromechanical function and the expression of key proteins important for action potential and mechanical activity were systematically investigated in different regions of the heart. The acquired data were integrated using an in silico model.

Methods: Adult male wildtype rabbits (n=7) were examined by phase contrast magnetic resonance imaging (MRI) to assess cardiac wall movement velocities in regional segments (AHA-17 scheme). Segmental velocities were transformed into a deformation curve using a simplified deformation model. Briefly, intersegmental distances were calculated over time. By regarding intersegmental links as mechanical springs, a linear correlation between regional contraction and the calculated deformation curve was established. Vital cardiomyocytes were isolated from the left ventricular (LV) apex as well as LV, septum and right ventricular base (full width at half maximum of the contraction curve: 156 vs. 136ms; n=6). Cav1.2, KCNQ1, Kv1.4, Kir2.1, Na1.5, SERCA, RyR2, Phospholamban (PL) and NCX expression were quantified by western blotting. APs were recorded using patch clamping. Cav1.2, KCNQ1, KV1.4, Kir1.2, Nav1.5, SERCA, RyR2, Phospholamban (PL) and NCX expression were quantified by western blotting (WB).

Results: Action potential (APD90) was longer in LV apex than in all three base regions (medial 291 vs. 202, 209, 196ms; n=6, 26, 23, 12; p<0.01, p<0.05, p<0.05). MRI revealed an earlier, longer and stronger contraction in LV apex vs. LV base (full width at half maximum of the contraction curve: 156 vs. 136ms; n=6 rabbits x 4 segments (apex), n=6x6 (base); p<0.001; peak deformation 3.48±2.23 vs. 2.56±0.73, p<0.001). WB showed downregulation of several proteins in LV apex vs. LV base: Cav1.2 (107 vs. 240 std. densitometric units; p<0.05), KCNQ1 (100 vs. 278; p<0.07), KV1.4 (23 vs. 44; p<0.05), NCX (60 vs. 76; p<0.01), PL (91 vs. 134; p<0.05). When quantitative differences were used in an in silico model, a contraction and action potential prolongation in LV apex vs. LV base could be reproduced (137 vs. 125ms; 208 vs. 193ms).

Conclusions: We demonstrate the presence of an electromechanical apico-basal gradient in healthy rabbit hearts, and identify regionally heterogeneous expression patterns, associated with the progression of the disease. In conclusion, isoform specific expression of the quantitative differences reproduced the experimentally observed gradient. Since effective mechanical activity is the sole purpose of the heart, one can reason that dominance of apical activity is important for efficient pumping, as otherwise the flow of apical volume through the constricted basal “pipe” would be hampered.

P6357 | BENCH
The role of pitx2c in generating regional action potential gradients in the murine left atrium
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Background: Genetic variants adjacent to the Pitx2c locus associate with atrial fibrillation (AF) in populations and with recurrent AF in patients. Pitx2c mRNA is expressed in the adult left atrium (LA), and is enriched in the posterior LA wall, close to the pulmonary veins (LA-PV).

Purpose: We studied regional variations in the electrophysiological properties of the LA, including the LA-PV, and assessed whether reduced Pitx2c expression impacts on regional LA AP gradients.

Methods: Transmembrane action potentials (TAPs) were recorded from superfused WT and Pitx2c−/− murine LA paced at 100ms. TAPs were recorded from 3 LA regions: 1) the LA towards the junction with the pulmonary vein (LA-PV), 2) the medial dome (LA-M) and 3) the LA lateral wall (LA-LW). High spatial resolution AP duration distribution maps were recorded via a custom murine atrial optical mapping system.

Results: In WT, action potential amplitude (APA) was larger in the LA-PV (84±2mV) than LA-M (78±1mV) and LA-LW (77±2mV, n=11 atria). APs in the LA-PV were also longer than the other 2 regions; APD90 LA-PV 28±2ms, LA-M 21±0.7ms, LA-LW 19±1ms. In Pitx2c−/−, APA was reduced in all regions but this was most evident in the LA-PV, thereby decreasing the regional APA gradient (LA-PV 76±2mV, LA-M 75±3mV and LA-LW 71±3mV, n=12 LA). APD90 was shorter in all regions compared to WT but this was exaggerated in the LA-PV (LA-PV 22±2ms, LA-M 16±1ms and LA-LW 15±1ms). APD distribution maps confirmed regional APD gradients and showed that the LA-PV exhibits the greatest level of electrical heterogeneity.

Conclusion: We identify regional AP gradients in the murine LA. Pitx2c deficiency causes a reduction in these gradients and evokes electrical modification throughout the LA, with the most prominent remodelling occurring in the LA-PV area.

P6358 | BENCH
Transmural 2D living cardiac tissue slice model for investigating spatial heterogeneity of intracellular calcium handling in the heart
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Background: The spatial heterogeneity of intracellular calcium handling, in particular the transmural difference in the ventricle and its effect on the electrophysiological substrate, is largely unexplored despite the well established importance of the electrophysiological heterogeneity of the heart.

Purpose: To develop a novel living cardiac slice preparation for studying ventricular spatial heterogeneity of intracellular calcium handling.

Methods: A 2D transmural tissue slice was prepared from adult CD1 mouse (12–14 weeks old) and was then perfused with Ca2+ indicator Rhod2. Ventricular slices were prepared by sectioning the heart transversely from apex to base with a vibratome (Precision Inc, USA) in ice-cold oxygenated HEPEPS buffer solution (pH = 7.4 at 4°C) and slices were then returned to 35°C gradually in 10 μM blebbistatin-containing bicarbonate buffered solution (pH 7.4). Slices were imaged by an optical mapping system equipped with an EMCCD camera (Evolve 128 Photometrics, USA) and paced at frequencies of 2–4 Hz by field stimulation.

Results: The optimal thickness of slice for CaT recording was found to be around 300 μm. A spatial heterogeneity of CaT (as shown in Fig.1) was observed in different regions of the heart characterised by CaT duration at 80% decay time (CaT80). CaT80 in endocardial regions was longer than in epicardial regions (left
ventricle examined) (94.2±0.49 ms (endo, n=10) vs. 92.0±0.34 ms (epi, n=10), p<0.01). CA T80 in left ventricular apex was significant shorter (80.6±0.4 ms, n=10, the mid (91.4±0.2 ms. n=10) and base (92.0±2.1 ms, n=10) regions (p<0.01, apex vs. mid or base).

Conclusion: The methodology described here thus provides a novel model system for the study of spatial heterogeneity of intracellular calcium handling in the heart.

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P6369 | BENCH Deletion of PDK1 causes cardiac sodium current reduction in mice Z.L. Han1, Y.J. Jiang1, Y.Q. Yang1, X.H. Li2, Z.Z. Yang3, K.J. Cao1, D. Wang1, 1The First Affiliated Hospital of Nanjing Medical University, Cardiology, Nanjing, China, People's Republic of; 2The First Affiliated Hospital of Nanjing Medical University, Geriatrics, Nanjing, China, People's Republic of; 3Ministry of Education Key Laboratory of Model Animal for Disease Study, Model Animal Research Center, Nanjing, China, People's Republic of

The AGC protein kinase family regulates multiple cellular functions. 3-phosphoinositide-dependent protein kinase-1 (PDK1) is involved in the pathogenesis of arrhythmia, and its downstream factor, Forkhead box O1 (Foxo1), negatively regulates the expression of the cardiac sodium channel, Nav1.5. Mice are known to die suddenly after PDK1 deletion within 11 weeks, but the underlying electrophysiological bases are unclear. Thus, the aim of this study was to investigate the potential mechanisms between PDK1 signaling pathway and cardiac sodium current. Using patch clamp and western blotting techniques, we investigated the role of the PDK1-Foxo1 pathway in PDK1 knockout mice and cultured cardiomyocytes. We found that PDK1 knockout mice undergo slower heart rate, prolonged QRS and QTc intervals and abnormal conduction within the first few weeks of birth. Furthermore, the peak sodium current is decreased by 33% in cells lacking PDK1. The phosphorylation of Akt (308T) and Foxo1 (24T) and the expression of Nav1.5 in the myocardium of PDK1 knockout mice are decreased, while the nuclear localization of Foxo1 is increased. The role of the PDK1-Foxo1 pathway in regulating Nav1.5 levels and sodium current density was verified using selective PDK1, Akt and Foxo1 inhibitors and isolated neonatal rat cardiomyocytes. In conclusion, MEF2C is one of the major transcription factors regulating SCN5A expression and its downstream factor, Forkhead box O1 (Foxo1), negatively regulates the expression of the cardiac sodium channel, Nav1.5. PDK1 deletion causes cardiac sodium current reduction in mice.

P6361 | BENCH Linagliptin, a dpp-4 inhibitor, suppresses the electrical remodeling and myocardial injury in rats N. Ishizue1, S. Niwano1, T. Igarashi1, T. Fujiishi1, T. Hashikata1, J. Kishihara1, M. Murakami1, H. Fukuya1, H. Niwano2, J. Ako1, 1Kitasato University, Department of Cardiovascular Medicine, Sagamihara, Japan; 2Tamagawa University, College of Education, Department of Education, machida, Japan

Background: The dipetidyl peptidase-4 (DPP-4) inhibitor is an incretin-based anti-diabetic medicine, whose cardioprotective and anti-fibrotic effects have been reported. However, the effect of DPP-4 inhibitor on the electrical and structural remodeling is unknown. We hypothesized that linagliptin, a DPP-4 inhibitor, suppresses cardiac remodeling in isoproterenol (ISP)-induced myocardial injury model. Methods and results: Sprague-Dawley rats were assigned to 3 groups; 1) Sham, 2) ISP treated, and 3) ISP+linagliptin (5mg/kg/day) treated groups. Myocardial injury was induced by subcutaneous injection of ISP (70mg/kg). In the ISP+linagliptin group, linagliptin was orally administered for 14 days starting 1 week preceding ISP injection. Left ventricular ejection fraction was not significantly different among the groups in echocardiogram (p>0.141). In the electrophysiological study performed 1 week after ISP injection, ventricular effective refractory period (VERP) and monophasic action potential duration (MAPD) were markedly prolonged in the ISP group in comparison with the control (MAPD20: 14±6 vs. 12±4 ms, MAPD90: 58±8 vs. 44±8 ms, VERP: 72±2 vs. 38±10 ms, p<0.05, respectively). In contrast in the ISP+linagliptin group, such prolongation was suppressed and the parameters were significantly shorter than the ISP group (MAPD20: 6±1 ms, MAPD90: 34±6 ms, ERP: 52±14 ms, p<0.05, respectively). In the histology, ISP treatment induced myocardial injury, cardio-myocyte necrosis and reparative fibrosis especially in the endocardial area in the ISP group. However, the injured area was reduced by 43% in the ISP+linagliptin group (p<0.003). Conclusion: Linagliptin suppressed electrical remodeling characterized by VERP and MAPD prolongations and reduced myocardial injury area.

MITRAL VALVE DISEASE

P6362 | BEDSIDE Impact of new echocardiographic scoring system for predicting procedural outcome of percutaneous transmid valvuloplasty in patients with rheumatic mitral stenosis S.J. Ha1, I.J. Cho1, C.Y. Shim1, S.K. Ryu1, H.J. Chang1, G.R. Hong1, J.W. Ha1, N. Chung1, 1Severance Hospital, Cardiology, Seoul, Korea, Republic of; 2Eulji University College of Medicine, Cardiology, Seoul, Korea, Republic of

Background: Current echocardiographic scoring system for percutaneous mitral valvuloplasty (PMV) have limitations for predicting acute procedural outcome. The purpose of this study was to evaluate the impact of new echocardiographic scoring system in the prediction of procedural outcome of PMV in patients with rheumatic mitral stenosis. Methods: 185 patients (mean age: 46±11 years, M/F= 37:143) who underwent PMV at our institution were enrolled. Procedural success was defined as increase of more than 50% of mitral valve area (MVA) for a final area of ≥1.5 cm², with no more than 1 grade-increase in mitral regurgitation (MR) severity assessed 24 hours after PMV. Logistic regression analysis was performed to predict the procedural success. Results: PMV was successful in 135 patients (72.9%) and suboptimal in 50 patients (27%). Patients who had successful PMV were younger, lower the total echocardiographic score (Wilkins), lower pre-MR grade, lower values of subvalvular thickening and calcification among echocardiographic determinants. In logistic regression analysis, independent predictors of outcome for suboptimal results were pre-MR grade (OR: 2.783, 95% confidence interval [CI], 1.042–7.434) and subvalvular thickening (OR: 7.998, 95% CI, 3.804–16.814). New scoring system for predicting the suboptimal results consisted of age, pre-MR grade and
cloned into pG3-L. Basic vector and transfected into cardiomyocyte using SuperFect reagent. Total RNA from cultured cells was isolated using RNAeasy mini kit. Real-time quantitative RT-PCR (RT-qPCR) was conducted to detect the target gene mRNAs.

Results: Ecotropic expression of MEF2C was achieved by adding doxycycline in human fetal cardiomyocytes infected with inducible MEF2C lentiviral particles. SCNSA mRNA expression increased by addition of doxycycline in a dose-dependent manner. Knockdown of MEF2C by siRNA reduced SCNSA mRNA level by 22.3% (P<0.001). Luciferase mRNA driven by human SCNSA 2kb promoter increased 3.81 fold by overexpression of MEF2C compared to control (3.81±0.71 vs 1.00±0.12, P=0.002). The MEF2C binding site was mapped between 750bp to 1000bp upstream of SCNSA transcription start site, which contains putative MEF2 binding sequences (ATATATAAA).

Conclusions: Our results demonstrate that MEF2C is one of the major transcription factors regulating SCNSA transcription. The effect that MEF2C enhances SCNSA expression might be through its binding the cis-element (ATATATAAA) located in the promoter region of SCNSA.

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P6360 | BENCH Cardiac transcription factor MEF2C controls cardiac sodium channel gene SCNSA expression A. Zhou1, N. Jiang1, L. Patel2, G. Shi1, A. Xie1, H. Liu1, M. Liu1, E.M. Jeong1, S.C. Dudley1, 1Brown University, Rhode Island Hospital, Providence, United States of America; 2Brown University, The Warren Alpert Medical School, Providence, United States of America

Introduction: It has been well documented that abnormal expression of cardiac sodium channel gene SCN5A is linked to arrhythmia, but phenotypic variability of mutations is a problem for genotype-phenotype correlations, suggesting that there are likely several mechanisms that control SCNSA expression. Elucidation of transcriptional regulators of SCNSA expression could provide insights into the fundamental mechanisms of cardiac arrhythmias as well as the identification of possible targets for developing novel antiarrhythmic therapeutics to correct the electrical remodeling associated with heart disease.

Methods: Lentiviral doxycycline Inducible MEF2C mammalian expression plasmid was constructed using standard cloning procedure and packaged in Lentiv-X 293 cells. Human fetal cardiomyocyte cells were infected with lent viral particles using TransDux virus transduction reagent. siRNA was transfected into cardiac cells using RNAiMAX reagent. Human SCNSA promoter fragments were
P6363 | BEDSIDE
Noninvasive estimation of left ventricular filling pressure in patients with mitral regurgitation: a speckle tracking echocardiography study
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Background: It is exceedingly important to estimate pulmonary capillary wedge pressure (PCWP) in patients with mitral regurgitation (MR) to decipher the cause of dyspnea and determine the therapeutic strategy. However, there was a conflict in the use of E/e' to estimate left ventricular (LV) filling pressure in MR and echocardiographic parameters to predict PCWP in MR are not yet elucidated. We reported that PCWP was able to be accurately estimated by the novel KT index which is defined as log10 (left atrial (LA) active emptying function/LA minimum volume).

Methods: Echocardiographic parameters including LA dimensions, LA volume, LA phasic function, E/e', LA peak strain and estimated PCWP by KT index (ePCWP) were measured in moderate to severe MR (n=58, age: 67±8) just before catheterization and in normal subjects (n=26, age: 67±11) during sinus rhythm. MR was divided into primary MR (n=27) and secondary MR (n=31). LA strain, phasic volume and emptying function (EF) were measured by speckle tracking echocardiography during sinus rhythm. The ePCWP was calculated as 10.8 ± 12.4 x KT index.

Results: LV mass was increased in MR compared to control (131 ± 37 vs. 100±112g/cm², respectively) and LV ejection fraction reduced in MR (55±13 vs. 63±6%, respectively). LA phasic volume was increased in MR compared to control and LA phasic EF decreased in MR. E/e' and ePCWP were increased in MR compared to control (E/e': 18.2±8.2 vs. 10.5±3.3 and ePCWP: 16.6±4.9 vs. 7.7±2.7 mmHg, respectively). There was correlation between PCWP and E/e' (r=0.72, p<0.01). Receiver operating characteristic curve (AUC) of 0.784 (95% confidence interval [CI], 0.810–0.799) (Fig). Bland-Altman analysis confirmed the agreement between estimated PCWP and PCWP (bias ± SD) 1.6±5.2 mmHg. Multiple regression analysis revealed that ePCWP was an independent predictor of PCWP in MR including both primary and secondary MR (r=0.67, r=0.70 and r=0.67, respectively, p<0.01). Bland-Altman analysis confirmed the agreement between PCWP and ePCWP (mean bias 1.6±5.2 mmHg). Multiple regression analysis revealed that ePCWP was an independent predictor of PCWP in MR including both primary and secondary MR (r=0.67, r=0.70 and r=0.67, respectively, p<0.01). Bland-Altman analysis confirmed the agreement between PCWP and ePCWP (mean bias 1.6±5.2 mmHg).

Conclusion: The KT index was the most useful and reliable echocardiographic parameter to predict PCWP in patients with MR including both primary and secondary MR and may have an incremental value in a clinical setting to decide therapeutic strategy in MR.

P6364 | BEDSIDE
Long-term follow-up after percutaneous mitral valve repair using the mitraclip systerm
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Introduction and aims: Percutaneous mitral valve repair (PMVR) using the MitraClip system has become a valid alternative to surgery for patients with severe mitral regurgitation (MR), anatomical suitability, and high surgical risk. We report long-term outcomes of PMVR.

Methods: Between march 2009 and February 2014, 148 consecutive patients (mean age 75±10 years, 39.2% female) with moderate–severe (3+) or severe (4+) MR underwent PMVR at the University Heart Center Zurich. Clinical and echocardiographic data were prospectively collected. Clinical endpoints on follow-up included all-cause death, mitral valve surgery/reoperation, hospitalization for congestive heart failure, heart transplantation and New York Heart Association (NYHA) functional class.

Results: MR etiology was degenerative in 37% and functional in 57%, and 6% mixed. Baseline, 82% of patients were in NYHA class III/IV. Left ventricular ejection fraction was 45±18% and STS mortality risk score was 8.3±16%. Median follow-up was 1.9 years (interquartile range, 0.8 to 2.7). Acute procedural success (APS, defined as successful clip implantation with residual MR grade ≤2+) was achieved in 93% of patients. On echocardiographic follow-up, MR severity was 1+ and 2+ in 71% of patients. At 12 months, 63% of patients were in NYHA class I and II. Fifty-two (35%) patients died during follow-up (average annual mortality 19%/year). Overall, the composite endpoint (death; Reoperation; Heart failure hospitalization; heart transplantation) occurred in 84/148 (57%) patients. The following variables were independent predictors for higher event rates: age (p=0.026), LVEF (p=0.027), MR at discharge (p=0.005) and NYHA at base line (p=0.001) and age (p=0.026). LVEF (p=0.75) and functional etiology of MR (p=0.529) had no influence on outcome.

Conclusion: PMVR with the MitraClip system allows durable reduction of MR severity and improvement in patients' symptoms and functional status. Event rates, however, remain remarkably high despite successful treatment, reflecting advanced age and high comorbidity status of our population.

P6365 | BEDSIDE
Predictors of exercise capacity in asymptomatic patients with significant primary mitral regurgitation undergoing stress echocardiography
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Background: Primary mitral regurgitation (PMR) is progressive & results in reduction in exercise capacity.

Purpose: We sought to assess predictors of exercise capacity in asymptomatic significant PMR patients undergoing exercise stress echocardiography (ESE).

Methods: We studied 884 asymptomatic patients (58±14 years, 67% men) with ≥ III PMR that underwent treadmill ESE between 1/2000 and 12/2011. Clinical & ESE parameters were recorded.

Results: Mean body mass index (BMI), left ventricular (LV) ejection fraction, indexed left ventricular end-systolic dimension, mitral effective regurgitant orifice & rest right ventricular systolic pressure (RVSP) were 26±4 kg/m2, 58±5%, 1.6±0.4 mmHg, 0.48±0.3 cm² & 31±12 mm Hg. There were 11% & 47% patients with coronary artery disease & hypertension; 31% were on beta blockers. 5% ESE were positive for ischemia; while 89% patients had a decrease in LV cavity with stress & 3% had increase in LV cavity. Mean metabolic equivalents (METS) & peak stress RVSP were 9.6±3 and 46±17 mm Hg. Regression analysis showed the association between METS & various predictors is shown in Table.

Predictors of exercise capacity (METS)

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Beta</th>
<th>p- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>-0.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.02</td>
<td>0.7</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>0.03</td>
<td>0.4</td>
</tr>
<tr>
<td>Bota blockers</td>
<td>-0.59</td>
<td>0.005</td>
</tr>
<tr>
<td>Resting LV ejection fraction</td>
<td>0.07</td>
<td>0.54</td>
</tr>
<tr>
<td>Indexed LV end systolic</td>
<td>0.02</td>
<td>0.7</td>
</tr>
<tr>
<td>Mitral valve effective regurgitant orifice area</td>
<td>0.008</td>
<td>0.8</td>
</tr>
<tr>
<td>Resting RVSP</td>
<td>-0.162</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV cavity response to stress</td>
<td>-0.29</td>
<td>0.02</td>
</tr>
<tr>
<td>Peak stress RVSP</td>
<td>0.03</td>
<td>0.4</td>
</tr>
<tr>
<td>Ischemic response on ESE</td>
<td>-0.59</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Conclusion: In asymptomatic patients with ≥III PMR undergoing ESE, increased age, female gender, higher RVSP & ischemic response were inversely associated with METS.

P6366 | BEDSIDE
Left ventricular function analysis with 2D and 3D speckle tracking in secondary mitral regurgitation treated with transcatheter mitral valve repair with the MitraClip system
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Background: In current practice MitraClip (MC) treatment is predominantly used in patients suffering from secondary mitral regurgitation (sMR) due to relevant left ventricular (LV) pathologies. The effect of the procedure on LV volumes and function has been reported controversial. 3D speckle tracking (ST) analysis of LV geometry and function, theoretically, overcomes the limitations of a 2D geometric approach.
We, therefore, sought to determine the impact of transcatheter mitral valve repair (TMVR) with the MC system on global and regional LV function using two- and three-dimensional (2/3D) ST and conventional echocardiographic parameters.

Methods and results: 109 consecutive patients with sMR (age 77±3.7 years) at high surgical risk (EuroScore 16.9±15.2%) underwent successful MC implantation and completed 6 months follow-up (FU) including standardized 2 and 3D transthoracic echocardiography (TTE) prior to MC and after MC. Conventional echocardiographic parameters as well as 2D strain values were reduced at baseline but did not improve significantly 6 months after MitraClip implantation (2D global longitudinal strain (GLS): −8.5±4.1%, p=0.47; LV ejection fraction (LVEF): 33.1±15.8%, 43.1±14.9%, p=0.97). Furthermore, 2D volumes were unchanged during FU (2D end systolic volume (ESV): 65.9±8.9ml, 67.4±9.2ml, p=0.12; end diastolic volumes (EDV): 181.1±73.8ml, 159.8±52.5, p=0.07).

In contrast to 2D echocardiography, 3D TTE analysis showed significant amelioration of LV volumes and ejection fraction (EF): 2D ESV (181.8±70.6ml, 131.4±54.9ml, p=0.008), 3D end diastolic volume (EDV) (231.6±76.6ml, 177.4±58.0ml, p=0.013) and 3D EF (33.1±9.2%, 37.6±11.3%, p=0.015) improved significantly. Interestingly, 3D GLS showed the most significant amelioration 6 months after MC (−7.8±3.3%, −11.2±5.9%, p=0.006).

Conclusion: In contrast to 2D echocardiography, 3D ST analysis showed beneficial effects of interventional mitral valve repair with the MC system on LV volumes und function in patients with sMR. These data suggest, that 3D imaging might be superior to 2D echocardiography in patients with complex cardiac pathologies.

P6367 | BENCH
Predictors of long term outcome post surgical treatment of ischemic mitral regurgitation - results from Polish multicenter registry - PIMAR
Purpose:

1. To explore the survival predictors for patients with ischemic mitral regurgitation (IMR) treated surgically.

2. To identify the independent predictors of long-term survival.

Methods:

The present study enrolled 194 consecutive patients treated with mitraclip. The median follow-up period was 484±432 days. Severe LVSD was defined as LVEF <30%.

Purpose:

In the present study, we aimed to clarify the impact of LVSD on the long-term outcomes of MR patients who underwent mitractip procedure.

Methods:

The present study enrolled 194 consecutive patients treated with mitraclep. The median follow-up period was 484±432 days. Severe LVSD was defined as LVEF <30%.

Survival rate after MitraClip
**Conclusion:** Severe LVSD was not associated with a worse outcome after mitraclip implantation. However, we need to carefully observe LVSD patients who are elderly, have a high NT-proBNP level, and AF, as these may be considered high-risk subjects.

**Acknowledgement/Funding:** Japan Society for the Promotion of Science

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**Results:**

At baseline biventricular dysfunction group had higher NT-proBNP level (8063 pg/ml, IQR 3258 - 13805 pg/ml vs 4725 pg/ml, IQR 2106 - 7547 pg/ml, p=0.006) and only LV dysfunction group (55±10 mmHg vs. 48±9 mmHg, p=0.036). Even in patients who died between 6 months and 1 year, RVEDD, <15mm AND right ventricular end-diastolic diame-

**Conclusion:** Approximately 9% of patients with IE had no microbiological diag-

**AORTIC VALVE DISEASE**

**P6372 | BEDSIDE**

Incidence, predictors and impact on prognosis of estimated systolic pulmonary artery pressure and its improvement after transcatheter aortic valve implantation; a multicenter registry

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**Background:** Elevated estimated systolic Pulmonary Artery Pressure (esPAP) represents a common finding in patients (pts) with aortic stenosis. Prognostic impact of esPAP after transcatheter aortic valve implantation (TAVI) remains to be determined.

**Purpose:** All-cause mortality of one year follow-up (FU).

**Methods:** All consecutive pts undergoing TAVI between January 2007 and December 2012 in 5 European Centre were retrospectively included and divided into two groups according to esPAP: ≤40 mmHg and >40 mmHg.

**Results:** From a total of 674 pts, 319 (47%) had esPAP ≤40 mmHg (median 50 [IQ, 41–60] mmHg vs 35 [IQ 30–38] in the other group). Pts with esPAP >40 mmHg had a lower ejection fraction (51±13.8 vs 55±6.5%; p=0.001), larger left ventricle volumes, and higher rate of diastolic dysfunction, significant mitral regurgitation and right ventricle dysfunction (p<0.05, Figure). esPAP >40 mmHg was associated with higher mortality both at 30-days (4.5% vs 8.5% p=0.03) and at a median FU of 477 days (17% vs 26% p=0.03). In this group, there was a reduction of esPAP from median values of 50 (41–60) to 40 (35–50) mmHg after TAVI. Improvement of esPAP from above to below 40 mmHg was reported in 113 (27%) pts. esPAP reduction was more frequent in the absence of moderate or severe mitral regurgitation and of right ventricle dysfunction (OR 2:1.3–4 and OR 4.20:2–16, respectively). At multivariate analysis, esPAP independently predicted all cause of death at mean FU (HR 2.3, 1.2–4.9, for esPAP >40 mmHg, HR 1.2, 1.05–1.5 for esPAP as a continuous variable).

**Conclusion:** Elevated esPAP represents a common finding in pts undergoing TAVI, leading to increased all-cause mortality at one-year FU. Therefore esPAP could be a useful tool to stratify the risk of TAVI pts.
Results: PH is frequent in patients presenting with severe aortic stenosis (AS) undergoing transcatheter aortic valve implantation (TAVI) and is an independent predictive factor of death and re-hospitalization after TAVI. PH was defined as a mean pulmonary arterial pressure (PAP) >25 mm Hg. The primary end-point combined the incidence of death and re-hospitalization for heart failure at one year.

Conclusions: PH is frequent in patients presenting with severe aortic stenosis undergoing transcatheter aortic valve replacement or transcatheter aortic valve implantation (TAVI). However, few studies have characterized PH by invasive right heart catheterization and the impact of pulmonary vascular resistance (PVR) has never been investigated.

Background: One hundred and seventy-seven one hundred patients with asymptomatic severe AS prospectively underwent invasive right heart catheterization before TAVI. PH was defined as a mean pulmonary arterial pressure (PAP) >25 mm Hg. The primary end-point combined the incidence of death and re-hospitalization for heart failure at one year.

Methods and results: Among 980 consecutive patients included in CoreValve Italian Registry, 284 (29%) presented with a diagnosis of CLD in 8 high volume centers.

One-year overall mortality was similar between patients without CLD and those with mild CLD (HR 1.4 (0.94–2.4), p=0.06). Patients presenting with moderate CLD (defined as FEV1 50% to 59% of predicted, and/or on chronic steroid therapy) had similar mortality after TAVR. However, the observed benefit in terms of NYHA class and the effect on re-hospitalization should always be considered when judging the clinical equipoise of the TAVR with respect to the standard medical therapy.

Conclusion: Chronic lung disease (CLD) is deemed to negatively affect the outcome of patients undergoing Transcatheter Aortic Valve Replacement (TAVR) although data from the literature are inconclusive and little is known concerning the different impact of the diverse grades of CLD in a real world setting.
Comparison of stroke rate between the balloon expandable Edwards Sapien valve and the self-expandable CoreValve for transcatheter aortic valve replacement

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Background: Transcatheter aortic valve implantation (TAVI) has been used increasingly to treat inoperable or high surgical risk patients with severe symptomatic aortic stenosis. Although mortality rates are declining, stroke continues to be an issue.

Aim of the study: The aim of our study was to compare thirty day rate between the balloon expandable Edwards Sapien Valve (ESV) and the self-expandable Medtronic CoreValve system (MCV).

Methods: 573 patients with severe aortic stenosis and high surgical risk underwent consecutively TAVI in local anesthesia between April 2010 and October 2014. Major and minor stroke was defined according to the VARC II criteria. 30 day stroke rate and 30 day mortality were evaluated.

Results: 361 pts (age 80.6±0.34 years) with severe aortic stenosis (pmean 43.1±0.77 mmHg, AVA 0.68±0.01 cm²) and high surgical risk (log Euroscore 18.6±0.82%) underwent successfully TAVI with the MCV and 212 pts (age 81.7±0.41 years, log Euroscore 22.0±0.67%) underwent successfully TAVI with the ESV.

Conclusion: TAVI was associated with a 30-day stroke rate of 2.1%. There was no significant difference in 30-day stroke rate between the two valve types (MCV vs ESV=1.7% vs 2.8%; p=0.264), but there were more major strokes in the ESV group compared to the MCV group (MCV vs ESV: 0.8% vs 2.4%; p=0.273). There was a trend to more pre-dilation in the 30 day stroke group, but this did not reach statistically significance. 83.3% in the stroke group vs 69.1% in the group without stroke, p=0.235. 30-day mortality was significantly higher in patients with stroke compared to those without stroke (25% versus 3.9%; p=0.013).

Conclusion: TAVI was associated with a 30-day stroke rate of 2.1%. There was no significant difference in 30-day stroke rate between the two valve types, although there was a trend of more major strokes in the ESV group. 30 day mortality was significantly higher in patients with stroke.

Early and Late Mortality Among Severe Aortic Stenosis Patients

P.6379 | BENCH

Unsupervised network analysis of genome wide association study data identifies the epidermal growth factor receptor as the most connected hub in aortic valve calcification

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Background: Aortic valve calcification (AVC) can lead to aortic stenosis and is independently associated with adverse cardiovascular events. Relatively little is known of the pathogenesis of this condition. A recent genome wide association study (GWAS) with 6492 subjects identified a single nucleotide polymorphism (SNP) in the LPA locus as being associated with AVC at genome-wide significance. However the stringent requirements for genome-wide significance means that analysing the data on a per-SNP basis misses many important findings. Network analysis allows additional information to be extracted from the data.

Purpose: To identify biologically relevant associations with AVC through network analysis

Methods: We used the AVC GWAS data publicly available from the Framingham Heart Study. We mapped the SNPs to associated genes using the Versatile Gene-based Association Study (VEGAS) implementation in Fast Association Tests (FAST). We then used the Protein-interaction-network-based pathway analysis (PINPBA) app in Cytoescape to map this data to the IntAct protein interaction network (PIN). An unweighted greedy search algorithm through gene-based p-values was used to identify non-overlapping subnetworks of interacting genes.

Results: After correcting for multiple testing, no single gene retained statistical significance. Greedy search of the PIN identified two subnetworks, one with 515 gene products and a smaller one with 25 gene products. As in many biological networks, the larger subnetwork had a power law distribution of in- and out-degree of the nodes, indicating the existence of high-degree hubs. Using a standard measure of centrality (Betweenness Centrality), Epidermal growth factor receptor (EGFR) was the most connected hub in the network.

Conclusions: This study highlights the power of network analysis of GWAS data. Previous studies in mice have shown that inhibition of EGFR leads to AVC. Our unsupervised network analysis identified EGFR as the most connected genomic hub associated with AVC in humans. The current use of EGFR inhibitors as can-
cer therapies should be monitored for signals of harm related to aortic valve disease.

Acknowledgement/Funding: National Institute of Health Research Oxford Biomedical Research Centre Programme

P6381 | BEDSIDE
Prognostic impact of electrocardiographic abnormalities in patients with severe aortic stenosis
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Background: ST-segment elevation (STE) in leads V1–2 is often observed in patients with severe aortic stenosis (AS), but its prognostic significance remains unknown.

Purpose: This study aimed to investigate the clinical significance of STE in leads V1–2 in patients with severe AS.

Methods: We retrospectively evaluated baseline electrocardiograms (ECG) and 5-year clinical outcomes in 211 consecutive patients with severe AS. Severe AS was defined as peak aortic jet velocity (Aortic Vmax) ≥ 4.0 m/s, or mean aortic pressure gradient > 40 mmHg, or aortic valve area (AVA) < 1.0 cm². The primary outcome measure was the composite of death or surgical aortic valve replacement (AVR).

Results: STE in leads V1–2 (J-point deviation > 0.15 mV) was present in 97 patients (46%). Patients with STE in leads V1–2 had greater Aortic Vmax and smaller AVA than patients without. With median follow-up period of 4.9 years, the cumulative 5-year incidence of death or AVR was significantly higher in patients with STE in leads V1–2 than in patients without (91.4% versus 77.1%; P<0.005) (Figure A). After adjusting for echocardiographic index of AS severity and other confounders, STE in leads V1–2 was independently associated with higher risk for death or AVR (hazard ratio, 1.58; 95% confidence interval, 1.11–2.27; P=0.01), but other ECG findings such as left ventricular hypertrophy and strain pattern were not. In 64 asymptomatic patients without any indication for AVR at initial diagnosis of severe AS, the cumulative incidence of death or AVR was significantly higher in patients with STE in leads V1–2 than in patients without (87.5% versus 44.1%; P<0.001) (Figure B).

Conclusions: STE in leads V1–2 independently predicted poorer prognosis and more frequent need for AVR in patients with severe AS.

AORTIC VALVE INTERVENTIONS

P6382 | BEDSIDE
Differences in the diagnostic ability and analysis of 18F-FDG-PET/CT-Angiography in infective endocarditis between prosthetic valves and intracardiac devices
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Background: Diagnosis of infective endocarditis (IE) in prosthetic valves and intracardiac devices represents a clinical challenge because modified Duke criteria (DC) and echocardiography (ECHO) have limitations. 18F-FDG-PET/CT-Angiography (PET/CTA) has shown in recent studies an added value in this clinical scenario. However, the diagnostic ability and the analysis of the PET/CTA may vary between valves and devices.

Purpose: To analyze the differences in the diagnostic yield and image analysis between valves and devices, in a cohort of patients included between Nov-2012 and Jan-2015 in a major prospective study conducted in our hospital, which counts with a multidisciplinary IE unit.

Methods: We analyzed 92 patients with suspected IE. The initial diagnosis with the DC, the PET-CTA results, and the DC adding PET-CTA information were compared with a final “expert team” diagnostic consensus. We made a visual interpretation of the images and we also evaluated the differences between the semi-quantification analysis.

Results: There were 64 prosthetic valves and tubes and 28 cardiac devices. PET/CTA was performed and compared with ECHO findings with an intermediate correlation (kappa: 0.26 for valves and 0.36 for devices). In our series, the sensitivity, specificity and positive and negative predictive values were similar between prosthetic valves (51%/92%/91%/55% for the DC, 87%/92%/85% for the PET/CTA and 94%/98%/92% for DC + PET/CTA) and devices (50%/100%/100% for the DC, 87%/100%/100%/86% for the PET/CTA and 94%/100%/100%/92% for DC + PET/CTA).

The semi-quantitative analysis showed that in prosthetic valves, a cut-off value of ≥4 m/s and a SUVmax-background ratio ≥ 2.8 discriminated positive cases with a sensitivity of 92% and a specificity of 72% and 11% respectively. Cut-off values of 6.89 and 3.45, respectively, achieved a specificity of 100% to confirm infection. This semi-quantification was not useful for devices, with cut-off values under the background of the patients (SUVmax 1.21 and ratio of 1.06) and a very low specificity (50%).

Conclusions: Although the image interpretation of devices is more complex, based on the visual analyses because the semi-quantification was not useful in all patients, the added diagnostic value of PET/CTA to the DC was significant in both valves and devices.

P6383 | BEDSIDE
A positive 18F-FDG PET/CT on admission predicts new embolic events but not mortality in patients with infective endocarditis
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Introduction: IE is associated with high mortality and severe complications. Among them, embolic events (EE) are the most severe and their prediction remains difficult. 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, the prognostic significance of a positive 18F-FDG PET/CT and its value in predicting embolic events are unknown.

Purpose: To assess the value of a positive 18F-FDG PET/CT in predicting EE and death in patients with IE.

Methods: From January 2011 to April 2014, 222 patients with definite IE by modified Duke criteria (168 (76%) men, mean age = 64 years) underwent 18F-FDG PET/CT. Among them, 98 (44%) presented with a positive 18F-FDG PET/CT (valvular or prosthetic valve uptake).

Results: Among the 98 patients with positive 18F-FDG PET/CT, valvular uptake was classified as absent, minimal, moderate, or severe, by semi-quantitative analysis.

Conclusion: An intense 18F-FDG PET/CT valvular or prosthetic valve uptake predicts new embolic events but not mortality in IE. The additional predictive value of a positive 18F-FDG PET/CT uptake as compared with traditional markers of embolic risk and death needs further investigations.

P6384 | BEDSIDE
The role of aortic valve velocity and stroke volume index in predicting the outcomes of severe aortic stenosis with preserved ejection fraction in elderly
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Background: The role of aortic valve velocity and transaortic flow on predicting the outcomes of severe Aortic stenosis with preserved ejection fraction is not well defined.

Purpose: To examined the incidence of aortic valve replacement and mortality in those ≥75 years of age with different transaortic velocities and flow.

Methods: We identified consecutive patients ≥75 years old presenting to our echo lab with an aortic valve area (AVA) < 1.0cm² and EF>50% regardless of symptoms. We strata patients depending on maximal transaortic velocity (Vmax ≥ 4m/s vs. <4m/s) and stroke volume index (SVI < 35 ml/m² vs > 35ml/m²). All patients were retrospectively followed for the occurrence of aortic valve replacement (AVR) or death.

Results: A total of 917 patients were included in analysis, of which 318 died and 90 had AVR. Mean follow up was 2.45±1.9 years. The mean age of this population was 85.4±5.6 years. In patients with a low peak velocity, those with a SVI ≥ 35 ml/m² were found to have significantly higher mortality [169/494 (37%)]
compared to those with a SVI >35 ml/m² [75/264 (28%); p=0.016]. Furthermore, the low velocity, low flow patients had similar mortality to patients with high velocities [74/199 (37.1%)]. AVR occurred much less frequently in the low velocity, low flow patients [21/454 (4.6%)], compared to the high velocity patients [49/199 (24.6%); p<0.001]. This discrepancy between mortality and surgical intervention is depicted in the graphs below.

Conclusion: In older patients with normal EF and severe aortic stenosis, those with low velocity, low flow as reflected by a SVI >35 ml/m², represent a high risk group. They are much less likely to have an AVR than elderly patients with high velocity aortic stenosis despite having the same prognosis.

Methods: Between 1993 and 2014, 25 (17 female) patients aged >65 years (median 70, range 65–82 years) underwent TT for PVT as a first-line treatment strategy. The TT regimens used were slow (24-hour) infusion of 1.5 million Units of Streptokinase in 2 patients, slow (6-hour) infusion of 25 mg recombinant tissue plasminogen activator (t-PA) in 11 patients, and ultra-slow (25-hour) infusion of 25 mg t-PA in 12 patients. The primary outcomes were treatment success and in-hospital adverse cardiovascular event (mortality, hemorrhage, embolism, rethrombosis, reoperation due to TT failure) rates.

Results: The overall success rate was 88%. Adverse events occurred in 5 (20%) patients. These included 3 (12%) patients with major (one death, one need for reoperation due to rethrombosis after initially successful TT, and one need for reoperation due to failed TT) and 2 (8%) patients with minor (one transient ischemic attack and one venous puncture site hematoma) events. Higher thrombus burden (thrombus area >1.1 cm² by reviewer operating characteristic curve analysis, sensitivity 100%, specificity 84%, area under curve 0.92, 95% confidence interval 0.81–0.99, p=0.004) and high New York Heart Association Class (III/IV vs I/I status, 44.4% vs 63.3%, respectively, p=0.04) were the predictors of adverse events. Age (p<0.1), elapsed time since valve surgery (p=0.44), coronary artery disease (p=0.27), hypertension (p=1), diabetes (p=0.6), stroke or transient ischemic attack (p=1), aspirin use (p=0.62), heart rhythm (p=1), leading symptom (p=0.06), thrombosed valve position (p=0.66), valve brand (p=0.75), presence of valve obstruction (p=0.13), baseline valve area (p=0.28), mean gradient (p=0.23), left ventricular ejection fraction (p=0.54), TT protocol (p=1), increasing number of TT sessions (p=0.08) and higher TT dose (p=0.19), did not seem to predict adverse events.

Conclusion: Prolonged infusions of low doses of TT (mostly t-PA) agents provide successful and safe thrombolysis in elderly patients with PVT. However, patients with excessive thrombus burden and poor functional capacity are still under higher risk of adverse events.

P6385 | BENCH Atorvastatin diminishes gene expression of tumor necrosis factor-alpha in left atrial appendage but not interferon-gamma and interleukin-4 in rheumatic heart disease A.C. Aykan, M.A. Astarcioglu, M. Biteker, M. Ozkan, S. Gunduz, M. Yesin, M. Kalcik, S. Karakoyun, M.O. Gursoy, Z. Bayram

Background: Atorvastatin is known to suppress TNF-α and increases gene expression of IL-4 as the inflammatory response in the myocardium. This was an experimental study, recruited 53 RHD patients. They were excised valves and Left Atrial Appendage (LAA) as the study outcomes.

Methods: This was an experimental study, recruited 53 RHD patients. They were planned to undergo cardiac valve surgery and given atorvastatin vs placebo 6 weeks prior to surgery. Gene expression method was applied to probe Messenger RNA (mRNA) TNF-α, mRNA IFN-γ and mRNA IL-4 IL-4 expression from excised valves and LAA in RHD patients undergoing transcatheter aortic valve implantation (TAVI). However, the AR index is contoured by several periprocedural characteristics such as heart rate or pre-procedural hemodynamics.

Results: There were no significant differences between the study groups, in terms of gender proportion, ages, echocardiographic and clinical indicators and treatments administered. Atorvastatin group presented lower gene expression of TNF-α in LAA with p=0.005 (95% CI 0.05–0.58) after being adjusted with gender and ejection fraction. There was no difference of IL-4 and IFN-γ gene expression in cardiac valves and LAA.

Conclusions: Atorvastatin diminishes inflammation in LAA patients of RHD by suppressing TNF-α gene expression. There were correlations between suppressed gene expression of TNF-α and IFN-γ with increased gene expression of IL-4 level.

Acknowledgement/Funding: Grants from National Cardiovascular Centre, Harapan Kita Hospital, Jakarta Indonesia

P6386 | BENCH Thrombolysis in elderly patients with prosthetic heart valve thrombosis S. Gunduz, M. Yesin, M. Kalcioglu, S. Karakoyun, M.O. Gursoy, Z. Bayram, A.C. Aykan, M.A. Astarcioglu, M. Biteker, M. Ozkan

Background: There is no previous study that has evaluated thrombolytic therapy (TT) in elderly patients with prosthetic valve thrombosis (PVT).

Methods: Thrombolysis in elderly patients with prosthetic heart valve thrombosis

Purpose: To investigate the safety and efficacy of low dose and/or slow infusion TT strategies in PVT patients aged >65 years.
Conclusions: The negative prognostic value of an AR Index below 25 is significantly attenuated in patients with an AR Index ratio > 0.50. A low pre-procedural AR index before the procedure indicates resilience against the clinical impact of complications.

P6388 | BEDSIDE
Influence of nutritional status on survival after transfemoral transcatheter aortic valve implantation
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Background: Suboptimal nutritional status is a known predictor for worse outcome after cardiac surgery. The nutritional status of fragile elderly patients is frequently suboptimal, and might be of paramount importance for outcome/survival after transcatheter aortic valve implantation (TAVI).

Purpose: We sought to provide insight in the influence of peri-procedural nutritional status on survival after TAVI in the fragile elderly TAVI population.

Methods: All patients (n=117) who underwent a transfemoral TAVI and a documented pre-procedural serum albumin level between 19-11-2010 and 20-1-2014 were included. Preprocedural albumin levels were assessed in all patients to reflect current nutritional status. Patients were subdivided in high and low albumin level based on a even distribution of the groups; the cutoff between low (group 1) and high (group 2) was defined as 41 g/L. We performed albumine-based comparison and Kaplan Meier analysis to evaluate differences in short and longer term survival after TAVI.

Results: Mean age was 79.6±8.8 years. Survival in the group of patients with high albumin levels was significantly higher as compared to the low-albumine group (p=0.029) with Log-Rank (Chi-Square: 4.779). (Fig. 1: Kaplan-Meier)

Conclusion: Short- and longterm survival after transfemoral TAVI is significantly lower in patients with suboptimal nutritional status, indicated by lower preprocedural albumin levels.

P6389 | BEDSIDE
Impact of paravalvular leak on mitral regurgitation change after transcatheter aortic valve replacement for aortic stenosis and its prognostic implications
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Background: The prevalence of at least moderate mitral regurgitation (MR) in patients with severe aortic stenosis reaches 20%. MR severity can improve after Transcatheter Aortic Valve Replacement (TAVR).

Purpose: To assess the echocardiographic determinants of MR change after TAVR and its impact on prognosis.

Methods: We evaluated 244 patients (48% Males, age 79.8±7.33) with severe aortic stenosis referred to our institution for TAVR from 2008.

Echocardiography was performed before implantation and within 6 months after. MR was graded according to the MR index, on a scale of 1 to 4+. MR change was defined as an improvement of at least 1 grade. Patients with organic mitral tricuspid disease (rheumatic, congenital and prolapse) were excluded.

The presence of Paravalvular Aortic Regurgitation (PAR) was evaluated and graded according to the Valve Academic Research Consortium-2 criteria. The combined endpoint was defined as death, myocardial infarction, stroke, heart failure hospitalization.

Results: 130 (53.3%) patients have a baseline MR degree >2+. Baseline MR degree, Ejection Fraction (EF), transaortic mean gradient (M0) were: 1.61±0.965, 52.15±14.26, 51.86±17.14, respectively. At 6 month echocardiographic follow-up, in the overall population MR degree was 1.41±0.88, EF 54.14±10.33%. Significant (r>2+) PAR was detected in 72 patients (32%). The prevalence of MR change was significant lower in patients with PAR >2+ than in patients without (22% vs 37.8%, p=0.01). Subgroups analysis showed that both patients with MR improvement and patients with no MR improvement have significant changes in pre and post EF (51.57±13.70 vs 54.80±10.30, p=0.0002; 53.84±14.17 vs 55.41±10.34, p=0.034).

At multivariate analysis, PAR >2+ was the only significant predictor of lack of MR improvement after TAVR (OR 3.2 (CI 1.2–8.4); p=0.001), whereas pre and post TAVR End Diastolic Volume, pre and post TAVR EF, pre and post TVAR MG did not enter in the model.

Conclusions: These data demonstrated that a significant percentage of patients present a MR reduction after TAVR; PAR >2+ is a predictor of lack of MR improvement after TAVR. Moreover, there is a trend in the excess of events in patients without improvement of MR after TAVR even though does not reach the statistical significance.

P6390 | BEDSIDE
Three-year outcomes of transcatheter aortic valve implantation in patients with STS score less than or equal to 7%: a comparative analysis between different risk strata from the ADVANCE study
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Introduction: Transcatheter aortic valve implantation (TAVI) has been increasingly offered to intermediate surgical risk patients with severe aortic stenosis (AS), and the impact of TAVI on morbidity and mortality remains poorly investigated.

Purpose: The purpose of this sub-analysis was to assess 3-year clinical outcomes among patients with Society of Thoracic Surgeons (STS) score less than or equal to 7% compared to the outcomes of patients with STS score greater than 7% who underwent TAVI.

Methods: Data were drawn from the ADVANCE study, which enrolled patients with severe AS treated with implantation of a self-expanding transcatheter valve. Events were independently adjudicated based on VARC-1 definitions. A total of 996 patients were implanted, and for the purpose of this analysis those with an available STS score were dichotomized into two groups: STS<7% (n=797, mean STS score 4.3±1.5%) and STS=7% (n=299, mean STS score 11.3±5.0%).

Results: At 3-years, the STS<7% group reported lower rates of all-cause mortality (28.6% vs. 45.9%, p<0.01) and cardiovascular mortality (19.0% vs. 30.2%, p<0.01) as compared with the STS ≥7% group. No differences were observed with regards to cerebrovascular accidents, vascular complications, bleeding and myocordial infarction during 3-year follow-up. Mortality at 3-years was higher in STS<7% patients with moderate/severe paravalvular regurgitation (PVR) measured at discharge that in those with mild or less PVR (39.9% vs. 22.9%; HR, 1.98; 95% CI, 1.37-2.6; p<0.001). In contrast, the severity of PVR at discharge did not affect mortality in STS>7% patients (42.8% versus 44.6%; moderate/severe vs. none/mild; HR, 1.04; 95% CI, 0.62-1.7; p=0.86; p for interaction=0.047).

Conclusions: In the ADVANCE study, TAVI was commonly offered to patients with STS score ≤7%. Compared with patients having STS >7%, they showed reduced all-cause and cardiovascular mortality rates at 3-year follow-up. Complication rates were low and stable in both groups, demonstrating the safety of this procedure across patients at varying levels of surgical risk.

Acknowledgement/Funding: Medtronic, Inc., funded the ADVANCE study
tured (27%), intensive care complications (20%) and vascular complications (11%). There was no difference in mortality according to the type of device used (8.5% vs 5.7%, p=0.28), but death occurred more frequently after transcatheter than transvalvular TAVI (16.8%, vs 4.7%, p<0.001). Mortality decreased over time: 11.9% in the first, 6% in the second and 4.5% in the third tertile (p<0.001). This difference was mainly due to a reduction in cardiac failure-related death (6.5% in the first tertile, vs 1.5% in the third, p=0.021). There were no vascular complications-related death in the third tertile (0 vs 1% in the first tertile, p=0.47). However, no decrease was observed in the rate of death related to cardiac rupture (2.5% in the first tertile, vs 0% in the third, p=0.72) as well as those due to intensive care complications (2% in the first tertile vs 1.5% in the third, p=0.39).

Conclusions: Procedural mortality after TAVI substantially decreased over time. The improvement was driven by a decrease in deaths due to post-TAVI heart failure (4.1% in the first tertile vs 1.5% in the third, p=0.021), as well as those due to vascular complications. However, efforts should continue to prevent the occurrence of cardiac rupture and to improve the management of patients requiring post-TAVI intensive care.

CARDIOMYOPATHIES

P6392 | BEDSIDE
Cardiac extracellular volume quantified by cardiac magnetic resonance imaging as a degree of cardiac and neurological involvement in familial transthyretin amyloidosis
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Introduction: Amyloidotic cardiomyopathy (AC) in familial amyloid polyneuropathy (TTR-FAP) determines prognosis and treatment options. CMR T1 mapping techniques are useful to assess myocardial extracellular volume (ECV) and might be useful to evaluate cardiac disease and neurological involvement in TTR-FAP.

Purpose: We hypothesized that ECV could detect AC in TTR-FAP patients and that cardiac ECV could reflect the degree of neurological impairment caused by TTR amyloid extracardiac deposits.

Methods: 31 genetically proven TTR-FAP patients (19 males; mean age 49±12 years; 26 V30M) underwent a T1 mapping CMR study and a neurological evaluation with NIS-LL score (examination of the sensory, motor and reflexes in the lower limbs), Norfolk-QOL questionnaire (symptoms and quality of life) and Karnofsky index (general health status). Confirmed AC was defined by a positive 99mTc-DPD scintigraphy (uptake grade ≥2) or by left ventricular hypertrophy with typical amyloid gadolinium kinetics/enhancement at CMR for those subjects without DPD-scan (10 patients).

Results: 5 patients had AC (4 determined by scintigraphy and 1 by CMR). Mean ECV was increased in patients with AC (0.490±0.131 vs 0.289±0.035; p=0.026). ECV correlated with age (R=0.467; p=0.008), NIS-LL score (R=0.484; p=0.004), C-reactive protein (R=0.583; p=0.000), left ventricular end-systolic volume index (R=0.485; p=0.000), left ventricular ejection fraction (R=-0.378; p=0.036), NIH-LL (RS=0.694; p=0.001), Norfolk-QOL (RS=-0.529; p=0.003) and Karnofsky index (RS=−0.517; P=0.004). A cut-off value of ECV=0.357 calculated by ROC curve, was diagnostic of AC with 100% sensitivity and specificity (P<0.001). ECV and NT-proBNP values were the only cardiac parameters that significantly correlated with neurologic scores.

Conclusions: ECV quantification by CMR allows identification of AC in TTR-FAP and correlates with the degree of neurological impairment. This non-invasive technique could be a useful tool for early diagnosis and to track cardiac and extracardiac amyloid disease.

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P6393 | BEDSIDE
Late gadolinium enhancement on cardiac magnetic resonance for the prediction of non-sustained ventricular tachycardia in patients with hypertrophic cardiomyopathy
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Introduction: Cardiovascular Research (CNIC), Advanced Imaging Unit, Madrid, Spain

Purpose: Amyloidotic cardiomyopathy (AC) in familial amyloid polyneuropathy (TTR-FAP) determines prognosis and treatment options. CMR T1 mapping techniques are useful to assess myocardial extracellular volume (ECV) and might be useful to establish non-invasive diagnosis tool for acute myocarditis. However, it is less established as a prognostic tool. Our aim was to assess the CMR findings after the first episode of acute myocarditis.

Methods: We studied 33 patients with acute myocarditis whose CMR was performed during clinically acute myocarditis and 9±3 months later. A CMR protocol was applied and the prognostic value was assessed using a combination of death, heart transplant, hospitalization for cardiac cause and recurrent myocarditis as main outcome.

Results: The mean age of 32±9 years and 24 (72%) patients were men. Troponin I elevation was found in all patients (mean peak value 22±23 ng/ml). Mean BNP, C-reactive protein values at admission were 241±443 pg/ml and 96±93 mg/dl, respectively. An abnormal ECG was present in 21 (64%) patients. CMR was displayed at 4±2 days after admission and mean left ventricular (LVEF) ejec-

Published online before print. Value 0.050. The area under the receiver-operating characteristics curve was 0.72 and a cut-off of 18% had a sensitivity and specificity of 62% and 69%, respectively, for the prediction of NSVT.

Conclusions: The extinct 33 patients was an independent predictor of NSVT in this population. LGE-CMR may represent an additional marker to enhance sudden cardiac death risk stratification in HCM patients, particularly in those with intermediate risk.
and IL-10) serum profile in Venezuelan Chagasic patients stratified with Lown and NYHA classifications and treated with amiodarone, an antiarrhythmic drug with reported trypanocidal activity, to evaluate progression and response to the treatment.

Methods: Sera samples from 38 chagasic patients, clinically classified by NYHA and Lown criteria, were analyzed for cytokines using a human Th1/Th2/Th17 cytokmeric bead array kit in a FACSComp cytometer. Treated and untreated patients were paired in function to their clinical status. The Wilcoxon rank-sum statistic was used for testing the hypothesis of significant difference between two groups (treated and untreated) and Principal Component Analysis (PCA) was used for reducing the data dimensionality, while keeping more than 98% of the original variance.

Results: Non-Treated (n=7) vs Treated (n=15) paired groups were quite different in IL-6, IL-2 and IL-4 (p<0.039), while IL-10 remains almost similar (p=0.2251). IL-10 high producers frequency was significant lower in patients with high risk for sudden death (Lown 3 and 4 stage, n=14) regarding to Lown stages 0–2 (n=24). IL-17 and IL-2 high producers was higher in advanced NYHA stage (3–4, n=8) while IL-10 remains similar. A significant association between Q-wave location and VT during follow-up was observed (p=0.001, Table).

Conclusions: In chronic Chagas’ disease, abnormal Q-wave in anterior and not in inferior wall is a long-term marker for cardiac death. Additionally, abnormal Q-wave in anterior wall is associated with spontaneous VT episodes in long-term. However, location of electrocardiographic markers of myocardial scar is weakly related to left ventricular systolic function in this population.

Acknowledgement/Funding: State University of Rio de Janeiro

P6396 | BEDSIDE
Effects of paediatric human immunodeficiency virus infection on electrical conduction of the heart
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Background: Heart conduction disorders, such as prolongation of QT interval, have been reported in HIV-infected adults. However, little is known about such disorders in paediatric HIV, particularly in relation to delineation of the effects of HIV infection from treatment.

Methods: This cross-sectional study was conducted in 165 perinatally-acquired HIV-infected and 99 newly diagnosed antiretroviral treatment (ART)-naive, 58 ART-exposed and 51 healthy age-matched children in Indonesia. We performed 12-lead ECG examinations to measure cardiac conduction parameters; QTc and QoTc (corrected using the Bazett's formula), and PR intervals. The associations between HIV infection/treatment status and ECG intervals were evaluated using general linear modeling with further adjustment for potential confounders or ex- planatory variables. Findings are presented as (adjusted) mean differences between each of the two HIV groups (ART-naive and ART-exposed) and healthy children.

Results: Compared to healthy children, QTc intervals were longer in ART-naive (difference 18.3 milliseconds, 95% confidence interval (CI) 7.3 to 29.3) and, to greater extent, in ART-exposed HIV infected children (difference 27.9 milliseconds, 18.3 to 37.4). Following adjustment for RR interval, age, and height, prolongation of QoTc interval was only in ART-exposed children, difference 12.8 milliseconds, 2.3 to 23.3). Neither cardiac mass or function, high sensitivity C-reactive protein, lipid profile, gycosylated haemoglobin levels, systolic and diastolic blood pressure, nor postnatal parental smoking exposure affected these associations. In no QTc interval was observed between the groups.

Conclusions: Prolongation of QTc interval occurs only in ART-naive HIV infected and, to a greater extent, in the ART-exposed children. In addition, ART-naive HIV infected children have a longer PR interval than healthy children.

P6397 | BEDSIDE
Abnormal Q-wave in anterior wall but not in inferior wall on surface ECG is marker for cardiac death in long-term follow-up of subjects with chronic Chagas disease
P.R. Benichiel Barbosa1, B.R. Tura3, A.C.L. Benichiel Barbosa2, E.C. Barbosa1, J. Barbosa-Filho1 on behalf of Search-Rio Study, 1State University of Rio de Janeiro (UERJ), Rio de Janeiro, Brazil; 2National Institute of Cardiology, Rio de Janeiro, Brazil; 3Fluminense Federal University, Niteroi, Brazil

Introduction: Abnormal Q-waves on surface ECG are markers of myocardial scar, cardiac dysfunction and life threatening arrhythmia. In chronic Chagas’ disease, ventricular tachycardia (VT) relates to the presence of myocardial scar. Prognostic value of the location of myocardial scar based on surface ECG is undefined.

Methods: In a prospective longitudinal long-term follow-up study (Search-Rio Study, 2001–2014), 63 patients (34 to 74 years old) with chronic Chagas’ disease and complaint of palpitation were admitted. Surface ECG assessed abnormal Q-wave, defined as >100 ms (deep) and >40 ms (width), as marker of myocardial scar according to the location: anterior (AW); V1-V4, and inferior (IW) wall:

Conclusions: In chronic Chagas’ disease, abnormal Q-wave in anterior and not in inferior wall is a long-term marker for cardiac death. Additionally, abnormal Q-wave in anterior wall is associated with spontaneous VT episodes in long-term. However, location of electrocardiographic markers of myocardial scar is weakly related to left ventricular systolic function in this population.

Acknowledgement/Funding: State University of Rio de Janeiro

P6398 | BEDSIDE
Electrocardiographic criteria and outcome in patients with arrhythmogenic right ventricular cardiomyopathy
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Current literature in arrhythmogenic right ventricular cardiomyopathy shows that electrocardiographic markers such as epsilon waves and the amount of T wave inversions of electroanatomical scar size predicts arrhythmic risk. The amount of T wave inversions with increasing electroanatomical scar size were normal T waves, negative T waves in V1 to V3, negative T waves in V1–V2 extending to lateral leads and negative T waves in both precordial and inferior leads. This study was conducted in a large number of patients to correlate ECG findings to the outcome of each patient.

Methods: In 321 patients (207 males, mean age 46.7±11.3 years) the amount of T-wave inversions and outcomes of the patients were correlated. T-wave inversions in 4 leads or more (high risk group) were found in 61 patients and T-wave inversions in a maximum of 3 leads (so-called low risk group) could be revealed in 260 patients.

Results: In 38 out of 61 patients with T-wave inversions in 4 or more leads re-current ventricular tachycardia or ventricular fibrillation occurred. In the low risk group at least 35 out of 260 patients were characterized by ventricular tachycardia or ventricular fibrillation. In the high risk group VT/VF were present in 62%, in the low risk group VT/VF occurred in 15%. These results were highly statistically significant with a p value <0.000001. Specificity was high with 86%, negative predictive value was higher with 90%.

Conclusions: It is known that the amount of T-wave inversions characterizes scar size and predict arrhythmic risk. In this analysis it was shown that the amount of T-wave inversions had a strong correlation to outcomes of the patients. T-wave inversion is an excellent predictor to ventricular tachycardia or ventricular fibrillation by the outcome of the patients with arrhythmogenic right ventricular cardiomyopathy.

P6399 | BEDSIDE
Exercise capacity in hypertrophic cardiomyopathy; predictors and effect of treatment with losartan
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Background: Reduced exercise capacity is common in hypertrophic cardiomyopathy (HCM) and a predictor of adverse outcome. Studies of animal models of HCM and pilot studies in patients have suggested beneficial effects of angiotensin II receptor blockers on structural and functional parameters including an increase in the exercise time.

Purpose: Our aims were to assess the effects of losartan on exercise capacity compared to placebo and to identify predictors of exercise capacity in patients with overt HCM.

Methods: We studied 130 adult patients (52±13 years, 35% female) who were randomly allocated to treatment with losartan (100 mg/d) or placebo for 12 months. Patients were assessed with a symptom-limited exercise test, echocardiography and CMR or CT (patients with ICD) before and after treatment.
Results: Mean exercise capacity remained unchanged from baseline to 12 months follow-up in both groups (placebo 7.6±2.9 to 7.7±2.8 METS, p=0.49 and losartan 7.7±2.4 to 7.5±2.5 METS, p=0.33) and did not differ between groups (mean difference −0.3 METS [95% CI −1.0 to 0.3], p=0.28). Exercise capacity correlated strongly with NYHA class (r=-0.44, p=0.0001) and patients in NYHA class 3 had a significantly higher exercise capacity than patients in NYHA class ≥2 (8.4±2.7 METS vs. 5.8±1.9 METS, p<0.0001). In multivariate analysis of baseline data, a small left ventricular end-diastolic volume (LVEDV) (<616MET) (95% CI −0.96 to −0.27) per 10 mL/m² decrease, p=0.010) elevated E/ e′ (r=−0.15 METS [95% CI −0.03 to −0.03], p=0.103) and waist circumference (r=−0.08 METS, p=0.73). Conclusion: Patient with LVEDV index in the lowest quartile achieved a significant lower exercise capacity than patients in the upper quartile (9.3±2.9 METS, p=0.0001). Losartan had no effect on the predictors of exercise capacity. There was a significant increase in left atrial volume in both groups from baseline to follow-up (placebo 7.2±14.0 mL/m², p=0.0013 and losartan 5.9±13.7 mL/m², p=0.0086). There was no correlation between the change in left atrial volume and the change in exercise capacity in the individual patient (r=−0.04, p=0.73).

Conclusion: Losartan could not improve the reduced exercise capacity seen in adults with overt HCM. Low exercise capacity was predicted by female sex, low left ventricular end-diastolic volume and elevated E/ e′. Future studies may reveal that angiotensin II receptor blockers can affect left ventricular structure and function and have an accompanying beneficial effect on physical capacity in earlier stages of HCM.

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P6400 | BEDSIDE
Obstruction in asymmetric hypertrophic cardiomyopathy: a multicentre study
C.E. Correia, I. Cruz, L. Teles, M. Oliveira, J. Almeida, C. Lourenco, R. Faria, J. Leao, K. Domingues, N. Marques Brazil on behalf of SUNSHINE group. 1Hospital Sao Teotonio, Viseu, Portugal; 2Hospital Garcia de Orta, Almada, Portugal; 3University Hospitals of Coimbra, Cardiology, Coimbra, Portugal; 4Alto Ave Hospital Center, Guimaraes, Portugal; 5Hospital Center of Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal; 6Hospital Centre do Tamega e Sousa, Penafiel, Portugal; 7Centro Hospitalar Menedo Ave, Vila Nova de Famalicao, Portugal; 8Hospital Center of Tras-os-Montes and Alto Douro, Vila Real, Portugal; 9Hospital of Santarem, Santarem, Portugal; 10Faro Hospital, Faro, Portugal

Introduction: Obstruction at rest is described in about 25% of patients with asymmetric hypertrophic cardiomyopathy (HCM) and determines the natural history of the disease.

Aim: Characterize a Portuguese population of patients with asymmetric HCM and compare patients with and without obstruction at rest.

Methods: Portuguese multicentre study including all patients diagnosed with asymmetric HCM in 11 hospitals. We evaluated the clinical, genetic, electrocardiographic, echocardiographic and cardiac MRI data. We compared these parameters between patients with and without HOCM.

Results: We included 346 patients with asymmetric HCM (61% male, mean age 61±14 years). About 60% of patients were symptomatic, and dyspnea (56%), angina (16%) and syncope (11%) were the most common symptoms. The average thickness of IVS was 19±5 mm and the posterior wall 11±3 mm. Obstruction at rest was present in 32% of cases and latent obstruction in 13% of cases. Mitril regurgitation was detected in 23% of cases. Delayed enhancement was found in 61% of patients undergoing cardiac MRI. Most patients were in sinus rhythm (80%). About 20% of patients had a history of atrial fibrillation and 18% had a history of non-sustained ventricular tachycardia (NSVT). About 6% of patients had pacemaker and 11% ICD. Cardiac death was found in 1.4% of cases. Family history of HCM was identified in 26% and family history of sudden death in 17% of cases. Genetic testing was performed in 167 patients (48%) and revealed genetic mutations in 67 cases (40%) in the following genes: MYBPC3 (10%), MYH7 (10%), TPM1 (4%), MYL2 (1%), TNNT2 (5%) and RYR2 (3%). Unique environmental strains in twin pairs. Two hundred and twelve twin siblings were recruited (65 monozygotic and 41 same-sex dizygotic twin pairs, mean age 57±14.6 years). Siblings with coronary artery disease, any cardiomyopathy or severe valvular disease were excluded. Beyond the standard echocardiographic protocol, parasternal short axis- and apical views were obtained, optimized for speckle tracking analysis. Using dedicated software, global circumferential (GCS), longitudinal (GLS) and radial (GRS) strains were calculated by averaging the corresponding values of the 16 LV segments. Apical counter-clockwise, basal clockwise rotation and their net difference, the LV twist were also measured. After adjusting for age and sex, the univariate additive genetic (A), dominant genetic (D) and unique environmental (E) effects model showed 76% additive genetic component in the variance of GCS, while 46% for twist. Similarly high, but dominant genetic effects (D) were found regarding GLS, GRS, apical rotation and basal rotation (D: 77%, 70%, 74% and 62%, respectively). Unique environmental effects were responsible for the rest of the variance (E: 23% to 54%).

Our study demonstrated high heritability of LV deformation. Role of unique environmental factors is less prominent. These results urge to search for the responsible genes determining LV deformation, whilst also highlight the importance of advanced echocardiographic screening.

ACUTE PULMONARY EMBOLISM

P6402 | BEDSIDE
Right-sided heart thrombus in the patients with atrial fibrillation and acute pulmonary embolism: impact on in-hospital prognosis
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Aim of the study: The aim of the study was to determine the prevalence of thrombus in the right side of the heart (RHT), and its potential impact on prognosis in patients with acute pulmonary embolism (APE). The secondary aim of the study was to assess the association between the presence of RHT and the presence of AF.

Methods: The study group consisted of 1006 consecutive patients with APE (598 females, 408 males), with a mean age 65±14.6 years. We excluded 31 patients due to a lack of information on the presence or absence of RHT.

Results: As compared to patients without RHT, patients with RHT had lower systolic blood pressure (108±48 vs 125±31 mmHg, p=0.004), higher heart rate (109±22 vs 40% of those with RHT as compared to those without RHT. (32.0% vs 13.5%, OR 3.02, p=0.001). There were no differences in the prevalence of RHT in patients with AF as compared to patients without AF (6.9% vs 4.5% OR 1.60, p=0.147).

The mortality rate in patients with AF and RHT was significantly higher than in patients with AF and patients without RHT.
higher as compared to those with AF but without RHT (50% vs 20.5% OR 3.86, \(p=0.014\)). In turn, in patients without AF but with RHT the mortality rate was twice as high as in those with neither AF nor RHT (24.2% vs 11.2%, OR 2.57, \(p=0.041\)). Univariate analysis revealed an association of death with age (\(p=0.03\), OR 1.23), fibrinolysis (\(p=0.01\), OR 4.30), history of heart failure (\(p=0.007\), OR 1.99), active infection (\(p=0.007\), OR 1.96), mmm7, CRTT (\(p=0.001\), OR 2.02), lower systolic blood pressure (\(p=0.001\), OR 0.77), higher heart rate (\(p=0.01\), OR 1.21), AF detected during admission (\(p=0.001\), OR 2.18), elevated ctTnt (\(p=0.001\), OR 2.75), catecholamines use (\(p=0.000\), OR 9.34), RHT (\(p=0.001\), OR 3.02) and RV overload (\(p=0.001\), OR 4.06). In multivariate analysis the independent predictors of death were: RHT (\(p=0.026\), OR 2.35), age (\(p=0.005\), OR 1.29), heart rate on admission (\(p=0.019\), OR 1.11), shock (\(p=0.000\), OR 9.96) and RV overload (\(p=0.012\), OR 2.53).

Conclusion: RHT was an independent predictor of death in patients with APE. The mortality rate was three times higher in patients with RHT as compared to those without RHT. The presence of RHT was comparable in patients with and without AF. The mortality rate in patients with AF and RHT was 3 times higher than the rate in patients with AF but without RHT.

### P6403 | BEDSIDE

**Predictive value of TDI assessment of right ventricular function in patients with acute pulmonary embolism**

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The aim was to determine whether the assessment of right ventricular function using tissue Doppler imaging (TDI) of the tricuspid annulus (TA) could be used as a prognostic marker in patients with pulmonary embolism (PE).

Materials and methods: Echocardiography (EchocG) and pulsed TDI were performed in 167 patients with acute PE and normal left ventricular ejection fraction, and in 35 matched healthy volunteers (CG). The tricuspid annulus systolic (S_tr,v) and diastolic velocities were acquired in apical four-chamber view using TDI.

Results: TDI EchocCG established: In patients with PE systolic and early diastolic TA velocities were significant lower that in CG (\(p<0.001\)). In 62 (37%) of PE patients we estimated signs of RV dysfunction: high atrial (RA) pressure (IVC diameter \(>2.1\) cm and inspiratory collapse \(-50\%) and RA dilatation \(-18\) cm). In PE patients with RV dysfunction S_tr was significant lower 10.6 \(+1.5\) cm/s that in patients with normal RV function 11.8 \(+1.8\) cm/s (\(p<0.005\)) during the 30-day follow-up period 8 (13%) patients with RV dysfunction and S_tr \(<10.5\) cm/s had recurrent PE and 4 (6.5%) patients died. In patients with S_tr \(<10.5\) cm/s we observed 1 patient with recurrent PE and no deaths occurred. The major complications (recurrent PTE and death) had a significant higher rate in patients with RV dysfunction (\(p<0.001\)).

Conclusion: In clinical settings TDI EchocG in PE patients was a valuable, non-invasive method for evaluation of RV function. The establishment of RV dysfunction was related with significant increase in major complications, which should enhance clinical attention and care to those patients at risk. According to our results, normotensive patients without signs of right heart failure or serious co-morbidity belong to a low-risk group which could be early discharged within 24 h and treated out of hospital.

### P6404 | BEDSIDE

**Computed-tomography-findings of inferior vena cava perforation after inferior vena cava filter deployment and its prognosis**

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Objective: The indication of inferior vena cava filter (IVC-filter) is inconclusive because of possible IVC-filter-related adverse events. Although several reports introduced the computed tomography (CT) findings of IVC-filter with IVC-perforation and its clinical significance, no enough evidence is available.

Methods: We introduced the computed tomography (CT) findings of IVC-filter with IVC-perforation. The indication of inferior vena cava filter (IVC-filter) is inconclusive because of possible IVC-filter-related adverse events. Although several reports introduced the computed tomography (CT) findings of IVC-filter with IVC-perforation and its clinical significance, no enough evidence is available.

Results: Obvious IVC-perforation was observed in 11/41 cases (27%) and no adverse events have occurred (0%) during follow-up period (287–279 days). Of these, 4/11 cases were planed to remove the IVC-filter and the IVC-filters were safely retrieved in all cases without any complications.

Conclusions: IVC-perforation is a kind of shocking finding, however, our data suggests it rarely causes clinically devastating events and can be retrieved safely.

### P6405 | BEDSIDE

**Patient selection in outpatient and short-stay treatment in pulmonary embolism - comparison of different criteria (PESI, sPESI, Hestia and RV on CT) in relation to ESC 2014 guidelines**

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Background: Over the latest decade wide spectrum of studies have presented possible solutions of how to select low-risk pulmonary embolism (PE) patients to home treatment. Several risk scores have been introduced as prediction tools for the recognition of low death risk individuals. Universal consensus for how to use these criteria is lacking and there is a need for clarification for which one to integrate.

Purpose: To compare three scores – Pulmonary Embolism Severity Index (PESI), simplified Pulmonary Embolism Severity Index (sPESI) and Hestia – and documented right ventricular dysfunction (RVD) on computer tomography (CT) to find out if these criteria recognized the same or different patients to be treated at home and also evaluate the current practice of patient selection in outpatient and short-stay treatment of PE in Finland based on ESC 2014 guidelines recommendations.

Methods: From January 2010 to July 2012, 276 patients with acute, symptomatic PE were screened retrospectively from electronic patient records. 233 patients, aged 16–93 years, were included in the final analysis. All patients were treated accordingly to local Finnish guidelines. Statistical computations were performed by R statistical software version 3.0.2 and IBM SPSS version 21. The concordance of the scores was analysed by Cohens' and Fleiss' kappa.

Results: The most significant difference was found when documented RVD on CT was compared to PESI, sPESI and Hestia - almost half of the patients were classified differently. The best concordance was found between PESI and sPESI, but still only 0.71 that means substantial agreement. All of the patients (n=19) who would have been sent to home using only PESI (n=9), only sPESI (n=1) or both of them simultaneously (n=9) had RVD on CT. There were 5 patients with PESI class I or II with clinical signs of RVD, one of these patients had PESI class III (young and tachycardic) and four patients had PESI class II (3 were tachycardic and 2 had oxygen demand). When all four criteria scores were revised in our study population, 40–60% of patients could have been treated early at home, but only 9 patients (3.9%) were discharged straight from the emergency ward to home. At or below 48 hours of hospital stay were discharged 43 patients (18.5%).

Conclusions: Although PE patient is classified as low risk group, there might still be RVD, and the patient should be treated in the hospital. The effort should be projected to accomplishing universal consensus of how to manage rapid and accurate risk stratification recognizing especially low mortality risk patients, patient safety being major concern.

### P6406 | BEDSIDE

**Usefulness of right ventricular rate pressure product to assess right ventricular dysfunction and mortality in acute hemodynamically stable pulmonary embolism**

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Introduction: Acute pulmonary embolism (APE) manifests with an acute increase in right ventricular afterload leading hemodynamic compromise. With neurohormonal activation, right ventricular (RV) compensatory response plays a crucial role in clinical progress. As a simple indicator of RV energy consumption, right ventricular rate pressure product (rRPP) may utilize determination of RV dysfunction (RVD). We aimed to investigate the relationship between rRPP and RVD in acute hemodynamically stable pulmonary embolism.

Methods: 218 consecutive patients admitted with APE (54% male, mean age 61.2±19.8) between 2010–2014 were included in the study and divided into tertiles with respect to rRPP. Patients were followed-up median 28.9 months. RVD was defined as right-to-left ventricular dimension ratio > 1.0 in the relevant transverse plane. rRPP was calculated as the product of admission heart rate documented by ECG and echocardiography derived systolic pulmonary artery pressure.

Results: The prevalence of RVD was highest in the highest rRPP tertile (34%, \(p=0.011\)), and rRPP had a close relationship with troponin levels (\(r=0.480\), \(p<0.001\)). In multivariate analysis, rRPP was delineated as an independent predictor of RVD (OR: 1.19, 95% CI: 1.008–1.678, \(p=0.003\)). In ROC analysis, a cut-off value of 4983.7 for rRPP has a 69% sensitivity and 63% specificity for predicting RVD in APE (AUC 0.732 \(p=0.001\)). Kaplan-Meier analysis for long-term mortality, demonstrated higher mortality rate in third rRPP tertile compared with other tertiles (\(p=0.010\), Chi-square = 6.551).

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Conclusion: As an indicator of RV compensatory response, rRRP seems to be an independent marker of RVD and mortality. A bedside examination, the assessment of this calculation may be beneficial in clinical assessment of these patients.

P6407 | BEDSIDE
Course of vascular obstruction after pulmonary embolism as assessed by ventilation-perfusion lung scan follow-up

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Background: We investigated the course of residual pulmonary vascular obstruction (RPVO) from discharge up to 3-6 months after pulmonary embolism (PE).

Methods: Prospective registry including 202 consecutive patients with PE who survived the acute phase (high risk PE: 12.4%, intermediate-risk: 65.8%, and low-risk: 21.8%). Patients with a prior history of chronic pulmonary disease were excluded. Ventilation-perfusion (V/Q) lung scan was performed in all patients before discharge, and again at follow-up (between 3 and 6 months after discharge).

Results: Between both lung scans, RPVO decreased from 29.1±15% to 10.9±11.4%, with an average relative change of 61.7±33.4%. Overall, 49 patients (24.2%) presented a full resolution of lung perfusion. Relative change in RPVO was constant, regardless of the level of RPVO at discharge (p<0.07). Patients who presented full resolution on the second lung scan (n=49) had significantly lower RPVO at discharge as compared to those without full resolution (21.7±10.1% vs 31.4±16.0% respectively, p<0.001), and almost 75% of those with full resolution had RPVO<30% at discharge. Multivariate logistic regression suggested that high-risk PE and right ventricle (RV) to left ventricle (LV) ratio (by quartiles) at discharge were independently related to unfavorable course of RPVO during follow-up (high-risk PE: OR 3.6, 95% CI 1.54–8.43, p<0.001; RV/LV ratio: OR 3.42, 95% CI 1.12–9.45, p<0.03).

Conclusion: Our findings suggest that systematic lung scan follow-up should not be considered after PE, except in patients with high-risk PE or those with echocardiographic signs of RV pressure overload at discharge.

P6410 | BEDSIDE
Effect of atrial fibrillation on the in-hospital prognosis of patients with acute pulmonary embolism

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Background: The novel guidelines recommend several novel anticoagulant drugs and vitamin K antagonists for the treatment of pulmonary embolism. However, in all studies which studied novel anticoagulants, patients who received them were not assessed by ventilation-perfusion lung scan follow-up. The aim of this study was the assessment of the combination of these agents and the exact protocol for the introduction of NOACS is not established.

Methods: Seventy-five consecutive patients with either high or intermediate risk PTE who admitted in the single coronary care unit of university hospital during the last 3 years. A retrospective analysis. AF through the therapy all patients were on continuous infusion of unfractionated heparin until hemodynamic stabilization when they started either bridging with enoxaparin and vitamin K antagonists or for rivaroxaban at dose 15 mg twice daily. Composite end point of death, major bleeding and need for mechanical ventilation at 30 days were compared between 34 and 41 patients who received vitamin K antagonists or rivaroxaban, respectively. Only patients who were on oral anticoagulant therapy (OAC) for at least 1 day are included in the study, and major bleeding was related to OAC if patient was on rivaroxaban for at least 2 doses and on vitamin K antagonists within the first 24 hours. The two groups were similar in relation to age (62±15 vs 59±17 y, p=0.401), gender distribution (p=0.817), simplified PESI score at admission (2.0 [1.0–5.0] vs 1.0 [0.5–3.0], p=0.735) and the distribution of major and minor risk patients (38% vs 42% adm vs 6 [16.4%], p=0.591). Only one patient in rivaroxaban group died from PTE. One patient on vitamin K antagonists and 2 patients on rivaroxaban fulfilled criteria for major bleeding on OAC. However, 5 (16.1%) and 6 (14.5%) patients had major bleeding related to thrombolysis before the OACs was initiated. Composite 30 days end point was similar between two groups (2 [5.9%] and 6 [14.6%], p=0.280), respectively. The average hospitalization stay was similar between two groups (10 [6–14] vs 8 [7–13] days, p=0.136).

Conclusion: There was no significant difference between major adverse events at 30 days between heparin plus Vitamin K antagonists compared to rivaroxaban group in PTE patients who received thrombolytic therapy.

P6409 | BEDSIDE
Comparison of rivaroxaban and vitamin K antagonists anticoagulant therapy after thrombolysis in patients with intermediate and high risk pulmonary embolism

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Background: The novel guidelines recommend several novel anticoagulant drugs and vitamin K antagonists for the treatment of pulmonary embolism. However, in all studies which studied novel anticoagulants, patients who received them were not assessed by ventilation-perfusion lung scan follow-up.

Methods: Between both lung scans, RPVO decreased from 29.1±15% to 10.9±11.4%, with an average relative change of 61.7±33.4%. Overall, 49 patients (24.2%) presented a full resolution of lung perfusion. Relative change in RPVO was constant, regardless of the level of RPVO at discharge (p<0.07). Patients who presented full resolution on the second lung scan (n=49) had significantly lower RPVO at discharge as compared to those without full resolution (21.7±10.1% vs 31.4±16.0% respectively, p<0.001), and almost 75% of those with full resolution had RPVO<30% at discharge. Multivariate logistic regression suggested that high-risk PE and right ventricle (RV) to left ventricle (LV) ratio (by quartiles) at discharge were independently related to unfavorable course of RPVO during follow-up (high-risk PE: OR 3.6, 95% CI 1.54–8.43, p<0.001; RV/LV ratio: OR 3.42, 95% CI 1.12–9.45, p<0.03).

Conclusion: Our findings suggest that systematic lung scan follow-up should not be considered after PE, except in patients with high-risk PE or those with echocardiographic signs of RV pressure overload at discharge.

P6510 | BEDSIDE
Identification of normotensive patients with pulmonary embolism at high risk of adverse clinical outcome: comparison of two clinical scores

S. Vanni1, D. Jimenez2, P. Nazerian1, C. Gigli1, G. Pепе1, B. Paladini1, F. Emrini1, C. Caviglioli1, F. Morello3, S. Grifoni1.

Background: Recently two clinical scores (Bova score and TELOS score) have been proposed for the identification of normotensive patients with acute pulmonary embolism (PE) at high risk of haemodynamic collapse and death. The present study compared the accuracy of the two scores and investigated the prognostic utility of their combination.

Methods: Bova score, based on the presence of mild hypotension (systolic blood pressure <95% [0.96;4.71], p=0.067). Univariate analysis revealed an association of death and almost 75% of those with full resolution had RPVO<30% at discharge. Multivariate logistic regression suggested that high-risk PE and right ventricle (RV) to left ventricle (LV) ratio (by quartiles) at discharge were independently related to unfavorable course of RPVO during follow-up (high-risk PE: OR 3.6, 95% CI 1.54–8.43, p<0.001; RV/LV ratio: OR 3.42, 95% CI 1.12–9.45, p<0.03).

Conclusion: Our findings suggest that systematic lung scan follow-up should not be considered after PE, except in patients with high-risk PE or those with echocardiographic signs of RV pressure overload at discharge.

P6409 | BEDSIDE
Comparison of rivaroxaban and vitamin K antagonists anticoagulant therapy after thrombolysis in patients with intermediate and high risk pulmonary embolism

S. Obrodovic1, B. Dzudovic1, S. Vukotic1, D. Vranes1, B. Subotic2, G. Koricovic1, N. Antonijevic3.

Conclusion: Patients with APE who experience AF during hospital admission had higher risk of death and complications as compared to patients without AF.

P6400 | BEDSIDE
Identification of normotensive patients with pulmonary embolism at high risk of adverse clinical outcome: comparison of two clinical scores

S. Vanni1, D. Jimenez2, P. Nazerian1, C. Gigli1, G. Pepe1, B. Paladini1, F. Emrini1, C. Caviglioli1, F. Morello3, S. Grifoni1.
pressure 90–100 mmHg), tachycardia (≥110/min), right ventricular dysfunction (RVD) and troponin elevation, categorized normotensive patients with PE into three groups: low, intermediate and high risk patients. TELOS score based on the presence of RVD, elevated troponin and plasma lactate (≥2mmol/l); when all three criteria are present, patients are considered at high risk of adverse outcome. We retrospectively applied the scores on a large cohort of patients derived from three prospective studies. The primary outcome was a composite of haemodynamic collapse and death within 7 days from diagnosis.

**Results:** Of 1276 screened patients, 21 patients with shock and 261 patients with missing values were excluded. Of the 994 (79.1%) patients included in the analysis, 63 (6.3%) reached the primary outcome. Bova score classified 775 (78.0%), 160 (16.1%) and 59 (5.9%) patients in low, intermediate and high-risk categories, with primary endpoint incidence of 3.7%, 14.4% and 18.6% respectively (c2 for trend P<0.01). Similarly to the Bova score, TELOS score identified 58 (5.8%) high-risk patients, with a primary outcome incidence of 20.7% (P<0.001 vs low risk). When we identified high-risk patients by using the combination of the two scores (high-risk patients according to Bova score together with high-risk patients according to TELOS score), patients included in the high-risk group increased to 91 (9.1%), without a reduction in the primary outcome incidence (18.7%).

**Conclusions:** Both Bova and TELOS scores identified a small group of normotensive patients at high risk of short-term adverse outcome, with no significant differences between scores. The combination of the two scores sensibly increased the proportion of high-risk patients.

**Methods:** This is a cross-sectional study of adults with CHD at a tertiary center. A control group was also recruited. The HADS-P is a 14-item rating scale with independent subscales for anxiety and depression (7 items each) was administered to both the study and control groups. A cut-off score of >8 points on either of the depression and anxiety subscale was used to determine their respective diagnoses.

**Results:** A total of 192 patients (92 patients with CHD and 100 controls) with a mean age of 33 years old were recruited. The proportion of cases with anxiety and depression were significantly higher among those with CHD (61% and 39% in the CHD group compared to healthy controls. Of the 92 patients with CHD, majority had an atrial septal defect, ventricular septal defect, and patent ductus arteriosus. Focusing on the CHD group, simple logistic regression identified employment status, a higher NYFC, low distance 6 minute walk test, traditional cardiopulmonary defects (AF, VSD) as predictors of anxiety; whereas a higher educational achievement, higher NYFC, right-to-left shunt or Eisenmenger physiology, low distance 6 minute walk test, and LV/RV failure were predictors of depression. Multiple logistic regression identified only employment status (i.e. being unemployed) as a significant predictor of anxiety [OR 4.54, p=0.012]; while having a right-to-left shunt or Eisenmenger physiology was a significant predictor of depression [OR 6.44, p=0.004].

**Conclusion:** This cohort of adult Filipinos with CHD has higher HADS-P scores, suggestive of a higher prevalence of depression and anxiety. Factors associated with the presence of anxiety and depression, and some interventions that may help improve their quality of life should be explored.

**Objectives:** To determine the prevalence of anxiety and depression in adult CHD Filipino patients compared to healthy controls using the HADS-P questionnaire.

**Methods:** We retrospectively applied the scores on a large cohort of patients derived from three prospective studies. The primary outcome was a composite of haemodynamic collapse and death within 7 days from diagnosis.
(Aprox) to postaortic (Adist) aorta (A=4/V2-V1) (Aprox/Adist).2) The calculated PG was compared to values yielded by the conventional Bernoulli equation (A=4/V2-V12) and to the noninvasively measured blood pressure difference between the right arm and leg, which served as standard of reference. In 10 patients measurements of the pre- and poststenotic VA were taken from noninvasive angiographies (CT or MRA) and added to the calculation. In all other patients, a ratio of 1 for Aprox/Adist was applied (A=4/V2-V12).

Results: Calculation of the PG across the CoA with the refined equation showed better performance in regression analysis than with the conventional equation (correlation 0.82), even if measurements of the pre- and poststenotic VA were included in the calculations (corrected R2 of 0.887). Accordingly, Bland-Altman-limits of agreement showed smaller confidence intervals compared to the calculations by the conventional Bernoulli equation.

Conclusion: Our study has shown that this refined equation yielded more accurate results of the PG in CoA compared to the conventional Bernoulli equation, especially when adding measurements of the pre- and postaortic VA to the calculation. Moreover we can state that the pre- and poststenotic VA have to be different if the PG deviates from the blood pressure difference and can be estimated by the novel equation if not available by noninvasive imaging. Hence we recommend using the novel equation for assessment of severity in CoA and furthermore, considering additional noninvasive imaging for assessing VA in cases where the PG by DVM differs substantially from the blood pressure difference.

P6416 | BEDSIDE
Anomalous connections or the coronary arteries: a prospective observational cohort of 472 adults. The ANOCOR Registry
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Introduction: Anomalous connections of the coronary arteries (ANOCOR) are rare. Management of high-risk ANOCOR may be difficult in the lack of life-threatening cardiac events. Need of risk stratification model is recognized. Large-scale multicenter registries dedicated to these congenital abnormalities are lacking.

Purpose: The multicenter ANOCOR Registry provides prospective collection of contemporary data regarding the profile and the management of patients with ANOCOR.

Methods: The cohort population comprised consecutive patients presenting to French interventional cardiologists (n=71) during the recruitment period (January 2010-January 2013). ANOCOR was documented by selective coronary angiography or cardiac computed tomography angiography. Follow-up was planned at 5 years by the coordinating center.

Results: 472 patients (72% male) were enrolled with a mean age 63±13 years. Young patients (≤35 years of age) were few (n=11). First imaging modality was selective coronary angiography in 89.2% (n=421) and cardiac computed tomography angiography in 10.8% (n=51). Initial clinical presentation was computed tomography in 89.2% (n=421) and cardiac computed tomography angiography in 10.8% (n=51). Initial clinical presentation was computed tomography in 89.2% (n=421) and cardiac computed tomography angiography in 10.8% (n=51). Initial clinical presentation was computed tomography in 89.2% (n=421) and cardiac computed tomography angiography in 10.8% (n=51).

Calculation of the PG across the CoA with the refined equation showed better performance in regression analysis than with the conventional equation, especially when adding measurements of the pre- and poststenotic VA to the calculation. Moreover we can state that the pre- and poststenotic VA have to be different if the PG deviates from the blood pressure difference and can be estimated by the novel equation if not available by noninvasive imaging. Hence we recommend using the novel equation for assessment of severity in CoA and furthermore, considering additional noninvasive imaging for assessing VA in cases where the PG by DVM differs substantially from the blood pressure difference.

P6417 | BEDSIDE
Multivariable mortality risk stratification in adult patients with Eisenmenger syndrome
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Background: Eisenmenger Syndrome (ES) is the extreme manifestation of pulmonary arterial hypertension (PAH) in patients with congenital heart disease, as defined by a gradient between the right and leg. Several clinical parameters were proposed as predictors of mortality but risk stratification remains challenging, as multiple variables associated with high mortality. Several single parameters were proposed as predictors of mortality but risk stratification remains challenging, as multiple variables are available in the clinical setting.

Methods and results: In total 334 adult patients with ES were identified (62% female, 36% with Down syndrome), including 190 (57%) patients with post-tricuspid lesion, 29 (9%) with pre-tricuspid shunt and 115 (34%) with complex anatomy. Over a cumulative follow-up period of 1120 patient-years 78 patients died. On univariable Cox regression analysis several parameters were related to mortality, including age, oxygen saturation (SO2), 6-minute walk test distance, presence of sinus rhythm, QRS duration, presence of pericardial effusion on echocardiography, treatment with advanced therapy for PAH (AT for PAH) and several biochemical parameters. On multivariable Cox regression analysis (Figure) only age, SO2, pericardial effusion, albumin and AT remained in the mortality risk stratification model. The model remained stable after adjustment for missing values using multiple imputation as well as after adjustment for AT as a time dependent variable.

Conclusions: Multivariable mortality risk stratification is feasible and may improve further management of patients with ES. Multivariate validation and adjustment of the risk stratification model is currently in progress and should enhance the risk stratification process and management of ES patients.
Release of growth-differentiation factor 15 and associations with cardiac function in adults with congenital heart disease

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Background: Growth-differentiation factor-15 (GDF-15), an oxidative stress-induced cytokine with broad cardiac and non-cardiac activity, has diagnostic and prognostic value in acquired heart failure. Purpose: We studied the release of GDF-15 in adults with congenital heart disease (ConHD), and assessed its association with cardiac function and functional capacity. Methods: A total of 587 consecutive adults with ConHD (median age 33 [IQR 25–41] years, 59% men, and 90% NYHA I II) underwent physical examination, electrocardiography, echocardiography, and venepuncture according to a standardised protocol. A subset of 143 patients underwent bicycle ergometry on the same day. Results: Median plasma GDF-15 was 618 [IQR 487–867] ng/L. In 87 patients (15%), GDF-15 was above the reference value of normal (1109 ng/L). GDF-15 levels were higher in older patients (p=0.367, p<0.001). GDF-15 was higher in patients with elevated pulmonary pressure than in patients with normal pulmonary pressure (p<0.001). NT-proBNP and GDF-15 above the reference value was associated with NYHA class (odds ratio for NYHA II: 3.5 [95% CI 1.8–6.8], p<0.001, and decreased exercise capacity: patients able to work out 41.6±22.9 mm to 33.7±15.3 mm; the size of the RA from 42.7±24.1 mm to 38.7±6.5 mm & from 52.7±13.3 mm to 43.5±7.6 mm and the SPAP from 34.3±7.0 to 26±4.5 mm Hg & from 52.0±14.5 to 36.8±11.4 mm Hg, respectively. The absolute changes of the SPAP and size of right chambers were significantly different in the groups. Symptoms of heart failure (HF) noted 27% and 75% of patients before surgery in groups 1 and 2. After the procedure, reducing the symptoms of HF noted 100% and 85% of patients in groups 1 and 2, respectively.

Conclusion: Closing of ASD is accompanied by improvement of clinical symptoms and decrease of the size of the right heart chambers is not dependent on the age of the patient. However, the most beneficial results are obtained in patients with less severe symptoms HF, right chambers overload and initially less increased pulmonary artery pressure. Closings hemodynamically significant ASD should be advised as soon as possible, at an earlier date after the diagnosis, especially in older patients.

Anticoagulation in adults with congenital heart disease and atrial arrhythmias. A report from a regional registry of congenital heart disease (RACCA)

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Patients with congenital heart disease (CHD) and atrial arrhythmias (AA) often do not have typical thromboembolic risk factors and typically present with arrhythmias other than non-valvular atrial fibrillation. The need for anticoagulation in intra-atrial re-entry tachycardia (IART) may be questioned, but the prevalence of intracardiac thrombi in this patients has been reported to be high. Thus, anti-coagulation is recommended in high-risk patients. We sought to evaluate current practice on anticoagulation therapy and the accordance with existing guidelines.

Methods: A total of 2,384 patients >14 years were prospectively included over a period of 2 years in the regional RACCA registry. We addressed the use of anticoagulation or antiplatelet therapy in 258 patients with paroxysmal or chronic atrial flutter, atrial fibrillation or IART. Patients with previous intracardiac repair, Fontan palliation, mechanical valves or subaortic right ventricle or with CHA2DS2-VASc ≥1 were considered as high-risk.

Results: A total of 158 patients, which accounted for 60.8% of all cases with AA, were on antithrombotic treatment: warfarin 66.4%; new oral anticoagulants (NACO) 0.63%; and antiplatelets (ASA) 29%. Of high-risk patients, only 50% were receiving anticoagulation with warfarin. Forty-five (39%) patients were maintained mild and 12 (11%) moderate to severe atrial fibrillation regurgitation. No re-occurrences occurred. In the open VSD group, six (4%) patients developed endocarditis. Nineteen (14%) spontaneous closures occurred.

Conclusions: Overall long-term survival in patients with VSD is excellent. Ninety-one percent of patients function in NYHA class I. Five patients needed pacemaker implantation after VSD closure. An important percentage of patients without congenital aortic valve malformations developed AS after VSD closure. A potential association with surgery needs to be further investigated.
P6423 | BEDSIDE
Risk factors for cardiovascular and cerebrovascular diseases among 4,752 adult hypertensive subjects in the primary care setting in Guangdong, China: a 5-year follow-up study

H.H.X. Wang1, J.J. Wang2, D.Y. Zhang2, J. Tang3, D.R. Yu2, L.C. Li1, X. Huang1, X.J. Li2, M.C.S. Wong1, S.M. Griffiths1

Background and introduction: In China, an increasing level of attention has been paid to the rising occurrence of disability and deaths caused by cardiovascular and cerebrovascular diseases (CCDs). Our previous study showed that the prevalence of hypertension was rising continuously, and more than one in ten of the general population had two or more chronic conditions simultaneously. The recent national health report showed that nearly 3 million people died from diseases related to CCD, accounting for 51% of the causes of total deaths annually in China.

Purpose: This longitudinal study aimed to explore factors associated with the prevalence of CCDs among an adult hypertensive population in the primary care setting in China.

Methods: The community health centres (CHCs) are the major primary care providers in mainland China. We selected six CHCs according to the geographic locations and population characteristics, wherein a national standardised protocol of community-based hypertension management strategy has been in place from August 2007 to July 2012. Information of adult hypertensive subjects enrolled in the care management of these CHCs were collected, and the prescription profiles of antihypertensive drugs were captured through face-to-face interviews as of August 2012. A multivariate Cox proportional hazards modelling analysis was performed.

Results: A total of 4,752 adult subjects with physician-diagnosed hypertension were enrolled, with an overall follow-up at 5 years. The age of the overall participants ranged from 23 to 98 years old, and there was a slightly higher proportion of females (58.4%, [2,774/4,752]). The mean survival time was 10.92 years (standard deviation 5.44 years). There were no significant differences (p=0.126) in the mean age years between males (67.02, standard deviation 11.23) and females (67.51, standard deviation 10.87). Factors associated with CCDs among hypertensive subjects included ageing (adjusted hazard ratio [aHR]=1.06, 95% CI 1.04 to 1.08), systolic dietary preference (aHR=1.53, 95% CI 1.01 to 2.33), smoking behaviour (aHR=1.77, 95% CI 1.11 to 2.81), abnormal level of body mass index (aBMI=1.75, 95% CI 1.01 to 1.12), and suboptimal blood pressure control (aHR=1.48, 95% CI 1.02 to 1.94).

Conclusion(s): Our study suggests that hypertensive patients in the primary care setting in China should be monitored closely for preventing secondary CCDs, especially for those who have risk factors of CCDs identified in the present study.

P6425 | BEDSIDE
NT-proBNP as a predictor of calcified coronary atherosclerosis progression

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Background: Coronary calcium score (CCS) is a well validated index of subclinical atherosclerosis with high negative predictive value in patients with intermediate risk and low/absent CCS. Predictors of CCS progression are not well understood, as traditional coronary risk factors show a low relation with CCS progression. Cardiac natriuretic peptides have been recently postulated as potential biomarkers of vascular remodeling beyond the presence of cardiac anomalies and have been associated with the amount of CCS. We analyzed the hypothesis that NT-proBNP could be also a predictor of CCS progression.

Methods: We analyzed 601 middle aged subjects without previous cardiovascular events and a baseline value of CCS <100 Agatson Unit (A.U.) from the screening program of the Montignoso Heart and Lung Project. These subjects underwent a second computed tomography (CT) scan 3 years after basal CT, using the same detector, and having the same level of irradiation. A trained cardiologist, who was blinded to previous data, evaluated calcium volumes with the software. Intraclass correlation coefficient for inter-rater reproducibility was 0.99. A total of 49 patients (7.8%) developed coronary calcifications. NT-proBNP was measured with a highsensitivity electrochemiluminescence immunoassay (ECLIA) and was performed on the day of the previous CT scans. The cut-off for NT-proBNP was 100 pg/ml.

Results: Among the 601 subjects, we observed an increase of CCS from 0 to 100 A.U. in 29% (173 patients) and no change in 71% (428 patients). In univariate analysis, age, female sex, smoking, diabetes, obesity, and systolic blood pressure were related to progression of coronary wall calcifications. After adjustment for confounding factors (i.e., age, sex, physical activity, smoking and eating habits, education program). Adult Treatment panel III (revise NCEP ATP III), the International Diabetes Federation (IDF) or the Harmonized definition. MS was defined using three definitions, provided by the National Cholesterol Education Program Adult Treatment panel III (revised NCEP ATP III), the Internatio- nal Diabetes Federation (IDF) or the Harmonized definition.

Results: The NCEP ATP III criteria for the MS were met by 20.0% of the sam- ple, while 48.9% met the IDF criteria and 51.0% the Harmonized criteria using the IDF cut points for waist circumference. After adjusting for various potential confounding factors (i.e., age, sex, physical activity, smoking and eating habits, using the MedDietScore), history of MS using the revised NCEP ATP III definition, was associated with 83% higher likelihood (95% CI: 1.24–2.72) of 10-year-CCVD incidence. Furthermore, using the IDF or the Harmonized definitions, insignifi- cant results were observed (OR=0.91, 95% CI: 0.62–1.35 and OR=0.98, 95% CI: 0.66–1.47, respectively).

Conclusion: After 10 years of follow-up, participants with MS defined by the re- vised NCEP ATP III definition had increased likelihood of CVD.

Acknowledgement/Funding: Demosthenes Panagiotakos and Ekavri Georgousopoulou received research grants by Coca-Cola SA.
**P6426 | BEDSIDE**

Impact of delay to reperfusion on infarct size and clinical outcomes in patients with ST-segment myocardial infarction

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**Background:** Longer delay from symptom onset to reperfusion has been associated with increased mortality and worse clinical outcome in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI). The effect of delay on clinical outcomes is not entirely clear. We aimed to evaluate the impact of the delay from symptom onset to reperfusion (<3 h vs. ≥3 h) on infarct size and clinical outcomes at 30 days in patients with STEMI treated with PCI.

**Methods:** We analyzed 482 consecutive patients presenting to a tertiary care hospital with STEMI who underwent PCI between July 2012 and April 2014. Peak CK, a measure of infarct size, and the incidence of major adverse events (defined as the composite of death, re-infarction or clinically driven target-vessel revascularization) and major bleeding (defined as BARC type-3) at 30 days were compared between 2 groups of patients regarding time from symptom onset to reperfusion, classified as <3 h vs. ≥3 h.

**Results:** There were 249 (52%) patients with <3 h delay and 233 (48%) with ≥3 h delay. Patients with longer delay were significantly older; anticoagulant/antiplatelet treatment and baseline TIMI flow score were similar in both groups. Patients with shorter delay had significantly smaller enzymatic infarct size, higher rates of final TIMI 3 flow and lower rates of the composite of major adverse events. Major bleeding rates were similar in both groups.

**Impact of the delay to reperfusion**

<table>
<thead>
<tr>
<th>Total (n=482)</th>
<th>Time to reperfusion</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 h</td>
<td>1870</td>
<td></td>
</tr>
<tr>
<td>≥3 h</td>
<td>2290</td>
<td></td>
</tr>
<tr>
<td>Final TIMI 3 flow</td>
<td>229 (92%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Ischemic MACE (death, re-MI, TVR)</td>
<td>42 (16.4%)</td>
<td>0.06</td>
</tr>
<tr>
<td>Major bleeding BARC ≤3</td>
<td>19 (8.32%)</td>
<td>0.7</td>
</tr>
<tr>
<td>Composite of major adverse events (ischemic and bleeding)</td>
<td>58 (23.92%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

**Conclusion:** In patients with STEMI undergoing PCI, longer delay to reperfusion negatively impacts clinical outcome. This effect appears to be mediated by less successful reperfusion and by a larger infarct size.

**P6427 | BEDSIDE**

Impact of delay to reperfusion on infarct size and clinical outcomes in patients with ST-segment myocardial infarction

M.-R. Taskinen1, C.P. Cannon2, D. Thompson3, D.A. Gipe3, M.T. Baccara-Dinet4, M.-R. Taskinen1, C.P. Cannon2, D. Thompson3, D.A. Gipe3, M.T. Baccara-Dinet4, 1Assiut University, cardiovascular medicine, Assiut, Egypt; 2Assiut University, Microbiology and Immunology, Assiut, Egypt; 3Assiut University, Clinical Pathology, Assiut, Egypt

**Background:** Myocyte necrosis and contrast induced nephropathy (CIN) occurs frequently in elective percutaneous coronary intervention (PCI) and is associated with subsequent cardiovascular events.

**Purpose:** This study assessed the cardio- and renoprotective effect of remote ischemic preconditioning (RIPC) in patients undergoing elective PCI.

**Methods:** Two hundred consecutive patients undergoing elective PCI with normal baseline troponin-I (cTnI) values were recruited. Subjects were systematically allocated to 2 groups: 100 patients received RIPC (created by three 5-minute inflations of a blood pressure cuff to 200 mmHg around the upper arm, separated by 5-minute intervals of reperfusion) ≤2 hours before the PCI procedure, and the control group (n=100). The primary outcome was incidence of PCI-related myocardial infarction (MI) and RIPC (defined as cTnI >0.2 ng/mL). Secondary outcome was incidence of CIN at 72 hours after contrast exposure.

**Results:** The incidence of MI 4a was lower in the RIPC group compared with the control group. Subjects who received RIPC had significant trend toward lower incidence of CIN and less chest pain during stent implantation compared to control group. No significant deference in the mean change of CRP was noted between both groups. At 3 month, the major adverse event rate was lower in the RIPC group (6 vs. 14 events; P=0.04).

**Conclusions:** The use of RIPC ≤2 hours before PCI, reduce the incidence of PCI-related MI 4a, tend to decrease the incidence of CIN and improve ischemic.

**P6428 | BEDSIDE**

Cardio- and renoprotective effect of remote ischemic preconditioning in patients undergoing percutaneous coronary intervention

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**Conclusions:** The use of RIPC ≤2 hours before PCI, reduce the incidence of PCI-related MI 4a, tend to decrease the incidence of CIN and improve ischemic.

**Abstract P6427 – Table 1. Effect on lipoprotein levels**

<table>
<thead>
<tr>
<th>Lipoprotein</th>
<th>Baseline ALI vs. EZE</th>
<th>W12 absolute change ALI vs. EZE</th>
<th>W12% change ALI vs. EZE</th>
<th>W24 absolute change ALI vs. EZE</th>
<th>W24% change ALI vs. EZE</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C</td>
<td>4.6 vs 4.6 (176.5 vs 177.7)</td>
<td>-2.1 vs -0.8* (-82.8 vs -31.4)</td>
<td>-47.4 vs -16.7*</td>
<td>-21 vs -0.8* (-79.2 vs -28.8)</td>
<td>-45.6 vs -14.8*</td>
</tr>
<tr>
<td>Apo B</td>
<td>[131.5 vs 128.0]</td>
<td>[-47.7 vs -16.4]</td>
<td>[47.8 vs -16.0]</td>
<td>-36.5 vs -11.6*</td>
<td>-36.5 vs -11.2*</td>
</tr>
<tr>
<td>Non-HDL-C</td>
<td>5.5 vs 5.5 (211.7 vs 210.8)</td>
<td>-2.3 vs -0.9* (-89.1 vs -36.2)</td>
<td>-41.9 vs -16.0*</td>
<td>-22 vs -0.9* (-84.9 vs -34.3)</td>
<td>-40.4 vs -14.7*</td>
</tr>
<tr>
<td>Lp(a)</td>
<td>[31.6 vs 31.5]</td>
<td>[-3.9 vs -1.7]</td>
<td>[-6.1 vs -4.5]</td>
<td>-23.3 vs -8.9*</td>
<td></td>
</tr>
<tr>
<td>Fasting triglycerides</td>
<td>1.9 vs 1.8 (170.2 vs 156.3)</td>
<td>-0.2 vs -0.2 (-22.0 vs -20.6)</td>
<td>-9.3 vs 7.4</td>
<td>-0.3 vs -0.2 (-29.4 vs -20.3)</td>
<td>-10.3 vs 6.0</td>
</tr>
</tbody>
</table>

ALI, alirocumab; EZE, ezetimibe. *Medians shown for absolute change and adjusted means are shown for % change. \( P<0.0001 \) vs EZE.
Risk reduction – clinical aspects

symptoms in patients undergoing elective PCI. The observed cardio- and renoprotection appears to confer sustained benefit on reduced MAE at 3 month follow-up.

P6429 | BEDSIDE
Prognostic value of coronary CT imaging in high-risk patients without symptoms of coronary artery disease
1 Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands; 2 Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands; 3 Erasmus Medical Center, Department of Internal Medicine, Rotterdam, Netherlands

Background: At present, traditional risk factors are used to guide cardiovascular management of asymptomatic individuals. Intensified surveillance may be warranted in those identified as high risk of developing cardiovascular disease (CVD).

Purpose: This study aims to determine the prognostic value of coronary CT angiography (CTCA) next to coronary artery calcium scoring (CACS) in high CVD risk patients without symptoms suspect for coronary artery disease (CAD).

Methods: A total of 665 high-risk patients (mean age 56±9 years, 417 males), having at least one important CVD risk factor (diabetes mellitus, or familial hypercholesterolemia) or a calculated European Systematic Coronary Risk Evaluation of >10% were included from outpatient clinics at two academic centres. Follow-up was performed for the occurrence of adverse events including all-cause mortality, non-fatal myocardial infarction, or acute coronary revascularization.

Results: During a median follow-up of 3.0 (interquartile range 1.3–4.1) years, adverse events occurred in 40 (6.0%) individuals. By multivariable analysis, adjusted for age, gender and CACS, obstructive CAD on CTCA (>50% luminal stenosis) was a significant predictor of adverse events (hazard ratio 5.9 [95% confidence interval 1.3–26.1]). Addition of CTCA to age, gender, plus CACS, increased the C-statistic from 0.81 to 0.84 and resulted in a total net reclassification index of 0.19 (p=0.01).

Conclusions: CTCA has incremental prognostic value and risk reclassification benefit beyond CACS in patients without CAD symptoms but with high risk of developing CVD. Whether CTCA based patient management will improve clinical outcome remains to be determined.

P6430 | SPOTLIGHT
Carotid intima-media thickness and aortic stiffness index are increased in normal healthy subjects with parental history of diabetes mellitus
M. Ghaleb1, Z. Ashour2, M. Abd Elghany1, A. El Damaty1. Cairo University Hospitals, Cardiovascular Department, Cairo, Egypt

Background: Previous studies have shown that high HbA1c concentrations considered within the normal range may detect individuals with increased propensity for developing type 2 diabetes mellitus in the near future. Available information has also suggested that in general population, high HbA1c concentrations may detect individuals at higher risk for cardiovascular mortality. However, little is known about the diabetic subject with a familial history of diabetes is at high risk for vascular damage or not. The aim of the present work was to evaluate the arterial status of healthy offspring of diabetic patients.

Methods: Fifty-six healthy subjects with parental history of diabetes were compared with 56 matched age and sex-matched healthy subjects without parental history of diabetes. Age, sex, body mass index, smoking habits, blood pressure, HbA1c, lipid profile were measured. Carotid intima-media thickness was measured by high-resolution B-mode ultrasound imaging, and aortic stiffness index was measured by M-mode echocardiography.

Results: HbA1c level, carotid IMT and aortic stiffness index were significantly higher in subjects with parental history of diabetes than in subjects without parental history of diabetes (5.6±0.38 vs. 5.42±0.33, P<0.009; 0.65±0.09 vs. 0.55±0.09, P<0.001; 5.12±2.36 vs. 4.52±1.51, P<0.001, respectively). In all healthy subjects, HbA1c level was positively correlated with Aortic stiffness index (r=0.235, P=0.013) and carotid IMT (r=0.289, P=0.002). Also we found a positive correlation between CCA IMT and Aortic stiffness index (r=0.685, P<0.001).

Conclusions: This study demonstrated that the CCA IMT and aortic stiffness index are significantly higher in subjects with parental history of diabetes compared with subjects without parental history of diabetes. Therefore, these findings suggest that glycemic control might have a pathophysiological relevance in the development of vascular disease, even in individuals without diabetes.

P6431 | BEDSIDE
Predictive and protective values of high-density lipoprotein cholesterol for cardiovascular events in statin-treated patients with acute myocardial infarction
J.S. Park1, K.S. Cha1, J.H. Choi1, B. Kim1, H.W. Lee1, J.H. Oh1, J.H. Choi1, H.C. Lee1, T.J. Hong1, M.H. Jeong1, 2 Pusan National University Hospital, Busan, Korea, Republic of; 3 Chonnam National University Hospital, Gwangju, Korea, Republic of

Purpose: A low level of high-density lipoprotein cholesterol (HDL-C) has been identified as a residual risk of cardiovascular events after lowering low-density lipoprotein cholesterol (LDL-C) in patients with stable coronary artery disease. Furthermore, a high HDL-C level is proven to have a protective effect for cardiovascular events in primary prevention studies. We evaluated whether the HDL-C level has predictive and protective values in patients with acute myocardial infarction (MI) following percutaneous coronary intervention (PCI) and statin treatment.

Methods: A total of 15,290 patients who had acute MI and statin treatment were selected from a nationwide MI registry. Baseline HDL-C level was used to identify patients with low HDL-C (Group A; normal HDL-C (Group B), or high HDL-C (Group C) levels according to the ATPIII criteria. The primary endpoint, defined as the composite of cardiovascular death and recurrent MI, was compared within the groups who were categorized according to adjusted and matched cohorts.

Results: At the median follow-up of 11.5 months, the primary endpoint occurred 2.7% (112/4098) in Group A, 1.4% (54/3910) in Group B, and 1.2% (8/661) in Group C. In the propensity adjusted cohort, low HDL-C level was associated with an increased risk of primary endpoint (hazard ratio [HR] 1.755, 95% confidence interval [CI] 1.724–2.417, P=0.001) and high HDL-C level was not associated with a reduced risk of primary endpoint (HR 0.562, 95% CI 0.275–1.146, P=0.113). In the propensity matched cohort, low HDL-C level was consistently associated with an increased risk of primary endpoint (HR 1.716, 95% CI 1.210–2.434, P=0.002) and high HDL-C level was associated with a reduced risk of primary endpoint (HR 0.449, 95% CI 0.214–0.946, P=0.035).

Conclusions: In acute MI patients treated with PCI and statins, a low HDL-C level was associated with an increased risk of cardiovascular death and recurrent MI. However, a high HDL-C level was possibly associated with a reduced risk of cardiovascular events, particularly in patients with ST-elevation MI.

P6432 | BEDSIDE
The efficacy of ischemic preconditioning for prevention of contrast medium-induced acute kidney injury
T. Iwaki, Yokohama Sakaie Kyojai Hospital, Department of Internal Medicine, Yokohama, Japan

Background: Contrast medium-induced acute kidney injury (CI-AKI) is a serious complication of angiography. Remote ischemic preconditioning (RPC) may prevent CI-AKI. In this study, we evaluated the effect of RPC for CI-AKI.

Methods: Patients with improved renal function (serum Cr < 1.4 mg/dL or eGFR > 60 mL/min/1.73m2) undergoing elective angiography were divided to standard care (continuous intravenous saline infusion 12 hours before to 12 hours after angiography 1mL/kg/hr), with (n=34) or without RPC (n=31). RPC was accompanied by performing 4-min cycles of 5 minutes ischemia and 5 minutes reperfusion at the standard upper-arm blood pressure cuff. RPC was started before angiography and the time between last inflation and the start of angiography was <45 minutes. The primary end point was the incidence of CI-AKI, defined as an increase in s-Cr >25% or >0.5 mg/dl above baseline at 48 hours after angiography. We also measured serum cystatin C (s-cysC) at baseline and 48 hours after angiography. More than 60 mL of contrast medium was used in all patients.

Results: There were no significant differences in age, sex, smoking status, and CI-AKI between control group and RPC group (control group 105±51mL versus RPC group 89±22mL). CI-AKI occurred in 4patients (6%), 4 (13%) in the control group and 0% in the RPC group (P >0.05). The change of s-cysC from baseline to 48hours after angiography was not different between 2groups. No major adverse events were related to remote ischemic preconditioning.

Conclusions: RPC before angiography prevents CI-AKI in high-risk patients.

P6433 | BEDSIDE
Long-term anti-hypertensive treatment with amlodipine/bendroflumethiazide results in lower carotid IMT at 3.5 years than with atenolol/bendroflumethiazide
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Introduction: Carotid Intimal Medial Thickness (CIMT) can identify patients at elevated risk of cardiovascular disease. It is an independent predictor of risk of myocardial infarction, stroke and cardiovascular death. The Anglo Scandinavian Cardiac Outcomes Trial (ASCOT) enrolled 19,257 patients in seven countries (UK, Ireland, Norway, Sweden, Denmark, Finland and Iceland) with elevated cardiovascular risk without established cardiovascular disease. Participants were randomly allocated to receive combination anti-hypertensive therapy with atenolol ± bendroflumethiazide or amlodipine ± perindopril. Its Hypertension-Associated Cardiac Outcomes Study (HACOS) sub-study collected detailed cardiovascular phenotypic data from 1,006 participants at two centres in London and Dublin.

Purpose: We hypothesised that anti-hypertensive therapy with the amlodipine ± perindopril based regimen would result in a lower burden of carotid atherosclerotic disease evidenced on CIMT.

Methods: Data were collected in two phases, ~1.5 years and ~3.5 years post-randomisation to treatment assignment at each HACOS site. Participants allo-
Conclusion: EOV subjects exhibited a higher prevalence of diabetes, worse exercise performance and ventilation efficiency. EOV determinants in this population were an index of RV systolic function, LV diastolic function and BMI. These findings may provide the bases for a more in-depth definition of abnormal exercise phenotypes in the prediction of CV risk.

P6435 | BEDSIDE
Prevalence and determinants of exercise oscillatory ventilation in a population at cardiovascular risk enrolled in the EUEROX trial
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Background: Cardiopulmonary exercise testing (CPET) with gas exchange analysis allows functional evaluation of cardiopulmonary diseases and definition of ventilatory and metabolic parameters that may add to define the level of cardiovascular (CV) risk. Among CPET-derived variables, the occurrence of exercise oscillatory ventilation (EOV), a pathological ventilatory pattern, in the general population at risk for CV diseases is not described in literature. We aimed at assessing the prevalence of EOV in a general population enrolled in the EUEROX study.

Methods: 599 healthy subjects (60±14 years; male 48.4%; BMI 28.6±5 kg/m²) underwent a maximal CPET with personalized incremental ramp protocol. Subjects had different CV risk factors, but no previous CV events. A subgroup (n=230; 62±13 years; male 48.7%; BMI 29.5±5 kg/m²) also underwent echocardiography within 6 months.

Results: A prevalence of 15.9% of EOV was observed. The EOV group showed higher prevalence of diabetes (25 vs 14%, p<0.05) and female sex (71 vs 47%, p<0.05). EOV patients showed reduced exercise tolerance (workload 109±46 vs 121±49 W, p<0.05), impairment of oxygen consumption (VO2-related variables (peak VO2 15.1±3.8 vs 20.7±2.2 ml/min/kg, p<0.01) and worse ventilator efficiency (VE/VCO2 slope: 27.7±4.6 vs 25.7±3.6; peak PETCO2: 36.5±4.5 vs 39.1±4.3 mmHg, p<0.01). A lower heart rate at peak exercise (125±21 vs 135±23 bpm, p<0.01) and heart rate recovery (142±9 vs 165±9 beats, p<0.05). Echocardiographic data showed a reduction of end-systolic dimensions of both ventricles (LV ESVi: 13.5±5.6 vs 15.5±6.6 ml/m², p<0.01; RV ESA: 6.9±1.6 vs 7.8±2 cm, p<0.01) and right atrial area (14.8±4 vs 16.8±4 cm², p<0.01) in the EOV group. At a multivariate analysis the EOV determinants were TAPSE, E/A and BMI.

P6436 | BEDSIDE
Simultaneously measured inter-arm & inter-leg systolic blood pressure differences and cardiovascular risk stratification: A systematic review and meta-analysis
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Background: Association of inter-arm systolic blood pressure difference (IASBDP) and inter-leg systolic blood pressure differences (ILSBPD) with cardiovascular (CV) morbidity and mortality remains controversial. Purpose: We aimed to thoroughly examine all available evidence on inter-arm blood pressure difference and its association with CV risk and outcomes.

Methods: We searched PubMed, Embase, CoINHAL, Cochrane library and Ovid for studies reporting bilateral simultaneous blood pressure measurements in arms or legs and risk of peripheral arterial disease (PAD), coronary artery disease (CAD), cerebrovascular disease, subclavian stenosis or mortality. Random effect meta-analysis was performed to compare effect estimates.

Conclusion: Inclusion criteria was met by 17 studies (18 cohorts) were suitable for analysis. IASBDP of 10 mmHg or more was associated with PAD (RR 2.2, 1.4–3.5; p=0.0006; sensitivity 16.6%, 6.7–35.4); specificity 91.9%, 83.1–96.3; 8 cohorts; 4,774 subjects), left ventricular mass index (SMD 0.21; 0.03–0.39; p=0.02; 2 cohort; 1,604 subjects) and carotid and brachial-femoral wave velocities (SMD 0.25, 0.03–0.47; p=0.05; 3 cohorts; 2,649). Association of PAD remained significant at cut off of 15 mmHg (HR 1.91; 1.28–2.84; p<0.001; 5 cohorts; 1,914 subjects). We could not find statistically significant correlation of IASBDP with ILSBDP, cerebrovascular disease, CV and all-cause mortality in subjects with IASBDP of 10 mmHg or more, 15 mmHg or more and inter-leg systolic blood pressure difference of 15 mmHg or more. Inter-leg blood pressure difference of 15 mmHg or more was strong predictor of PAD (P=0.0001) and brachial-ankle pulse wave velocity (P<0.0001). Two invasive studies showed association of IASBDP and subclavian stenosis (estimates couldn’t be combined).

Conclusions: Inter-arm and leg blood pressure differences are associated with PAD, subclavian stenosis, high left ventricular mass effect and higher brachial-ankle pulse wave velocities. A BP difference of more than 10 or 15 mmHg is predictive of occlusive vascular disease, however lack of BP difference is less informative. Inter-arm and inter-leg BP difference measurements are inexpensive tools which can help clinicians in cardiovascular risk stratification of the patients.

P6437 | BEDSIDE
Surgical and pharmacological reassignment image on transsexuals' cardiovascular risk profile
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Purpose: To evaluate the cardiovascular effects and to stratify early cardiovascular risk in transsexual subjects undergone pharmacological and/or surgical gender reassigment. We stratified early cardiovascular risk in transsexual patients who underwent sexual reassignment surgery or only hormone replacement therapy.

Methods and results: We enrolled 56 transsexual patients. 6 undergone female-to-male (FIM) reassignment surgical therapy, 16 not-operated FIM, 13 operated male-to-female (MIF) and 21 non-operated MIF subjects. All underwent anthropometric, laboratory and instrumental [carotid artery intima-media thickness (C-IMT) and flow mediated vasodilation (FMD) of brachial artery] evaluations. We compared operated versus hormone replacement therapy (HRT) patients. We distinguished: group 1-transsexual patients who underwent gonadectomy (orchietomy for MIF subjects and hystero-anesthesia for FIM subjects); group 2-transsex-uals treated with HRT desmet inclusion criteria but without FMD (FIM subjects and androgens for MIF subjects). Our results showed a statistically significant difference (p<0.0001) between group 1 and 2 patients according to FMD values. FMD percentage (%) in patients who underwent gonadectomy was lower than not-surgical treated patients, who take only hormone replacement therapy (5,711 in group 1, 7,339 in Group 2, respectively). Mean C-IMT values were higher in go-nadectomized patients than in no-operated patients one (0.733 in Group 1; 0.582 in Group 2). The duration of hormone therapy correlates positively with mean C-IMT (R=0.90; p<0.001) and negatively with FMD% (R=-0.90; p<0.001).

Conclusions: Cardiovascular risk, which is expressed in terms of endothelial (FMD) and morphological (C-IMT) dysfunction, increases in subjects undergoing gonadectomy as compared to those receiving cross sex reassigment therapy.
alone. Previous sex does not affect the results. Therefore, a protective role of the gonads might be suggested.

P6438 | BEDSIDE
The mediating effect of adherence to Mediterranean diet on the association between fibrinogen and 10-year cardiovascular disease risk: Results Of The 10-year Follow-up of the ATTICA study (2002-2012)
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Objective: Thrombosis markers such as fibrinogen have been associated with increased cardiovascular disease (CVD) risk and are usually managed with pharmaceutical ways. On the other hand, adherence to Mediterranean diet is a widely accepted protective habit against CVD, but mainly through the management of cardiovascular disease. Moreover, there is a potential antithrombotic and antithrombosis role of Mediterranean diet that needs further research. The aim of the present study was to investigate this role under the prospective design of the ATTICA study.
Methods: The study sample were the volunteers of the ATTICA study (that included information from 1514 men and 1528 women). At baseline, the fibrinogen levels were measured, as well as assessment of dietary habits was based on the MedDietscore, that evaluates adherence to Mediterranean diet. In 2012, the 10-year follow-up was performed in 2009 participants and development of CVD (coronary heart disease, acute coronary syndromes, stroke, or other CVD) was defined according to WHO-ICD-10 criteria.
Results: The 10-year incidence was 19.7% in men and 11.7% in women (p<0.001). Unadjusted analysis showed that increased fibrinogen levels increased CVD risk (Relative Risk (RR) per 1 mg/ml = 1.006, 95%Confidence Intervals (CI)=1.003, 1.008). After adjusting for age, gender, history of diabetes mellitus, hypertension and hypercholesterolemia, smoking, family history of CVD the association remained significant (RR=1.003, 95% CI: 1.000, 1.006, p=0.05), but when adherence to Mediterranean diet was included, the association regained significance (RR=1.002, 95% CI: 1.000, 1.004, p=0.045), and thus, stratified analysis according to MedDietscore tertiles revealed that increased fibrinogen levels were significantly promoting CVD only among subjects that were away of the Mediterranean dietary pattern, but lost significance as regards to subjects that were close and very close to Mediterranean diet.
Conclusion: Adherence to Mediterranean dietary pattern might have an important antithrombotic effect apart from other beneficial effects against CVD risk. Promotion of Mediterranean diet could be an important target for public health strategies, especially under the emerging need for reducing the CVD prevention cost.

P6439 | BEDSIDE
Living alone and depressive symptoms are associated with major cardiovascular events in patients with chronic coronary heart disease
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Background: There is evidence from population-based and observational studies linking psychosocial stress, such as emotional stress and depression, to risk of coronary heart disease (CHD) and mortality. Patients with previous myocardial infarction report a higher degree of depressive symptoms, stress at work and at home, and financial strain. However, most studies evaluating psychosocial stress and CHD have not assessed its association with risk for CHD in the general population.
Purpose: The aim of the analysis was to describe the association between patterns of self-reported psychosocial stress and cardiovascular (CV) outcomes in patients with chronic CHD.
Methods: The MONICA/CAAN study (Monitoring Atherosclerotic Plaque by Initiation of darapladib Therapy (STABILITY)) trial randomized 15,826 patients with chronic CHD in 39 countries. At baseline, data on CHD risk factors were obtained from 15,456 patients completing a lifestyle questionnaire with specific information on: level of (never, sometimes, often, always) depressive symptoms; home, work and financial stress; home- and work-related sense of control; and if the subject was living alone. Psychosocial stress variables were analysed with multivariable Cox proportional hazards models, by category change, related to major adverse cardiovascular event (MACE, CV death, non-fatal myocardial infarction, non-fatal stroke) during a median of 3.7 years of follow-up, adjusted for CV risk factors, co-morbidities, prior diseases and education.
Results: Increased risk of MACE occurred in patients reporting feeling down (HR 1.14, 95% CI 1.06–1.23), lost interest in hobbies (HR 1.11, 95% CI 1.04–1.18) or experienced financial stress (HR 1.11, 95% CI 1.04–1.18). No significant evidence of a relationship was observed for home-related stress (HR 1.06, 95% CI 0.99–1.14), home- (HR 0.99, 95% CI 0.94–1.04) or work-related lack of control (HR 0.96, 95% CI 0.81–1.13). Of the patients, 52.4% were working and 47.6% were retired or did not work for other reasons such as unemployment. Among employed patients, stress at work was associated with a lower risk of MACE (HR 0.82, 95% CI 0.69–0.98) compared to those reporting no stress. Patients living alone had a higher risk of MACE (HR 1.28, 95% CI 1.11–1.48). Conclusion: Financial stress, depressive symptoms and living alone were associated with an increased risk for ischaemic events and death. These findings suggest a need for additional support in patients with chronic CHD. Conversely to prior data, self-reported work-related stress was associated with improved prognostic value. This finding warrants further investigation.
Acknowledgement/Funding: The STABILITY study was funded by GlaxoSmithKline

P6440 | BEDSIDE
Marital status is associated with a prevalence of metabolic syndrome in men based on the 2013 Korean National Health Examination and Nutrition Survey
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Objective: This study aims to investigate the gender-specific associations between socioeconomic status and metabolic syndrome (MetS) in Korean adults.
Methods: We examined the relationship between socioeconomic status and the prevalence of MetS in 4,689 Korean adults aged 20 to 79 years (2,024 men and 2,665 women) who participated in the 2013 Korean National Health Examination and Nutrition Survey. Occupation status was classified as none, manual, non-manual based on a self-reported questionnaire. Marital status was classified as single, married, divorced, and widowed. A modified Asian criterion based on a harmonized definition of MetS was adopted. Adjusted odds ratios (ORs) for MetS were calculated using multiple logistic regression models.
Results: The prevalences of MetS in men and women were 30.9% and 24.8%, respectively. Significant differences in the association between marital status, occupational status, household income, education, and MetS were found between men and women. The ORs for MetS in the highest income and the highest educated group (-12 years) were 0.831 (0.461–0.864) and 0.460 (0.315–0.670), respectively.
Conclusions: Marital status was significantly related to the prevalence of MetS in men, but not in women. Economy and education status was related to the prevalence of MetS in women, but not men. These findings suggest that gender-specific public health interventions that consider socioeconomic status are needed for targeting MetS prevention and treatment.
Acknowledgement/Funding: No financial support

P6441 | BEDSIDE
The role of uric acid as early marker carotid atherosclerosis in subjects without cardiovascular disease
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Recent studies have suggested that hyperuricemia is a risk factor for cardiovascular disease in the general population. Carotid intima-media thickness (C-IMT) measured noninvasively by ultrasonography is now widely used as a surrogate marker for atherosclerotic disease and directly associated with increased risk of cardiovascular disease.
Objective: We aimed to investigate whether elevated serum uric acid (SUA) concentrations are associated with higher risk of carotid atherosclerosis in patients without cardiovascular disease.
Methods: The study included 136 participants, without manifested cardiovascular disease (mean age 66.07 years, 82% (S2) (male) were included. For all patients was determined: presence of risk factors for cardiovascular disease (hypertension, hyperlipidemia, smoking, diabetes, obesity, age), SCORE risk, laboratory analysis and anthropometric measurements. The carotid artery intima-media thickness (C-IMT) and carotid atherosclerotic plaques were measured by B-mode ultrasonography.
Results: The patients were divided into 2 groups according to level serum uric acid. The first group (I) consisted of subjects with normal SUA, n=95 (69,85%), the second (II) group patients with elevated level SUA, n=41 (30,15%). The average carotid C-IMT level was 295 ±58,77 in the first group vs. 443 ±34,451 in the second group (p<0.0001). Patients with high SUA had significantly higher mean age (p=0,058), average number of risk factors (p=0.03), SCORE risk (p=0.005), body mass index (p=0.002), the prevalence of diabetes (p<0.005).-C-
IMT were significantly higher in the second group compared to the first group (1.002±0.21 vs 0.81±0.16, p < 0.0001). The high C-IMT values (~0.90 mm) were observed in 68% of patients in II group vs 20% in I group, p < 0.0001. Patients with elevated SUA had more frequently one or more carotid plaques (p = 0.003). Also, they had a higher average number of carotid plaques (p = 0.0001) and percentage of stenosis (p = 0.0001). In the first group, plaques were mostly fibrous (30.0%), followed by fibrocalcified (17%) and calcified (7%). In the second plaques were mostly fibrocalcified (36.6%). After multiple linear regression analysis, SUA levels were identified to be independently correlated with C-IMT (R=0.34, p<0.001); number of carotid plaques (R=0.25, p=0.003); percentage of stenosis (R=0.22; p=0.017); characteristic of plaque (R=0.26; p=0.024).

Conclusions: There is an association between elevated serum uric acid concentrations and subclinical carotid atherosclerosis in patients without clinically evident cardiovascular disease.

P6442 | BEDSIDE
Relation between parameters of arterial stiffness and endothelial function among patients with and without severe periodontal disease
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Introduction: Periodontal disease has been described as playing a role in the atherosclerosis process, and its relation with intimal thickness and vascular endothelial function has been investigated.

Purpose: To determine whether there are differences in parameters of arterial stiffness and endothelial function between patients (P) with and without severe periodontal disease (SPD).

Methods: Patients referred to School of Dentistry, University of Buenos Aires-Argentina were consecutively evaluated. All P were given their informed consent to participate in the study. Demographic characteristics, atherogenic risk factors, and concomitant pathologies were determined. P with known cardiovascular pathology were excluded from the study. Previously calibrated dentists determined gingival-periodontal indexes. Using carotid Doppler ultrasound, a single operator assessed arterial stiffness parameters: compliance (COP), elastic modulus (EM) and β stiffness index (βSI). Vascular endothelial function (FE) was assessed by brachial artery flow-mediated dilatation. The patients were divided into two groups: with and without SPD. Statistical analysis was performed by ANOVA and Pearson’s correlation coefficient with an alpha error < 0.05 and 95% confidence intervals, using SPSS 20.

Results: Sixty P were included; 60% were women; 25 P were in the group with SPD and 35 in the group without SPD. Respective results of the studied variables were: age 56.53±17.58 vs 51.12±12.97 years (pNS), diabetes 8% vs 8.57% (pNS), hypertension 68.29% vs 54.28% (pNS), tobacco 8% vs 11.42% (pNS), hypercholesterolemia 12% vs 14.28% (pNS), probing depth (PD) 2.53±1.30 (COP1 1.98±1.33) vs 2.15±0.51 (COP2 1.93±1.73) p=0.02, clinical attachment level (CAL) 4.80±2.00 (COP1 3.69±0.91) vs 1.72±0.93 (COP2 1.31–2.53) p=0.001, intimal thickness (IT) 0.10±0.17 (COP1 0.095–0.11) vs 0.82±0.18 (COP2 0.70–0.98) (pNS), COP2 2.41±1.32 vs 3.08±1.02 (p=0.004); EM 48.33±12.53 vs 38.86±7.69 (p=0.005); βSI 4.21±0.35 vs 3.64±1.02 (p=0.004); EF 57.25±14.50 (p<0.0001). Correlation between COP and CAL r=−0.60 (p<0.001), EF and CAL r=−0.59 (p<0.001).

Conclusions: Parameters of arterial stiffness and endothelial function were worse in P with severe periodontal disease, and correlated moderately with clinical attachment level. Correlation with compliance and endothelial function was negative.

P6443 | BEDSIDE
High protein intake supplementation to compensate changes in ventricular repolarization due to 21-days of bedridden immobilization
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Prolonged inactivity induces reduction of lean body and bone mass, glucose intolerance, and weakening of the cardiovascular system. Increased protein intake supplementation to compensate changes in the effects on ventricular repolarization (VR) of supplementing high protein intake (1.2 g/kg/d plus 0.6 g/kg/d whey protein) and alkaline salts (90 mmol KHCO3/d) the night period (23:00–06:30) was selected for analysis and vectorcardiogram computed from X,Y,Z leads derived using inverse Kors regression. Selective beat averaging was used to obtain averages of P-QRS-T complexes preceded by the average, T-wave amplitude (Tmax) and area, RTapex and RTend, R/T amplitude ratio, ventricular gradient (VG) and ORST angle were measured.

Results: BR induced RTapex and RTend shortening, T-wave amplitude and area decreasing, higher R/T and lower VG. At HDT21, when nutritional CM was given, most of the effects seemed reversed. At POST, all parameters restored to their premanipulation control values.

Results with and without nutritional CM
<table>
<thead>
<tr>
<th>Parameter</th>
<th>PRE</th>
<th>HDT21 CTRL</th>
<th>HDT21 CM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tmax (mV)</td>
<td>567±118</td>
<td>464±127*</td>
<td>563±180*</td>
</tr>
<tr>
<td>T wave area (mV ms)</td>
<td>71±4.07</td>
<td>60.5±2.17*</td>
<td>69.5±2.23*</td>
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<td>RTapex (ms)</td>
<td>275±17</td>
<td>264±21*</td>
<td>259±20*</td>
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<tr>
<td>RTend (ms)</td>
<td>383±227</td>
<td>366±22*</td>
<td>359±22*</td>
</tr>
<tr>
<td>R/T (a.u.)</td>
<td>2.84±0.42</td>
<td>3.87±1.37</td>
<td>3.25±0.94</td>
</tr>
<tr>
<td>VG (mV)</td>
<td>77±36</td>
<td>60±29*</td>
<td>98±28*</td>
</tr>
<tr>
<td>ORST (angle)</td>
<td>49±28</td>
<td>54±27</td>
<td>50±27</td>
</tr>
</tbody>
</table>

*p<0.05 paired t-test vs PRE. *p<0.05 paired t-test CTRLs vs CM.

Conclusions: Sustained reduced gravitational stimulus and immobilization affected AV during the night period. High protein intake supplementation appeared to reverse the majority of the changes, thus decreasing ventricular heterogeneity and arrhythmogenic risk.

Acknowledgement/Funding: This study has been funded by the Italian Space Agency (contract 2013-033-R.0, recipient E.G. Caiani)

P6444 | SPOTLIGHT
Trajectories of body mass index before the diagnosis of cardiovascular disease
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Background: Individuals at the time of diagnosis for cardiovascular disease (CVD) might have different levels of body mass index (BMI). Our aim was to characterize patterns of BMI and other metabolic risk factors among middle-aged and elderly individuals before CVD diagnosis.

Methods: We included 6125 individuals free of CVD at baseline from the population-based Rotterdam Study. Individuals were followed from 1989–2012 with clinical examinations every 4 years. Latent class trajectories of incident CVD cases were used to identify patterns of BMI before CVD diagnosis. Additionally, mixed-effect models were used to characterize trajectories of other cardio-metabolic risk factors.

Results: During follow-up (median 16.7 years) 1748 participants developed CVD. Among the CVD patients, we identified 3 patterns of BMI. The “stable overweight” group compromised 87.8% of patients with steady BMI levels over time accompanied by a decrease in high density lipoprotein (HDL) cholesterol and an increase in waist circumference. Two other groups which compromised 6.4% and 5.8% of CVD patients were termed “progressive weight gainers” and “progressive weight losers”. The progressive weight gainers experienced an increase in BMI levels over time accompanied by increases in diastolic blood pressure and glucose and a decrease in HDL cholesterol. The progressive weight losers experienced a decrease in BMI levels 10 years before CVD development. Despite the decrease in their cardiovascular risk factors over time, this group experienced an increase of predicted CVD risk.

Conclusion: Our findings highlight a substantial heterogeneity in BMI development prior to CVD diagnosis accompanied by different trajectories of other cardiovascular risk factors. Most of the CVD patients were in the stable overweight category.

P6445 | BEDSIDE
Statin is associated with lower incidence of deep vein thrombosis confirmed by CT angiography in patients undergoing total knee replacement arthroplasty
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Background: Statin has potential to reduce the occurrence of venous thromboembolism in apparently healthy persons.

Purpose: To investigate whether statin is associated with lower incidence of deep vein thrombosis confirmed by CT angiography in patients undergoing total knee replacement arthroplasty.

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vein thrombosis (DVT) in patients undergoing total knee replacement arthroplasty (TKRA).

Methods: We retrospectively enrolled consecutive 414 patients who received TKRA from Feb. 2006 to Jan. 2015. All the patients received computed tomographic angiography (CT-angiography) of both lower extremities 7 days after index surgery and some patients received pulmonary artery CT-angiography. DVT and/or pulmonary thromboembolism were confirmed by expert blinded to the study group. They were analyses according to state of their chronic use of statin of any kind.

Results: One hundred and ten patients are statin users and 304 are non-statin users. The occurrence of DVT is significantly higher in statin naive patients as compared in statin users, 33.5% vs. 10.5% (HR 0.35, CI 0.15–0.752, p=0.035).

By multiple regression analysis, statin use was an independent risk factor for the occurrence of DVT (HR 3.02, CI 1.536–6.382, p=0.021). Age and smoking were also independent predictors for DVT. Pulmonary thromboembolism (PTE) did not occur in statin group (0%) but occurred in 20 patients (8.2%) in non-statins users with significant difference (HR 0.60, CI 0.385–0.852, p=0.041). No mortality was found during hospitalization in both groups.

Conclusion: Statin may be associated with lower occurrence of DVT and PTE in high risk patients who are undergoing TKRA. This results warrant further prospective randomized studies to evaluate the statin as prophylactic measures against DVT.

INTERVENTIONS IN PRIMARY AND SECONDARY PREVENTION

P6446 | BEDSIDE
A critical appraisal of safety and efficacy of statins in primary prevention of HIV patients

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Background: Statins are largely prescribed in HIV patients on highly active anti-retroviral therapy (HAART) for primary prevention, but their clinical benefit is to date far from being clearly established in this peculiar population.

Purpose: To assess the effectiveness and safety of various dosages of different statins in HIV patients on HAART.

Methods: Studies including HIV patients on HAART treated with statins for primary prevention were included. Total cholesterol reduction was the primary end point; LDL cholesterol, HDL cholesterol, triglycerides and discontinuation related meta-regression analysis.

Results: One hundred and ten patients are statin users and 304 are non-stain users. The occurrence of DVT is significantly higher in statin naive patients as compared in statin users, 33.5% vs. 10.5% (HR 0.35, CI 0.15–0.752, p=0.035).

By multiple regression analysis, statin use was an independent risk factor for the occurrence of DVT (HR 3.02, CI 1.536–6.382, p=0.021). Age and smoking were also independent predictors for DVT. Pulmonary thromboembolism (PTE) did not occur in statin group (0%) but occurred in 20 patients (8.2%) in non-statins users with significant difference (HR 0.60, CI 0.385–0.852, p=0.041). No mortality was found during hospitalization in both groups.

Conclusion: Statin may be associated with lower occurrence of DVT and PTE in high risk patients who are undergoing TKRA. This results warrant further prospective randomized studies to evaluate the statin as prophylactic measures against DVT.

P6447 | BEDSIDE
One-year follow-up from the CUT-IT trial: a randomized trial comparing a low energy diet with aerobic exercise in overweight individuals with coronary artery disease

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1 Bispebjerg Hospital of the Copenhagen University Hospital, Department of Cardiology, Copenhagen, Denmark, 2Amager Hospital, Department of Internal Medicine, Copenhagen, Denmark.

Background: Physical inactivity and overweight are major risk factors in coronary artery disease (CAD) and physical activity and weight loss are central in secondary prevention. The objective of this study was to evaluate a low energy diet (LED) combined with aerobic training (AIT) and intensive AIT as secondary preventive strategies.

Methods: 70 participants with CAD, BMI ≥ 28 kg/m² and no diabetes were randomized (1:1) to 12 weeks supervised AIT at 90% maximal heart rate 3 times/week or weight loss using a LED (800–1000 kcal/day). Both groups continued supervised AIT 2 times/week for 40 weeks following the initial intervention. The intervention was evaluated by a cardiopulmonary exercise test, dual X-ray absorptiometry based bone composition, body weight and VO2peak.

Results: 57 (81.4%) participants were men, median age was 63 (IQ range 58–67) years, median BMI was 31.3 kg/m² (IQ range 29.7–33.7) and mean VO2peak was 21.0 m/l/min/kg (SD 5.1). No between-group difference on relevant baseline data was seen. 29 participants in the LED and 26 in the AIT group completed 1-year follow-up. Results of the intervention are presented in table 1 (mean and SD). The combination of LED and training led to significantly greater weight loss without loss of lean body mass and similar improvement in exercise capacity as the AIT only.

Conclusion: The results indicate that a LED regimen followed by AIT may be a superior prevention strategy for overweight CAD patients. Further analyses will evaluate the effects on cardiovascular and metabolic risk markers.

Acknowledgement/Funding: Danish Heart Foundation and the Danish council for independent research.

P6448 | BEDSIDE
1146 Upcoming risk factors / Interventions in primary and secondary prevention

Abstract P6448 – Table 1. Results of the intervention (mean and standard deviation)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>AIT only</th>
<th>Between group difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T-year</td>
<td>p-value</td>
<td>T-year</td>
</tr>
<tr>
<td>V02 peak (ml/kg/min)</td>
<td>20.5 (4.9)</td>
<td>0.0001</td>
<td>21.0 (4.9)</td>
</tr>
<tr>
<td>V02 peak (ml/kg/min fat free mass/kg)</td>
<td>126.5 (25.4)</td>
<td>0.0454</td>
<td>132.4 (23.2)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>95.6 (10.7)</td>
<td>-0.0001</td>
<td>96.2 (12.8)</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>36.7 (6.8)</td>
<td>-0.0001</td>
<td>34.5 (6.5)</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.98 (0.07)</td>
<td>0.4266</td>
<td>1.00 (0.07)</td>
</tr>
<tr>
<td>Lean body mass (kg)</td>
<td>56.3 (8.3)</td>
<td>0.1716</td>
<td>58.4 (9.1)</td>
</tr>
</tbody>
</table>

LED, low energy diet; AIT, aerobic interval training.
We assessed the impact of the control of RF at baseline on long-term cardiovascular (CV) morbidity and mortality. Nonetheless, few data exist on gen-
as compared to subjects presented all RF controlled. For subjects presented none RF, a higher number of deaths occurred (389 vs. 212, p < 0.001), and the hazard ratio (HR) for subjects presented 1 non-controlled RF and for subjects presented 2 or more non-controlled RF was 1.70 [0.84–3.42] (p=0.138) and 3.67 [1.85–7.29] (p < 0.001), respectively, as compared to subjects presented all RF controlled or none RF (adjusted HR for subjects presented none RF as compared to sub-
jects presented all RF controlled was not significant (p=0.56 [0.17–1.83]; p=0.338)).

Conclusions: Failing to control RF (high blood pressure, high LDL-cholesterol, diabetes and smoking) increases significantly long-term all-cause and cardiovas-
cular mortality.

**P6450 | SPOTLIGHT**

Impact of cardiovascular risk factors management on long-term all-cause and cardiovascular mortality: an observational study

E. Berard1, V. Bongard1, D. Arveiler2, J. Dallongeville3, A. Wagner1, P. Amouyel1, B. Hass2, D. Cottel3, J. Ferrieres4, J.B. Ruidavets1.

**Background:** In clinical trials, lowering cardiovascular risk factors (RF) reduce cardiovascular disease morbidity and mortality. Nonetheless, few data exist on the general population of three French areas. Vital status and causes of death were obtained through questionnaire (10 questions) with specific focus on indication, side effects, pre-
itment and control at the time of recruitment. All-cause and cardiovascular mortality: an observational study

Purpose: To identify, summarize and analyze studies reporting multidisciplinary educational programs involving scholars and their relatives. Objective: To identify and summarize studies reporting multidisciplinary educational programs involving scholars and their relatives. Methods: A pre-defined protocol in accordance with the PRISMA was used. Electronic searches in Medline, Pubmed, Embase, Cochrane Library, IBECs, SciELO and LILACS were conducted through March 2014 involving multidisciplinary educational programs with parallel groups design. Reported outcome variables were health status, high cholesterol (HDL), low density cholesterol (LDL), diabetes, systolic blood pressure (SBP) and diastolic blood pressure (DBP).

Results: Of 4253 studies found, four reached the inclusion criteria for the systematic review and two were included in the meta-analysis contributing with three separate samples. Included studies involved 787 children (3–11 years) and 711 adults, who received educational interventions lasting 12–13 months and the prevalence of CVRF varied from 14% to 35%.

Conclusion: Evidence on scholarly programs involving LM is weak. Paucity of studies and the absence of some methodological criteria indicate that research in cardiovascular primary prevention involving scholars and their relatives is warranted.

**P6451 | BEDSIDE**

Effect of multidisciplinary educational programs delivered to scholar children on cardiovascular risk profile of their relatives- systematic review and meta-analysis


**Background:** Multidisciplinary educational programs involving scholar children and their relatives could be an easy and scalable preventive measure to face the increasing burden of cardiovascular diseases. Nevertheless such programs are not common in our context.

Method: A systematic review (with meta-analysis) and a narrative review were conducted. Six databases were searched. The review protocol was registered at PROSPERO (CRD42017066462).

Results: Of 4253 studies found, four reached the inclusion criteria for the systematic review and two were included in the meta-analysis contributing with three separate samples. Included studies involved 787 children (3–11 years) and 711 adults, who received educational interventions lasting 12–13 months and the prevalence of CVRF varied from 14% to 35%.

Conclusion: Evidence on scholarly programs involving LM is weak. Paucity of studies and the absence of some methodological criteria indicate that research in cardiovascular primary prevention involving scholars and their relatives is warranted.

**P6452 | BEDSIDE**

Patients’ understanding of chronic antithrombotic therapy in the era of direct oral anticoagulant therapy


**Background:** Patients’ warfarin understanding is generally poor and contribute to suboptimal anticoagulation and subsequent complications.

Purpose: To investigate knowledge of antithrombotic therapy among a population of patients receiving chronic anticoagulant therapy with vitamin K antagonists (VKA) or direct oral anticoagulants (DOA).

Methods: We conducted a prospective study among 193 patients consecutively admitted in a cardiology unit for various causes and receiving anticoagulant ther-

apy for more than 3 months. All patients were invited to independently fill in a questionnaire (10 questions) with specific focus on indication, side effects, pre-
cautions and risks of under/over dosing of anticoagulation therapy. The question-
naire was handed out by a nurse in a face-to-face interview. Patients with severe cognitive impairment or psychiatric disorders were excluded.

Results: Mean age was 73 y, 135 patients were male (70%), 67 (35%) of them had sociocultural level medium or high. Atrial fibrillation was the main indication of therapy (n=128; 66%). VKA and DOA concerned respectively 68% (n=132, group 1) and 32% (n=61, group 2) of the patients.

Conclusion: The majority of patients were aware of the anticoagulant therapy (n=173; 90%), most of them did not know risks and precautions needed with these drugs

<table>
<thead>
<tr>
<th>Need (VKA) or absence (DOA) of biological control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>VKA n=108 (82%)</td>
<td>0.06</td>
</tr>
<tr>
<td>DOA n=64 (33%)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Food interaction (VKA) or not (DOA)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>VKA n=39 (36%)</td>
<td>0.001</td>
</tr>
<tr>
<td>DOA n=15 (25%)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bleeding risk</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>VKA n=42 (25%)</td>
<td>0.001</td>
</tr>
<tr>
<td>DOA n=43 (75%)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Embolic risk</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>VKA n=18 (14%)</td>
<td>0.60</td>
</tr>
<tr>
<td>DOA n=18 (16%)</td>
<td>0.30</td>
</tr>
</tbody>
</table>
Introduction: This study describes the incidence and predictors of permanent disability pension (PWP) in patients ≤ 50 years old who underwent percutaneous coronary intervention (PCI).

Materials and methods: 910 patients undergoing PCI at 4 hospitals in 2002–2012. Patients records were reviewed for baseline and procedural data and late adverse events. Data on permanent work disability (PWP) pension allocation was obtained from national register for Pensions, which governs the statutory pension security in the country.

Results: Mean follow-up was 41±31 months. Altogether 103/910 (11.3%) of patients were on PWP by the end of follow-up, 60 (58.3%) for cardiac diagnoses. Incidence of PWP among PCI patients was comparable to prevalent patients continuing statin therapy during follow-up (n=147); the reduction in plasma total-cholesterol concentrations was more pronounced in the intervention group. 1.71 mmol/L vs. 1.44 mmol/L (P=0.027).

Conclusions: Patients ≤ 50 years old undergoing PCI are at a high risk for subsequent permanent disability for cardiac diagnoses. This finding underscores the need for reinforcing understanding of the disease and its preventive measures. Two years ago, we implemented a transition program (TP) for youth and young adults led by an advanced practice nurse, offering individualized patient education on IE and dental hygiene.

Acknowledgement/Funding: Finnish Foundation for Cardiovascular Research

P6454 | BEDSIDE

Adults with congenital heart disease: individualized structured patient education to improve patients’ knowledge on infective endocarditis

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Introduction: Adults with congenital heart disease (CHD) are at increased risk of infective endocarditis (IE). Previous studies have shown that they have a poor understanding of this disease and its preventive measures. Two years ago, we implemented a transition program (TP) for youth and young adults led by an advanced practice nurse, offering individualized patient education on IE and dental hygiene.

Methods: From 11/2012 to 02/2014, a descriptive cross-sectional study among patients with CHD and regular follow-up at our Center has been carried out. 187 consecutive CHD patients with current or former indication for IE prophylaxis according to the European Society of Cardiology Guidelines were included. Demographic and clinical variables were obtained from the medical records. IE knowledge was assessed using the “Leuven Knowledge Questionnaire for Congenital Heart Disease” (by P. Moons, 2009). Adjustments to the questionnaire with respect to oral hygiene and dental visits were made. The answers were scored according to their accuracy (maximum score 40).

Results: Out of the 187 patients (39% female), 54 visited the TP. TP patients were younger (mean age 21.4± 40. year ± 14 years) than the remaining CHD patients. There was no difference in gender, CHD complexity and history of previous valve replacement or previous IE between patients with and without TP participation. TP patients were less likely to have a college or university degree (TP 35% vs 50%). Despite a lower educational background, TP patients achieved a significantly higher IE knowledge score (TP 26±8 vs 21±10, p<0.001) compared to adults without structured IE education. The IE knowledge score remained high (26±8) even in patients with TP participation only the year before the current visit (n=26). All patients had good results regarding dental hygiene (i.e. brushing their teeth at least twice a day; TP 85% vs. 80%) and dental visits (at least once a year; TP 81% vs. 81%).

Conclusions: Systematic patient education as part of a TP improves IE knowledge independent of the patients’ educational background. This knowledge was sustained one year after participation in the TP. All patients showed fairly good results regarding dental hygiene and dental visits. More emphasis could be put on early patient and parent education, as well as on regular repetition.

P6455 | BEDSIDE

Visualization of coronary artery calcification: influence on preventive therapy and risk modification

R. Elmoose Mols1, J. Moeller Jensen1, N.P. Sand2, C. Fuglesang Christensen1, D. Bagdaz2, P. Vedsted1, H.E. Boecker1, L. Huche Nielsen2, B.L. Nørgaard1, 1Rigshospitalet University Hospital, Department of Cardiology, Copenhagen, Denmark; 2Sydvestjysk Hospital-Esbjerg, Department of Cardiology, Esbjerg, Denmark

Background: Direct health provider to patient presentation of coronary computerized tomography angiography (CTA) findings and recommendations on preventive therapy and risk modification. The purpose of this study was to assess the influence of visualization of coronary artery calcification (CAC) and lifestyle recommendations on cholesterol concentrations and other risk variables in symptomatic patients with hyperlipidaemia and non-obstructive coronary artery disease (CAD).

Methods: Prospective two-centre randomized controlled trial. Patients were randomized to intervention or standard follow-up in general practice. The primary end-point was change in plasma total-cholesterol concentration at 6-months follow-up.

Results: We included 189 patients (mean ± SD age 61 ±12 years, 57% males). Median (IQR, range) Agatston score was 166 (101–334, 70–2054). The reduction in plasma total-cholesterol concentrations tended to be higher in the intervention than in the control group, 1.32 mmol/L vs. 1.16 mmol/L (P=0.181). In a subgroup analysis, including patients continuing statin therapy during follow-up (n=147), the reduction in plasma total-cholesterol concentrations was more pronounced in the intervention than in the control group, 1.71 mmol/L vs. 1.44 mmol/L (P=0.027).

Conclusions: Visualization of CAC and brief recommendations about risk modification after coronary CTA in symptomatic patients with hyperlipidaemia and non-obstructive CAD may have a favourable influence on plasma total-cholesterol concentration, adherence to statin therapy and risk behaviour. Further investigations are needed to delineate the findings.

Acknowledgement/Funding: This study received financial support from Lillebaelt Hospital-Vejle Research Foundation (U-08-01), the Novo Nordisk Foundation (1-01-5087), and the T

P6456 | BEDSIDE

Closing the treatment gap: coaching patients on achieving cardiovascular health (COACH)

C.F. Sku1, M.J. Vale2, V. Chalmers3, G. Bennett1, K. McFarlane4, M.V. Jelinek1, J. Neumann5, D.R. Thompson1, 1Australian Catholic University, Centre for the Heart and Mind, Melbourne; 2The University of Melbourne, Department of Medicine, Melbourne; 3Queensland Health, Health Contact Centre, Brisbane, Australia

Background: In 2011 almost one third of all deaths in the Australian population were attributable to cardiovascular disease, of these 80% were preventable. Telephone coaching programs are flexible, multifaceted and integrated with the chronic care model.

Purpose: This study aimed to measure changes in cardiovascular risk factors among patients with coronary heart disease (CHD) and/or type 2 diabetes enrolled in a national state-wide telehealth coaching program in the public health sector in the Australian state of Queensland.

Methods: A population-based analysis of cardiovascular risk factor data collected prospectively as part of The COACH Program delivered through Queensland Government’s Health Contact Centre. Participants were patients with CHD (n=1962) and type 2 diabetes (n=707), of whom 145 were Indigenous. Changes in fasting lipids, fasting glucose, glycylated haemoglobin (HbA1c), blood pressure, body weight, body mass index (BMI), waist circumference, alcohol consumption and physical activity, as measured at entry to, and completion of, the program were assessed using paired-wise comparison.

Results: Improvements in cardiovascular risk factor status, from entry to completion of the program, were found across all biomedical and lifestyle factors in patients with CHD and/or type 2 diabetes. For both diseases, reductions in serum lipids, blood glucose, smoking habit and alcohol consumption combined with an increase in physical activity were the most notable findings. Those not statistically significant were: a decrease in mean LDL-cholesterol from 2.4 mmol/L to 1.8 mmol/L (CHD) and from 2.5 to 2.0 mmol/L (diabetes); a decrease in mean alcohol ingestion from 1.4 to 1.1 (CHD) and 1.3 to 0.9 (diabetes) standard drinks; and an increase in physical activity from 142 to 229 minutes (CHD) and from 127 to 182 minutes (diabetes) per week, and a decrease in mean HbA1c from 8.2% to 7.4% for diabetes patients (p<0.001 for all comparisons). Similar differences were found in mean change scores in cardiovascular risk factors between Indigenous and non-Indigenous participants.

Conclusion: A centralised state-wide telehealth coaching program overcomes obstacles of distance and limited access to health services and facilitates guide-line concordant decrease in cardiovascular risk.
P6457 | SPOTLIGHT
Women’s awareness, perceptions and knowledge of heart disease - three country comparison
N. Walker, C. Lawes, V. Parag, A. Rolleston, R.N. Doughty. The University of Auckland, Auckland, New Zealand

Background: A critical step towards improving the uptake of cardiovascular disease (CVD) prevention and treatment strategies in women is ascertaining their awareness of CVD, including the barriers to taking preventive action.

Purpose: To undertake a cross-sectional survey in New Zealand women aged ≥25 years looking at their CVD awareness, perceptions and knowledge, and compare the findings to those from corresponding studies undertaken in the USA (2012) and Austria (2011).

Methods: Participants were recruited via “citizen panels” managed by an on-line survey research company. Panel membership was broadly representative of the New Zealand population. Participants completed an on-line questionnaire previously developed by the American Heart Association and adapted for the New Zealand environment.

Results: A total of 724 women completed the survey. CVD was identified as the leading cause of death by only 21% of women, compared to 56% in the USA and 75% in Austria. Between 40–50% of women were aware of the atypical signs of a heart attack (i.e. fatigue and nausea), compared to 10–18% in the USA. Over 70% were aware of hypertension and diabetes mellitus. Mean number of risk factor was 2.0±1.01 in patients with marked CA, 1.8±0.9 in those with moderate CA, 1.68±1.1 in those with mild CA, and 1.31±0.8 without plaque (P=0.009 vs marked CA, P=0.021 vs moderate CA).

Conclusions: Clear differences exist between countries in terms of women’s awareness of risk factors and knowledge of CVD. These findings highlight the importance of undertaking country-specific surveys so that heart health messages and interventions for women can be targeted appropriately.

Acknowledgement/Funding: Heart Foundation of New Zealand (Project Grant, Douglas Senior Fellowship, Māori Cardiovascular Fellowship, and Chair in Heart Health)

P6458 | BEDSIDE
Usefulness of carotid ultrasonography for prevention of cerebral infarction
T. Tomaru. Toho University Medical Center, Sakura, Japan

Carotid plaques in neurologically asymptomatic subjects have been reported to be markers of generalized atherosclerosis and sources of thromboembolism. Then, we evaluated association between carotid plaque and cerebral infarction.

Methods: We evaluated 184 patients who were suspected of cerebral infarction and underwent head MRI and carotid ultrasonography (US) (120 males, 64 females) in a period of 50 years.

Results: CI or lacunar infarction was observed in 6 (27.2%) out of 22 patients without plaque, 0 (41.1%) out of 68 patients with PS of less than 5 (mild), 29 (48.3%) out of 60 patients with PS between 5 and 10 (moderate), and in 23 (67.8%) out of 34 patients with PS of more than 10 (marked). Incidence of CI or lacunar infarct was greater in patients with PS than in those without. CI score was 1.32±1.3 in patients without plaque, 1.5±1.4 in mild, 1.6±1.36 in moderate, and 2.32±2.2 in marked (P=0.34 vs cases without plaque). CAVI was 10.86±1.39 in cases with CI or lacunar infarct and 8.66±1.12 in those without (P=0.001).

Out of 42 cases with atherosclerotic cerebral infarction, mean thickness of internal carotid plaque in the artery responsible for infarction was 1.86±0.94 (P=0.05 vs 1.25±0.82 in contralateral artery). No plaque was observed in 8 internal carotid arteries for infarction. PS was greater at contra lateral carotid artery in 14 patients.

Mean number of risk factor was 2.0±1.01 in patients with marked CA, 1.8±0.9 in those with moderate CA, 1.68±1.1 in those with mild CA, and 1.31±0.8 without plaque (P=0.009 vs marked CA, P=0.021 vs moderate CA).

Conclusions: In general, carotid arteriosclerosis is associated with degree of cerebral ischemia and aortic stiffness, however, cerebral infarction may occur in patients with none or mild carotid arteriosclerosis. Internal carotid plaque or CAVI may also be associated with development of CI in most of patients, but not in all. Increase of RF or CAVI may predict CI in patients without severe carotid arteriosclerosis.
P6461 | BEDSIDE
The burden of cardiovascular diseases in Europe - results of the global burden of disease study 2013
G.A. Roth1, G. Saade2, M. Naghavi1, M. Fourrozantar1, A.H. Mokdad1, T. Vos1, C.J.L. Murray1. 1University of Washington, Institute for Health Metrics and Evaluation, Seattle, United States of America; 2Lebanese University, Beirut, Lebanon

Purpose: To better examine patterns in cardiovascular disease (CVD) in Europe, we analyzed results from the Global Burden of Disease (GBD) 2013 Study. GBD is a multinational study of disease burden by age and sex for 184 countries from 1990 through 2013, using all available data for risk factors, death and disability.

Methods: GBD produces consistent and comparable results over age, sex, time and space. Total health loss due to premature mortality plus disability is reported as a disability-adjusted life year (DALY). CVD burden is the aggregate of separate mortality and disease prevalence estimates created for ischemic heart disease, ischemic stroke, hemorrhagic stroke, atrial fibrillation, peripheral vascular disease, aortic aneurysm, hypertensive heart disease, endocarditis, rheumatic heart disease, and a category for other CVD conditions.

Results: In Western Europe, the 5 lowest CVD-specific DALY rates, standardized for age, are found in Andorra, Switzerland, France, Iceland, and Italy while the 5 highest rates are in Ireland, Malta, Germany, Finland, and Greece. Significantly higher DALY rates are found in Central and Eastern Europe and the Mediterranean. The figure below shows age-standardized CVD DALY rate per 100,000 in 2013. There is a distinct west-to-east gradient for CVD health across Europe that is only partially explained by the distribution of known CVD risk factors and health system performance.

P6462 | BEDSIDE
Trends in clinical profile, medical treatment and risk factors control in patients with stable coronary heart disease in Spain between 2006 and 2014
A. Cordero1, E. Galve2, H. Bueno3, L. Facila4, A. Cerquier5, E. Alegria6, A. Sanchez-Juan1. 1University of Washington, Institute for Health Metrics and Evaluation, Seattle, United States of America; 2University Hospital Vall d’Hebron, Barcelona, Spain; 3University Hospital Forcados, Barcelona, Spain; 4Donostia University Hospital, Peralta Galdos, Donostia-San Sebastian, Spain; 5University Hospital Sirio Libanes, Sao Paulo, Brazil; 6Hospital Clinic, Barcelona, Spain

Introduction: Patients with stable coronary heart disease are considered as high-risk patients and deserve the highest medical treatment intensive to control risk factors. Medical treatments have evolved

Methods: We compared to nationwide registries performed in Spain in 2006 (n: 7020) and 2014 (n: 1110) that included stable patients with coronary heart disease from outpatient clinics. Optimal medical treatment was considered the sum of antiplatelet, statin, ACE or ARB and betablockers. Atrovastatin 40–80 mg/daily and rosuvastatin 20–40 mg/daily were considered intensive statin treatment.

Results: Annualized treatment withdrawals and primary endpoint events. Annualized treatment withdrawal and primary endpoint events. Results: In both registries (2006 and 2014) the prevalence of antiplatelet, statin, ACE or ARB and beta-blockers was 83.8% in 2006 and 88.8% in 2014. In 2014 there was a significant improvement of statin and antiplatelet use (78% to 87% vs. 60% to 70% respectively) (p<0.001). Other predicators of withdrawals on study power and duration will raise awareness for the importance and cost of cardiovascular (CV) outcome trials. Understanding the implications of withdrawals on study power and duration will raise awareness for the need of improved retention efforts. Identifying subgroups of patients at higher risk of withdrawal may allow for more focused retention strategies.

Background: Treatment withdrawals can jeopardize the interpretability and success of long term cardiovascular (CV) outcome trials. Understanding the implications of withdrawals on study power and duration will raise awareness for the importance and cost of cardiovascular (CV) outcome trials. Understanding the implications of withdrawals on study power and duration will raise awareness for the importance and cost of cardiovascular (CV) outcome trials.

Methods: We examined rates and predictors of withdrawal from treatment in dal-OUTCOMES (clinicaltrials.gov NCT00658515), a trial that compared an HDL cholesterol-raising agent (dalcetrapib) with placebo in 15,871 patients with acute coronary syndrome who were followed for a median of 31 months. We used Monte-Carlo simulation to investigate the dependence of study power on baseline and anticipated risk improvements, and treatment withdrawal rate. Proportional hazards regression was used to assess dependence of treatment withdrawal on clinical and demographic characteristics and prior occurrence of CV endpoint events.

Results: Annualized treatment withdrawal and primary endpoint event rates in dal-OUTCOMES were 8.8% and 3.4%, respectively, with no differences between treatment groups. Simulation indicates that under such assumptions loss of study power can be up to 20%. Twenty-five variables related to study logistics (country, linearity, CV in substudy), CV in parent trial, and CV in parent trial event rates were considered together as independent variables. The strongest predictor was occurrence of a non-fatal CV event after randomization (HR=2.3; 95% CI [1.9, 2.7]; p<0.001). Other predic-
tors for treatment withdrawal included country (HR=5.5 for most vs least), gender (HR=0.83 for males), eGFR (HR=1.04 per 10 mL/min x 1.73m²), age (HR=1.01 per year), total cholesterol (HR=1.04 per 10 mg/dL), smoking (HR=1.24), and BMI (HR=0.98 per kg/m²). The risk of withdrawal from treatment decreases with time (50% lower in 3rd vs 1st year of dal-OUTCOMES).

**Conclusion:** Even with an "expected" range for large clinical trials, treatment withdrawals have a strong, adverse influence on study power. Occurrence of non-fatal CV events significantly increases the likelihood of subsequent treatment withdrawal. Clinical and demographic factors may identify patients more likely to withdraw from treatment and hence allow targeted strategies for patient retention. Independent confirmation of our results from other trials is desired.

**Acknowledgement/Funding:** F. Hoffmann-La Roche Ltd

### Table 1. Key outcomes for SMRE and MRC

<table>
<thead>
<tr>
<th>Overall subjects</th>
<th>Simv (n=8,855)</th>
<th>EZ/Simva (n=8,851)</th>
<th>p value</th>
<th>Simv (n=5,831)</th>
<th>EZ/Simva (n=5,791)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All rhabdomyolysis*</td>
<td>0.2%</td>
<td>0.1%</td>
<td>0.273</td>
<td>0.2%</td>
<td>0.1%</td>
<td>0.643</td>
</tr>
<tr>
<td>w/o renal dysfunction*</td>
<td>n=5</td>
<td>n=9</td>
<td>n=6</td>
<td>n=6</td>
<td>n=6</td>
<td>n=6</td>
</tr>
<tr>
<td>w/o renal dysfunction**</td>
<td>n=5</td>
<td>n=6</td>
<td>n=3</td>
<td>n=4</td>
<td>n=2</td>
<td>0.036</td>
</tr>
<tr>
<td>Myopathy*</td>
<td>0.1%</td>
<td>0.2%</td>
<td>0.393</td>
<td>0.1%</td>
<td>0.2%</td>
<td>0.823</td>
</tr>
<tr>
<td>&quot;Yes&quot; to possible MRC</td>
<td>19%</td>
<td>16%</td>
<td>18.9%</td>
<td>20.4%</td>
<td>0.039</td>
<td></td>
</tr>
<tr>
<td>MRC &quot;Yes&quot; led to stopping study drug at same or next visit</td>
<td>2.4%</td>
<td>2.3%</td>
<td>0.808</td>
<td>2.6%</td>
<td>2.6%</td>
<td>0.973</td>
</tr>
</tbody>
</table>

*Adjusted by independent blinded muscle clinical events committee. **MRC with CK > 5x ULN on repeated measures or > 10x once and not rhabdomyolysis.
Surveillance of risk factors and interventions / Diet and exercise: prevention begins here

myocardial infarction (AMI) recommend, as an adjunct to lifestyle modification, aspirin, beta-blockers (β-blockers), angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), and statins as lifelong treatment.

**Purpose:** To investigate potential determinants of long-term adherence to these evidence-based cardioprotective medications (EBCMs) in patients with AMI, and to estimate the effect of adherence on all-cause mortality.

**Methods:** Patient-based retrospective cohort study of 1-year survivors of AMI, members of a health organization in Israel, between 2005 and 2010. Adherence was measured using the proportion-of-days-covered (PDC) metric, and defined as PDC≥80%.

**Results:** Of 4655 patients prescribed at least one medication, 864 died during an 8-year follow up (median 4.5 years). Nonadherence to each EBCM approximately 50%, and 80% for combined therapy of all EBCMs. In multivariable analyses, adherers to at least one EBCM were more likely to be of Jewish origin (adjusted odds ratio [AOR], 2.11; 95% confidence interval [CI], 1.60–2.78), and attending a cardiologist at least once during the first year of follow up (AOR, 1.26; 95% CI, 1.05–1.51). Increasing number of outpatient visits to primary physicians and cardiologists was associated with improved adherence and followed a significant dose-response gradient. Factors significantly associated with reduced adherence were presence of comorbid conditions, and readmissions within the first year of follow up (AOR, 0.65; 95% CI, 0.55–0.78). Results were consistent when evaluating adherence of each EBCM separately. Except for β-blockers, medication nonadherence was significantly associated with increased all-cause mortality risk for aspirin (Adjusted hazard ratio [AHR], 1.28; 95% CI, 1.11–1.47), statins (AHR, 1.36; 95% CI, 1.18–1.57), and ACEIs/ARBs on the ischaemic heart disease patients with documented heart failure (AHR, 1.57; 95% CI, 1.16–2.14). Multidrug combined therapy exerted incremental survival benefit in a dose-response gradient, exceeding that of single component treatment, with the highest risk of mortality observed in patients adherent to none of the EBCMs as compared to adherents to all EBCMs (AHR, 1.38; 95% CI, 1.06–1.80).

**Conclusions:** Mortality risk profile for nonadherents to EBCMs will not improve unless strategies are implemented to improve long-term adherence. Further research is needed to elucidate the role of ACEI/ARB in patient subgroups.

P6469 | BEDSIDE

Comparative care model in patients with high cardiovascular risk: lessons from the EuroASPIRE database


**Introduction:** The EuroASPIRE III survey primary care arm, carried out in 66 general practices in 12 European countries, was one of the largest epidemiological trials focused towards uncovering unhealthy lifestyles.

**Purpose:** The aim of our study was to create a comparative care model implemented on high-risk patients followed over 18 months, in order to improve cardiovascular prevention and risk management according to the ESC guidelines.

**Methods:** Study population was selected from the 489 subjects who had previously participated in EuroASPIRE III – Primary Care Arm. We enrolled 325 incident participants. Of the patients enrolled in our study were dysglycemic. At the 18 months follow-up, we found that 80% of the subjects had systolic hypertension (SBP ≥ 140 mmHg), 78% were men. High triglycerides were present in 58% of the men and 42% of women. 16% had a mean age of the patients was 55.9 years. 80% of the subjects had systolic hypertension while 66% diastolic hypertension. Out of the entire population who had total cholesterol over 190 mg/dl 78% were men. However, 75% of the women had increased LDL-cholesterol as compared to low HDL-cholesterol where 80% were men. High triglycerides were present in 58% of the men and 42% of women. 16% of the patients enrolled in our study were dysglycemic. At the 18 months follow-up we observed that hypertension was the best controlled risk factor (p<0.001), as well as total cholesterol and LDL-cholesterol which had improved significantly (p<0.001).

**Conclusion:** Primary prevention needs a multidisciplinary approach, which addresses lifestyle and risk factor management by general practitioners, nurses and other allied health professionals, in order to improve guidelines adherence.
and decreased with CR (216±44 to 203±40 mg/dl; p=0.01). HDL, LDL, apoAl, apoB decreased in the CR group. ApoB increased in the RSV group. Glucose, insulin, NEFA, lipoprotein (a) and antioxidant capacity did not change in either group. Expression of Sirt1 gene by RT-PCR was higher in the CR group (11.0±1.24 to 12.4±2.19; p<0.001) but not in the RSV group (11.07±1.44 for 11.24±1.57; p=0.93).

Conclusion: CR and RSV increased plasma levels of Sirt1. Long-term impact of these interventions on atherosclerosis must be assessed.

P6472 | BEDSIDE
Can we LEARN to be effective in reducing obesity-related cardiovascular risk in women? Conventional vs internet-based program administration: interim analysis

Background: The LEARN (Lifestyle-Exercise-Attitudes-Relationships-Nutrition) program is an established weight management program that may have positive impact on cardiovascular disease (CVD) risk, but is limited in application due to physical requirement of weekly face-to-face sessions.

Purpose: To study the efficacy of a novel electronic format of the LEARN program compared to a traditional face-to-face format in achieving both weight loss and reduction of CVD risk factors in women.

Methods: Subjects include women (n=90) with 1 ≥ 2 CVD risk factors prospectively randomized to either weekly face-to-face LEARN classes or weekly online podcasts of LEARN classes with an online message board. Baseline, 3- and 12-month studies include body composition, cardiopulmonary exercise, endothelial function, and laboratory testing. Analysis was done by ANOVA and matched pairs analysis.

Results: The first 34 women (mean age 52±9.1 years, mean BMI 34.3±5.5, 68% dyslipidemic, 41% hypertensive, 41% glucose intolerant) to complete baseline and 3 month testing are included in this interim analysis. Mean weight loss was 4.2 kg (p=0.0001), with similar weight loss between each group (p=0.6011). All subjects experienced significant reductions in body fat (mean –1.4%) and body volume (mean –4.5 L). Although there was a trend for improved exercise capacity and respiratory exchange rate (RER), no significant differences were observed (Table 1).

<table>
<thead>
<tr>
<th>All patients (n=34)</th>
<th>Face-to-face (n=14)</th>
<th>Online (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Lost (kg)</td>
<td>-4.2 (p=0.0001)</td>
<td>-3.6 (p=0.008)</td>
</tr>
<tr>
<td>% Fat</td>
<td>-1.4 (p=0.0015)</td>
<td>-1.0 (p=0.017)</td>
</tr>
<tr>
<td>Body Volume (L)</td>
<td>-4.5 (p=0.0003)</td>
<td>-4.3 (p=0.0331)</td>
</tr>
<tr>
<td>RER</td>
<td>0.06 (p=0.0536)</td>
<td>0.09 (p=0.1252)</td>
</tr>
<tr>
<td>Peak VO2 (mL/kg/min)</td>
<td>-0.4 (p=0.6359)</td>
<td>-1.05 (p=0.5295)</td>
</tr>
<tr>
<td>% HR Achieved</td>
<td>2.5 (p=0.2630)</td>
<td>2.1 (p=0.1784)</td>
</tr>
<tr>
<td>Reactive Hyperemic Index</td>
<td>-0.05 (p=0.7335)</td>
<td>0.03 (p=0.8851)</td>
</tr>
</tbody>
</table>

Conclusions: In women with CVD risk exposed to 3 months of LEARN program, online lessons appear to be as effective as traditional face-to-face classes in initial achievement of body weight, fat and volume loss. We await the final results of this year-long study regarding longer term maintenance and physiological effects of weight loss upon CVD risk in women.

Acknowledgement/Funding: Internal Funding – Mayo Clinic Foundation – CV Prospective Study Grant

P6473 | BEDSIDE
J-shaped curve relationship of daily salt excretion and electrocardiographic left ventricular hypertrophy in first-visit outpatients
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Background: High dietary salt intake is a well-known risk factor for developing hypertension and left ventricular hypertrophy (LVH). However, there is no report investigating the relationship between daily salt excretion and LVH in first-visit outpatients.

Purpose: The aim of this study is to clarify the relationship between daily salt excretion and electrocardiographic LVH in first-visit outpatients.

Methods: Four hundred eight consecutive patients aged 40 to 80 years, visiting outpatient cardiology clinic for their first time were recruited. Patients with advanced renal dysfunction, congestive heart failure, myocardial infarction and other confounding electrocardiographic abnormalities were excluded. The relationship between daily salt excretion and Sokolow-Lyon voltage criterion or other clinical variables was examined.

Results: The patients were classified into four groups according to the quartiles (Q) of daily salt excretion: Q1: <9.0 g/day; Q2: 9.0–12.0 g/day; Q3: 12.1–15.0 g/day; Q4: ≥15.1 g/day. Both the prevalence of LVH assessed by Sokolow-Lyon criterion and the mean value of the Sokolow-Lyon voltage showed J-shaped curve with the lowest in Q2 of daily salt excretion among the group. (Q1: 3.0±1.0 mV; Q2: 2.5±0.7 mV; Q3: 2.7±0.6 mV; Q4: 2.8±0.8 mV; p=0.002). After adjusting for age, sex, and other clinical variables, Sokolow-Lyon voltage again demonstrated J-shaped curve with the lowest in Q2 of daily salt excretion.

Conclusions: Not only high daily salt excretion but also low daily salt excretion were correlated with the high prevalence of LVH. Low daily salt excretion in first-visit outpatients may suggest LVH.

P6474 | BENCH
Plasma levels of c-type natriuretic peptide in normal, overweight and obese young population
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Purpose: In recent years natriuretic peptide (NP) entered in the “lipolytic arena” and novel physiological functions have been discovered. The role of atrial NP (ANP) and B-type NP (BNP) during lipolysis/lipogenesis was largely defined, while the action of C-type NP (CNP), the third member of the NP family, was not. Recent evidence suggested CNP as an important, natural regulator of adipogenesis. Aim of the study was to evaluate plasma levels of CNP in normal (N), overweight (OW) and obese (O) young population.

Methods: CNP plasma levels were measured in 82 subjects (age:13.0±2.3; BMI-N=20.3±0.5; BMI-OW=25.3±0.05 BMI-O=30.3±0.6) by a specific radioimmunoassay. To better describe the neuroendocrine profile, NT-proBNP and MR-proANP were also measured in the same samples. Biochemical parameters were also evaluated. Advanced glycated endproducts (AGEs) dependent skin autofluorescence was measured by the AGE reader apparatus.

Results: CNP plasma levels resulted progressively reduced in OW: 8.8±3.3; n=10 and O=6.7±0.9, n=43 with respect to normal (N=10.4±1.6 pg/ml, n=29; p=0.04 N vs. O) while NT-proBNP and MR-proANP (N=29.1±1.7; OW=31.8±5.4; O=30.5±1.7 pmol/l) resulted similar in all groups. Insulin (p=0.0001), cholesterol (p=0.003), triglycerides (p=ns) and LDL (p=0.0005) were progressively higher in O and OW in comparison with normal subjects. Higher amount of AGEs were observed in OW (1.45±0.6) and O (1.45±0.6) in comparison with normal (1.28±0.4 AF; p=0.02 N vs. OW). Visceral trunk fat was also measured and resulted significantly higher in OW (36.1±2.39) and O (39.4±0.69) with respect to N (23.5±1.6; p<0.0001 respectively). CNP correlated significantly with age (p=0.011), fat mass (p=0.007), insulin (p=0.01), cholesterol (p=0.0001), LDL (p=0.0006), NT-proBNP (p=0.01) and MR-proANP (p=0.01). Circulating CNP values were similar in males and females. A significant correlation (r=0.313, p=0.006) was observed between AGEs and trunk fat.

Conclusion: In the population studied we observed lower plasma CNP levels confirming previous data. The correlations observed suggested that these alterations might be in part due to endocrine-metabolic deregulation. AGEs being involved in oxidative stress at vascular level, contributed to endothelial damage. The direct relationship between visceral trunk fat and skin AGEs confirms the increased risk of vascular disease due to accumulation of abdominal fat in our population, while the relationship between skin AGEs and circulating levels of total cholesterol and LDL reflects an incorrect food eating.

Acknowledgement/Funding: Unique Project Code B55E09000560002, supported by the Regione Toscana (Tuscany Region) under the Research Call “Innovation in Medicine 2009”.

P6475 | BEDSIDE
Real-time longitudinal monitoring of patients diet, exercise and weight loss has substantial positive effects on metabolic syndrome parameters
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Background: Intensive lifestyle change programmes are utilised in cardiovascular disease prevention, but their efficacy is variable. Real-time monitoring of patients is feasible.

Purpose: To evaluate the efficacy of real-time adherence monitoring of pa-
tient’s diet and exercise plan, in targeting metabolic syndrome parameters of weight/BMI, blood pressure (BP), and total cholesterol (TC) in overweight/obese (OWO) individuals.

Methods: 28 OWO (BMI > 25 & < 40) persons were enrolled. At entry, 16 had elevated BP (>140/90), 12 elevated TC (>5 mmol/l). Baseline resting metabolic rate (RMR) and BMI was calculated. Participants had a reduced daily calorie intake (~300–500 Kcal below RMR) and increased daily exercise (10,000–12,500 steps). Phone app training tracked caloric intake, while a wireless weighing-scale and pedometer, enabled daily weight tracking and exercise adherence monitoring. Non-responders received motivational emails, SMS or phone-calls. Participants were met weekly, either face to face or via video-link. The primary aim was to assess the effects on weight loss; also, BP and TC were analysed at specific time points.

Results: Significant weight loss was achieved at weeks 4 (n=28), 8 (n=21), and 12 (n=12) with an average weight reduction of 5.6%, 9.6% and 10.1% (P<0.01 for each time point). In 16 hypertensive subjects, by week 8 average systolic BP declined 17.1% and diastolic BP by 14.7%. Average TC in 12 hypercholesterolaemic subjects reduced from 6.21 mmol/l to 4.97 mmol/l or 19.94% by week 10, (see Figure).

Conclusion: Intense lifestyle and behavioural intervention, coupled with real-time remote monitoring of patients diet, exercise and weight has a substantial positive effect on metabolic syndrome parameters and may have a seminal role to play in cardiovascular disease prevention.

### P6476 | BESIDE

#### Increased consumption of fat and carbohydrates is associated with severe coronary artery disease

G. Siasos1, E. Kokkou1, E. Georgoussopoulou1, E. Oikonoumel1, T. Psaltopoulou2, M. Mourouzis1, M. Zaromytidou3, S. ‘salamandris1, E. Dimitropoulos1, D. Tousoulis1,1 University of Athens Medical School, 1Cardiology Department, “Hippokration” Hospital, Athens, Greece; 2University of Athens Medical School, Department of Hygiene, Epidemiology and Medical Statistics, Athens, Greece

Background: The association of dietary pattern with cardiovascular disease is well established.

Purpose: To examine the association between different dietary patterns and the severity of coronary artery disease (CAD).

Methods: The study population consisted of 188 consecutive symptomatic CAD patients recruited from the outpatient cardiology department of our Hospital. All patients underwent coronary angiography and they were categorized in subjects with one, two or three vessel disease (1VD, 2VD, 3VD respectively) and in subjects with left main (LM) disease. Patients with LM disease (stenosis>50%), 3VD, or 2VD marked by stenosis of the proximal left anterior descending artery >70% were characterized as having angiographically severe CAD. Among several other demographics and clinical characteristics all subjects were tested with a validated semi quantitative food frequency questionnaire. Univariate and multivariate (principal components analysis) analyses were used in order to evaluate the relationship between dietary habits and the severity of CAD, adjusting for potential confounders.

Results: After adjusting for all traditional risk factors (diabetes mellitus, hypertension, hyperlipidemia, family history of CAD and smoking habits), an increase in red meat consumption lead to a 47% increase in the probability of having severe CAD (p<0.01). Body mass index did not differ between patients with severe and non-severe CAD (p=0.11). Moreover, dietary pattern consisting of high consumption of red meat, sweets, pasta, potatoes and low consumption of fruits and vegetables (western type diet) was associated with higher probability of having severe CAD (p<0.01). This association between “Western type” diet and severe CAD was also evident even after adjustment for several cardiovascular risk factors (OR=1.9, p=0.022).

Conclusion: Dietary patterns affect the progression and severity of CAD. Western type diet is associated with the extent of CAD independently from traditional cardiovascular risk factors. Further studies are needed to elucidate the impact of different dietary patterns on cardiovascular health.

### P6477 | BESIDE

#### Aerobic high-intensity exercise training improves coronary flow reserve velocity and endothelial function in individuals with chest pain and normal coronary angiogram

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Purpose: Patients with impaired coronary flow reserve and chest pain despite normal coronary angiogram constitute a therapeutic problem with considerable residual morbidity associated with functional limitation and reduced quality of life.

Exercise training has been shown to improve endothelial function and symptoms in coronary artery disease. The aim of the current study was to assess the effect of high intensity aerobic exercise training on coronary flow reserve, endothelial function and functional capacity in this population.

Methods: Sixteen patients with typical exercise induced chest pain and normal coronary arteries assessed by coronary angiography at our university hospital were included. Twelve patients underwent a 3 months high intensity aerobic exercise-training program with 1 to 1 monitored exercise session on treadmill in a 4 min x 4 manner 3 times a week. A four patients served as controls.

Conclusion: Intense lifestyle and behavioural intervention, coupled with real-time remote monitoring of patients diet, exercise and weight has a substantial positive effect on metabolic syndrome parameters and may have a seminal role to play in cardiovascular disease prevention.

#### P6478 | BEDSIDE

#### Acute effects of energy drink consumption on endothelial function

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Background: Energy drink consumption is increasing especially among adolescents and young adults. Cases of fatal arrhythmia linked to energy drink consumption have been reported. Vascular effects of energy drinks are not known.

Purpose: This study investigates the effects of energy drinks on endothelial function and clinical characteristics all subjects were tested with a validated semi quantitative food frequency questionnaire. Univariate and multivariate (principal components analysis) analyses were used in order to evaluate the relationship between dietary habits and the severity of CAD, adjusting for potential confounders.

Methods: 30 healthy volunteers (15 male) aging 19 to 46 years were included in the study. Demographic variables, baseline heart rate and blood pressures were recorded. Flow mediated dilation measurements of the brachial artery were performed and recorded per protocol. FMD values were calculated. The volunteers were asked to drink 355 ml of energy drink containing 53,25 mg caffeine after baseline measurements, and all measurements were repeated 60 minutes later.

Baseline and post energy drink values were compared.

Results: Systolic blood pressure (p=0.59), diastolic blood pressure (p=0.71), and heart rate values (p=0.056) were similar before and after energy drinks. Baseline arterial diameters (p=0.24) and peak arterial diameters (p=0.79) in hyperemia also did not change after energy drink consumption. There was a 1.58% absolute decrease in FMD levels after energy drink consumption (9.7±4.6% at baseline vs 8.1±4.7% after energy drink) but the difference did not reach statistical significance (p=0.176).

Baseline and post energy drink parameter

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Post energy drink</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>111±12</td>
<td>114±13</td>
<td>0.59</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>72±8</td>
<td>73±8</td>
<td>0.77</td>
</tr>
<tr>
<td>Resting heart rate (beats/min)</td>
<td>73±10</td>
<td>70±10</td>
<td>0.056</td>
</tr>
<tr>
<td>Baseline arterial diameter (mm)</td>
<td>3.7±0.7</td>
<td>3.8±0.6</td>
<td>0.24</td>
</tr>
<tr>
<td>Peak arterial diameter (mm)</td>
<td>4.1±0.7</td>
<td>4.1±0.7</td>
<td>0.176</td>
</tr>
<tr>
<td>Flow mediated dilation (%)</td>
<td>9.7±4.6</td>
<td>8.1±4.7</td>
<td>0.176</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SD.

Conclusion: Energy drinks containing 53.25 mg of caffeine/355 ml did not have any significant influence on blood pressure, heart rate or endothelial functions in healthy volunteers.
Previous exercise training improves the lipid profile and the autonomic modulation in a model of menopause

R.K.P. Palma1, C.P.S. Santos1, M.R.H.D. Dutra1, N.B. Bernarde2, A.B.L. Lopes2, K.D.A. De Angelis1, C.M. Malfitano1, 1 Nove de Julho University, Sao Paulo, Brazil; 2 University of Sao Paulo, Institute for Biomedical Sciences, Sao Paulo, Brazil

Purpose: Exercise training has been indicated as a intervention non pharmacological to attenuate and prevent cardiovascular dysfunctions triggered by the advent of menopause. However, lipid metabolism and the cardioprotective effects of previous exercise training (PT) are unknown in this condition. Thereby, the aim of the present study was to investigate the effects of previous exercise training on cardiovascular autonomic control and lipid profile in ovariectomized rats.

Methods: Female Wistar rats were divided into 4 groups (n=8 each): control (C), sedentary ovariectomized (SO), trained ovariectomized (TO) and previously trained ovariectomized (PTO). The training was performed on a treadmill, in which were 4 weeks before ovariectomy and more 8 weeks after ovariectomy for PTO (5d/pw, 40–60%), and 8 weeks after ovariectomy for TO (5d/pw, 40–60%). Arterial pressure (AP) and heart rate (HR) were directly recorded and an autonomic modulation was evaluated by frequency-domain. The parametrial, retroperitoneal and subcutaneous adipose tissues were dissected and weighed in euthanization. Lipolysis was assessed in adipocytes and in content extracted from glycerol of parametral adipose tissue. The level of plasma triglycerides (TG) was measured.

Results: The ovariectomy induced rising in AP (CS: 103.03±6.3; SO: 113.13±12.2). PTO: 114.02±7.2 mmHg), increase of body weight (CS: 294.38±10.6; SO: 349.29±6.6; TO: 345.5±4.8; PTO: 336.43±2.9) and parametral fat, subcutaneous fat and lipolysis parametral. Both trained groups induced bradycardia (TO: 355.32±14 and PTO: 331.14±17.92 bpm) in compared to SO (274±6.5). Both groups induced an increase in the percentual of fat (subcutaneous, retroperitoneal and parametral), the diameter of adipocytes (parametral and retroperitoneal) in compared to the other groups. Lipolysis in PTO group was similar to the CS, with decreased parametral TG in relation to the other groups. Cardiac performance in this study demonstrated that exercise training performed prior ovariectomy induced an improvement in autonomic modulation and lipid profile, suggesting a beneficial role of this approach in the prevention of damage caused by the menopause in this experimental model.

Acknowledgement/Funding: CNPQ (Conselho Nacional de Desenvolvimento Científico e Metodológico)

Natural antioxidant ice cream improves vascular function and exercise performance in healthy subjects

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Diet is a major lifestyle factor in primary and secondary prevention of cardiovascular diseases. The role of natural antioxidants showed an increasing evidence of a beneficial role in between the intake of polyphenols-containing foods and coronary artery disease mortality. Cocoa and nuts are polyphenol-rich nutrients which elicits artery dilatation by reducing oxidative stress and increasing nitric oxide generation. We hypothesized that an antioxidant ice cream, product with a selected blend of cocoa, hazelnut and other ingredients from organic farming, could improve vascular function and exercise performance in healthy subjects via an oxidative stress-mediated mechanism. Thus, we performed an interventional study in which we measured the acute effect of natural antioxidant ice cream, on oxidative stress and artery dilatation in a population of healthy subjects. 14 subjects (7 male,7 female), mean age 38 years, were randomly allocated to a treatment sequence with 100mg of antioxidant ice cream or milk ice cream in a cross-over, single-blind design. Total polyphenol content (mg/100g) was significantly higher in antioxidant ice cream compared to milk ice cream (1817 vs 96). There was at least 1 week washout between the 2 phases of the study. Flow mediated dilatation (FMD), oxidatve stress (assessed by measuring plasma hydroperoxides, analytic method d-ROMs), exercise test (exercise double product: blood pressure x heart rate) were measured before and after baseline, after a 24 hours abstinence from food rich in polyphenols, and 2 hours after ingestion of ice cream. Compared to baseline intake of antioxidant ice cream showed a decrease of the average values of oxidative stress by reducing plasma hydroperoxides (31±17 vs 28±13; p<0.01), while no effect was observed with milk ice cream (302±53 vs 308±52). Compared to baseline FMD increased significantly after intake of antioxidant ice cream (2.5±0.6 vs 6.3±1.3;p<0.001) but not after milk ice cream intake (2.45±0.9 vs 2.34±0.5). The exercise test performed 2 h after intake of antioxidant ice cream showed comparable improvement of physical performance, over time by a reduction of the double product on the peak exercise for the same load reached (26.055±2646 vs 21.501±2351;p<0.01) while no difference was observed with milk ice cream (26.055±2646 vs 25.284±2739). Our results suggest that short term administration of a natural antioxidant ice cream improves vascular function and physical activity with a mechanism involving its high content of polyphenols mediated by an oxidative stress mechanism. This may be a novel approach in prevention of cardiovascular disease.

Does statin therapy unavourably influence healthy lifestyle? The results of the lipiogram survey

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Introduction: Recently it has been suggested that statin therapy might have an unfavourable effect on healthy lifestyle, including diet, physical activity, weight and smoking, compared with statin non-users.

Methods: Through 675 primary care centres in 444 Polish cities, 17,065 individuals were included to conduct a cross-sectional nationwide population-based survey in 2004 (LIPIDORGRAM 2004 survey). A separate prospective randomized sample of 1,842 individuals recruited in 2004 had a 5-year follow-up (LIPIDORGRAM 5- years survey). The parameters of healthy lifestyle – changes in diet, physical activity, body mass index (BMI) and waist circumference (WC), as well as smoking habits - were evaluated 3 times (in 2004, 2006 and 2010).

Results: 1190 patients (65%) completed the LIPIDORGRAM 5-Years study in 2010. Within this group there were 520 patients with dyslipidaemia (43.7%) in 2004, of whom 189 (36.3%) were treated non-pharmacologically, and for the rest (n=331; 63.7%) statins were administered. In 2010 (compared with 2004) there were almost 2 times fewer patients on diet in the group of statin users compared with statin non-users (25.7 vs 49.2%; p<0.001). At study baseline (2004) regular physical activity was declared by 40.2% dyslipidaemia patients without statin therapy and by 23.9% by statin users (p<0.001). After 5-year follow-up, regular physical activity was continued only in 3.7% statin non-users and 6.3% of patients on statin therapy (p=0.199). In 2010 there were numerically less individuals with BMI<25 kg/m2 (who kept a normal lifestyle compared with 2004) in statin users than in statin non-users (49.2% vs 75.7%; p<0.019). Opposite results were observed for smoking habits, as significantly more statin users stopped smoking after 5-year follow -the were in 12.2% smoking patients in 2010 in statin users and non-users, respectively (p<0.015).

Conclusions: A small proportion of patients with dyslipidaemia, both on and not on statin therapy, complies with a healthy lifestyle; a great challenge for physicians. The application of healthy diet and the number patients with correct statin therapy and by 23.9% by statin users (p<0.001). After 5-year follow-up, regular physical activity was continued only in 3.7% statin non-users and 6.3% of patients on statin therapy (p=0.199). In 2010 there were numerically less individuals with BMI<25 kg/m2 (who kept a normal lifestyle compared with 2004) in statin users than in statin non-users (49.2% vs 75.7%; p<0.019). Opposite results were observed for smoking habits, as significantly more statin users stopped smoking after 5-year follow -the were in 12.2% smoking patients in 2010 in statin users and non-users, respectively (p<0.015).

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Unfractionated vs. low-molecular weight heparin immediately after heart valve surgery

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Introduction: A number of studies have suggested that low molecular weight heparin (LMWH) may be used for early anticoagulation after heart valve surgery. This is unfractinated heparin (UFH) is used, but yet, there is no consensus which LMWH is better to use.

Purpose: We wanted to investigate efficacy and safety of early anticoagulation by using the UFH vs. two different LWWMH, immediately after heart valve surgery. For this prospective, non-randomized, multicenter study we evaluated patients with correct over-anticoagulate (aPTT>70) patients at the beginning of treatment but not...
in the middle, nor at the end of therapy, when majority of patients were opti-

mally anticoagulated (apTT 45–70s) (p<0.0001). Patients treated with enoxa-

parin were steadily optimally anticoagulated (anti-Xa 0.5–1 IU/ml) during the follow-

up (p<0.001). On the other hand, dalteparin treated patients were con-

stantly under-anticoagulated (anti-Xa 0.5 IU/ml), predominately on the first day (p<0.0001), which was also evident on the second day (p=0.028) and the last day of treatment (p=0.024). There was no difference between the groups in terms of thromboembolic and major bleeding events rate (p=NS). UFH treated patients had more pleural and pericardial hemorrhagic effusions (5/55), comparing with enoxaparin treated (0/57) and dalteparin treated patients (1/58) (p=0.022). Over-

all mortality was 5.3%. Mortality rate was similar in all groups, 2/55 among UFH treated patients, 3/57 among enoxaparin treated and 4/58 among dal-

teparin treated patients (p=NS).

**Conclusions:** Using the LMWH for early anticoagulation after heart valve surgery is as safe and effective as using the UFH, but there is a difference between level of anticoagulation achieved by enoxaparin and dalteparin, which could be attributed to their different low-molecular characteristics.

P6483 | BEDSIDE

Conventional mitral surgery in patients with left ventricular dysfunction: a single centre experience

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**Background:** Left ventricular (LV) dysfunction is often underestimated in patients with severe mitral regurgitation. Even in the presence of "normal" LV function, volume or pressure overload can lead to adverse consequences affecting survival. Decision making for these high-risk patients poses a real dilemma in the daily practice since trans-catheter therapies are rapidly expanding as alternative to conventional surgery.

**Purpose:** To evaluate the early and mid-term outcomes of patients undergoing conventional mitral surgery with a moderate/severe ventricular dysfunction.

**Methods:** From 2004 to 2014, 178 patients (115 males, mean age 66±10.6 years) with an ejection fraction (EF) less than or equal to 45% underwent mitral valve repair (50) or replacement (128). Mean preoperative EF was 37±6.2%. Mean PAPs was 48±13.8 mmHg while mean creatinine was 1.24±0.88 mg/dl. Thirty-eight patients had diabetes and 92 had an associated coronary disease. Variables with a P value <0.10 at univariate analysis entered the multivariate logistic regression to determine predictors of in-hospital death. Kaplan–Meier esti-

mates were calculated and compared using a log-rank.

**Results:** Operations were performed in urgent/emergent conditions in 9.3% of cases. Cardiopulmonary-bypass and cross-clamp times were 168±60 and 118±42 minutes. CABG was performed in 61 patients. Forty-seven patients (26.4%) required IABP. Eleven patients died in hospital (6.2%). Two patients had a stroke. Five required a continuous veno-venous hemolitration. Median post-

operative stay was 14 days (range 6–156). Median FU-time was 16.2 months (IQR 4–50). Nine patients died and 9% was lost at FU. Survival rates were 92.6 at 1y and 87.9 at 5 and 8 years. Freedom from mitral reoperation was 95.6 at 1y, 94.4 at 5y, and 92.4 at 8 years. Age (P<0.04), OR 1.032, C.I. 1.015–1.053, CPB time (P<0.04), OR 1.019, C.I. 1.001–1.038) and preoperative creatinine (P=0.03; OR 3.04, C.I.1.11–8.3) were independent predictors of in-hospital death. Type of surgery (repair vs. replacement) didn’t impact on death as well as the presence of diabetes (OR 1.04; P=0.54) and EF (OR 0.49; P=0.69). Median EF didn’t change at discharge (37.71±9.2%) and at last FU (38.5±10.5%).

**Conclusions:** Conventional mitral surgery still represents a satisfactory option in very complex patients with moderate/severe myocardial dysfunction. A lower EF doesn’t affect early outcomes while age, creatinine and cardiopulmonary bypass time are independent predictors of in-hospital deaths. Older patients with a combined cardio-renal impairment can probably benefit from alternative/trans-

catheter therapies.

P6484 | BEDSIDE

Effects of concomitant MAZE procedure in patients with functional mitral regurgitation undergoing isolated mitral valve annuloplasty using the HeartPort technique

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**Background:** Significant functional mitral regurgitation (FMR) is frequently associ-

ated with atrial fibrillation (AFIB). The HeartPort technique is a minimally invasive endoscopic video-assisted approach via the right chest avoiding sternotomy.

**Objective:** To study effects of concomitant MAZE procedure in patients with FMR undergoing isolated mitral valve annuloplasty (MVA) using the HeartPort tech-

ique.

**Methods:** The study population consisted of 139 patients (age 67±12y, 60% males, 47% coronary artery disease, 69% AFIB) with FMR undergoing isolated MVA (P6484). Concomitant MAZE procedure was performed in 56 (40%) patients (the MVA+MAZE group). The remaining patients underwent MVA alone (the MVA-alone group).

**Results:** The performance of MAZE was not associated with increased 30-day mortality (0% in both groups, NS). During a median follow-up of 3.6 y (IQR 2.2–4.9 y), the cumulative rate of death from any cause was similar in the MVA+MAZE (13%) and the MVA-alone (19%) group (HR, 0.49; 95% CI 0.21–1.16; p=0.11). In contrast, the MVA+MAZE group showed significantly lower rate of hospitalizations for heart failure than the MVA-alone group (13% vs 30%, adjusted HR, 0.41; 95% CI 0.19–0.83; p=0.024) (Figure). In addition, reverse left ventricular remodeling was observed only in the MVA+MAZE group (Δ end-systolic volume, −18 ml vs + 4 ml; p<0.05; Δ ejection fraction, +5.5% vs −2.2%; p<0.05).

P6485 | BENCH

We bring down long-term survival in patients with severe ischemic mitral regurgitation when replace mitral valve: propensity-matched analysis?

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**Background:** Severe ischemic mitral regurgitation (IMR) is associated with re-

duced long-term survival and optimal treatment still remains controversial. Our study focused on patients with severe compromised ischemic left ventricle and functional IMR to understand how mitral valve replacement versus repair affects survival and provide the predictors of long-term mortality.

**Methods:** 1068 patients (mean age 57.9±8.3 years) with coronary artery dis-

eases and ischemic mitral regurgitation were operated – in 989 patients mitral valve (MV) repair and in 79 patients MV replacement were combined with CABG. Groups were matched by propensity score using LV remodeling, MR grade by quantitative echocardiography, demographics dates and co-morbidity. Survival (with mean follow-up 7.34±1.8 years) and NYHA class were compared. Uni- and multivariate analyses were performed and the predictors of long-term mortality were identified.

**Results:** Before matching 10-year survival was significantly worse in replace-

ment group (HR– 2.14; 95% CI 1.43–3.21; p<0.001). After propensity matching 1:1 we’ve received cohort of 138 patients with severe compromised LV (EDD 71,1±7,9 mm, ESD 59,±7.7 mm, EDV 126±33.9 ml/m2 with EF 31,±5.7%) and severe MR (ERO PISA 0,43±0,18 mm2). In matched cohort four patients who underwent mitral valve repair died at 30 days postoperatively and five patients died after valve replacement (p=0.5). The fact of mitral valve replacement versus re-

pair did not impact long-term survival (HR: 1.35; 95% CI 0.82–2.29; p=0.26) and overall in 1- and 5-year were 91,8±0.14% and 57.2±0.48% respectively (long-rank p=0.251). Distribution of NYHA functional class in follow-up improved (Wilcoxon signed-ranks test p=0.001 for both group) and was comparable between matched groups (with mean 2.38±0.68 after MV replacement vs. 2.25±0.92 for MV re-

pair, z² = 5.29, p<0.49). In multivariate Cox regression LV ESD (HR: 1.038, 95% CI 1.004–1.072, p=0.013) and advanced NYHA (HR: 2.55, 95% CI 1.57–6.1, p=0.037) were found as independent risk factors for an increased long-term mor-

tality after surgery.

**Conclusion:** The mitral valve chordal-sparing replacement versus repair did not take down survival in patients with severe damaged ischemic LV. The functional status of patients is comparable between repair and replacement group in long-
term follow-up. Survival mostly depends on factors related to the patient’s condition at the time of surgery.

**OPTIMISING TECHNIQUES AND OUTCOME AFTER CARDIAC SURGERY**

P6486 | BENCH

Should Ross procedure be considered a feasible alternative for adult patients who require AVR? Single centre 357 patients long-terms outcome, clinical and echocardiographic study


**King Faisal Specialist Hospital & Research Centre, The Heart Centre, Riyadh, Saudi Arabia**

Aim of the study is to evaluate clinical and echocardiographic characteristic and mid-long term results of Ross operation in different groups of age with emphasis
Ross procedure should be considered a feasible alternative for adult patients who require AVR, especially for people with an active lifestyle and young women who plan to become pregnant. Technical expertise is required to ensure optimal benefits and enhanced durability for the patients.

P6487 | BEDSIDE
Systemic inflammation and oxidative stress contribute to acute kidney injury after transcatheter aortic valve implantation
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Background: AKI is common after conventional valve surgery with cardiopulmonary bypass (CPB) and has been linked to preexisting comorbidities, peri-procedural hypotension and systemic inflammation. TAVI does not require CPB but post-procedural AKI is still common. The extent of systemic inflammation and the mechanism of AKI after TAVI is not fully understood.

Objective: To characterize the inflammatory response after trans-catheter aortic valve implantation (TAVI) and evaluate its contribution to the mechanism of post-procedural acute kidney injury (AKI).

Methods: 105 consecutive patients undergoing TAVI at our institution were included in this study. We analysed the peri-procedural inflammatory and oxidative stress responses by measuring a range of biomarkers (including C-reactive protein [hsCRP], cytokine levels and myeloperoxidase [MPO]), before TAVI and 6, 24 and 48 hours post-procedure. We correlated this with changes in renal function and patient and procedural characteristics.

Results: We observed a significant increase in plasma levels of pro-inflammatory cytokines (hsCRP, IL-18, TNFα receptors) and markers of oxidative stress (MPO) after TAVI. The inflammatory response was significantly greater after trans-apical (TA) TAVI compared to trans-femoral (TF). This was associated with a higher incidence of AKI in the TA cohort compared to TF (42% vs 8%, respectively; P<0.0005). The incidence of AKI was significantly lower when the reactive oxygen scavenger N-Acetylcysteine (NAC) was given peri-procedurally (11% vs 39%, P<0.001) with a 3x lower relative risk of developing AKI with NAC (RR 4.7; 1.4–18.3). In multivariable analysis only the TA approach and no use of NAC before the procedure were independent predictors of AKI.

Conclusion: TAVI creates a significant post-procedural inflammatory response, more so with the TA approach. The mechanisms of acute kidney injury after TAVI are complex. Inflammatory response, hyperfusion and oxidative stress may all play a part and may therefore be therapeutic targets to reduce/prevent AKI in the future.

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P6489 | BEDSIDE
Conventional aortic valve replacement in medium/high risk patients
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Introduction: Medical treatment of aortic stenosis is associated with a poor prognosis and the advent of transcatheter valve implantation (TAVI) seems to be a good option to those ineligible for surgery. However, its use in medium and high risk patient still able to go for surgery is still under debate.

Purpose: To evaluate short and long-term results of medium/high risk patients who underwent conventional aortic valve replacement (AVR).

Methods: From January 2006 to December 2010, 125 patients with isolated or predominant aortic stenosis, logistic EuroSCORE > 10 (mean 17.2±7.8; range10–50.8; 23% with EuroSCORE ≥ 20), from a total of 798 (15.7%) were submitted to conventional AVR. Mean age 77.0±5.5 years (62–90); female 87 (67%); 50.8; 23.2% with EuroSCORE ≥ 20. Delay from previous surgery was 6.5±5.5 years in group 1 vs 13.2±3.6 years in group 2, (p<0.0001). Freedom from surgery after 10 years was 66% in group 1 and 81% in group 2 (p=0.025), after 20 years 62% vs 72% (p=0.0625) respectively.

Results: A bicuspid valve was found in 15 (12%) and calcified aorta in 33 (25.4%) (one case of porcelain aorta). Biological valves implanted in 115 (92%), mean size 21.8±1.2mm. Septal myectomy performed in 102 (82%) and aortic root enlargement in 39 (31.2%). Thirty-day mortality was 1.6% (2 patients), comparable to that observed in those with Euscore<10 (6.6%; P=0.232). Inotropic support used in 23 cases (18%). Complications included pacemaker implantation in 6 (4.8%) and major stroke in 7 (1.6%). Major strokes in 6 (4.8%) and minor strokes in 7 (1.6%) and major strokes in 6 (4.8%) and minor strokes in 7 (1.6%) and major strokes in 6 (4.8%) and minor strokes in 7 (1.6%). Mean postoperative creatinine 1.6±1 mg/dL. Mean systolic pulmonary artery pressure 54±17 mmHg.

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Conclusion: Despite the growing trend towards the use of TAVI in patients considered to be at high/medium risk for surgery, conventional AVR, when feasible, remains the best option, as it can be performed with low early mortality and morbidity, comparable to lower risk populations, but with impaired late survival, probably because of associated comorbidities.

P6490 | BEDSIDE
Ross operation: is it possible to identify the ideal candidate?
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Purpose: Autograft and homograft reintervention are possible complications after Ross operation. Our aim was to identify, in a prospective series of Ross autograft cardiovascular surgery, the variables that identify those patients free of reintervention in any valvular substitute in the long term.

Methods: Since November 1997 to July 2009, a total of 107 patients diagnosed of severe aortic valve disease requiring surgical treatment underwent Ross surgery (mean age 30±11years, 71 male, 86 patients: 18 years). In all of them, a comprehensive clinical and echocardiographic evaluation was performed before the intervention and at discharge, at 6, 12 months and annually after surgery. Groups were divided in 15 years (mean follow-up: 11 years) and patients with aortic valve function ≤ 1.611 mg/dL, Mean hospital stay was 8.8±6 days. No significant paraprostatic leak was detected at discharge. Survival at 1, 3 and 6 years was 93.4±2.3%, 86.0±3.2% and 65.3±5.2%, respectively, which was significantly lower than the 673 patients in the Euroscore≥20 group (93.1% vs 92.1%, p=0.006). Freedom from reintervention of both valve substitutes at 5 and 10 years was 88% and 81%, respectively.

Conclusion: The Ross valves have a potential to be used for tailor made therapy in valve surgery and satisfy the higher requirements of the systemic circulation maintaining the histological character as autologous tissues.
respectively. Women had better reintervention-free survival at median follow-up (85% versus 75%), as well as adult patients (≤18 years, 80% versus 67%) and the 34 patients with pulmonary annulus <22 mm in the echocardiogram previous to surgery (82% versus 76%), but none of these differences were statistically significant. However, the subgroup of 16 adult women with pulmonary annulus <22 mm had a significantly better reintervention-free survival at median follow-up (100% versus 73%, p=0.04, figure).

Conclusion: In our series, none of the adult women with pulmonary annulus <22 mm required reintervention of the autograft or homograft in the long-term. Further confirmation of this finding in larger series could be useful to identify the ideal candidate for Ross surgery.

P6491 | BEDSIDE
Impact of small annulus on valve hemodynamic and mid-term outcome following transcatheter aortic valve implantation compared with surgical aortic valve replacement
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Purpose: The aim of this study was to investigate the impact of small annulus on valve hemodynamic and mid-term outcome in patients with severe aortic stenosis (AS) following transcatheter aortic valve implantation (TAVI) compared with surgical aortic valve replacement (SAVR).
Methods: From Jan. 2013 to Aug. 2014, a total of 206 consecutive patients underwent aortic valve replacement in our institute were retrospectively enrolled. We defined annulus with 20mm or less measured by pre-procedural transesophageal echocardiography as small annulus. We compared the post-procedural valve hemodynamics including prosthesis-patient mismatch (PPM) and mid-term outcome between TAVI and SAVR patients.
Results: The age of the 75 severe AS patients with small annulus ranged from 63 to 95 years (mean±SD, 80.7±7.0 years, SAVR [n=52] 78.4±6.1 years vs TAVI [n=23] 85.9±6.1 years, P<0.001)). Post-procedural transaortic peak velocity (peakV), mean aortic pressure gradient (mPG), and effective orifice area (EOA) were significantly better in the TAVI group than in the SAVR group (peakV, SAVR 2.81±0.55m/sec vs TAVI 2.51±0.37m/sec, P<0.007; mPG, SAVR 17.0±6.4mHg vs TAVI 13.2±4.4mHg, P=0.005; EOA, SAVR 1.23±0.34cm² vs TAVI 1.37±0.16cm², P=0.046). Severe PPM defined as EOA ≤0.65cm² was seen in the SAVR group (26 cases, 50%) while no severe PPM was occurred in the TAVI group (P=0.03). In the light of these results, device success rate was significantly higher in the TAVI group (78.3%) than in the SAVR group (53.9%, P=0.045), whereas 1-year mortality was similar between the two groups (P=0.80).

Conclusion: In the severe AS patients with small annulus, TAVI was hemodynamically superior to SAVR and significantly reduced the incidence of PPM, though it did not affect 1-year mortality.

P6492 | BEDSIDE
Type 2 diabetes and prosthesis-patient mismatch are associated with faster structural valve degeneration in bioprosthetic aortic valves
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Introduction: Bioprosthetic aortic valves have been progressively more frequent due to excellent hemodynamic properties and freedom from warfarin. The main problem is long-term durability that is limited by structural valve degeneration (SVD). The patients that develop SVD have a poor prognosis.

Aims and methods: The aim of this study was to assess clinical risk factors for early SVD in aortic bioprostheses. From 1999 until 2014 the patients after cardiac surgery were prospectively followed up. The inclusion criterion was the patients who underwent aortic bioprostheses without in-hospital mortality. In the follow-up the patients were seen after discharge, third and twelfth months. During each visit an echocardiogram was performed. SVD was defined as stenosis type if the progression of mean aortic transprosthetic gradient double from baseline with thickening of leaflet. The incompetence type SVD was diagnosed when aortic regurgitation was either moderate or severe.

Results: 257 patients were discharged after the surgery. Median follow-up was 3.8 years, 96.1% follow-up was completed. Mitroflow was the most frequent bioprosthesis model (61%) followed by Carpentier-Edwards (18%). Mean transprosthetic gradient was higher in bioprostheses with prosthesis-patient mismatch (PPM) than those without PPM (16±5 mHg vs. 13±5 mHg, P<0.001 at baseline and these differences persisted at the first year after valve replacement. During the follow-up the diagnosis of SVD was carried out in 21 patients at mean 3±2.3 years. SVD as stenosis was observed in 16 cases and regurgitation in 5 cases. On univariable analysis, SVD was associated with diabetes (57% vs. 31% P=0.01). At 3 and 5 years after valve replacement freedom from SVD was 95% and 79% in diabetic patients, significantly lower than in non-diabetic patients (97% and 95%, respectively) (Log-Rank, P=0.005). Free from SVD in patients with PPM was 92% and 81% significantly lower than patients without PPM (99% and 95%) (Log-Rank, P=0.001) at 3 and 5 years. Clinical risk factors to develop SVD in multivariable analysis revealed that diabetes and PPM were independent predictors of SVD. The combination of both predictors for SVD shows that in diabetic patients with PPM, survival with SVD was 81% at 5 years.

Conclusions: In the present study, diabetic patients and PPM in aortic bioprostheses are strong predictors of SVD. When both clinical predictors are combined, the free-SVD survival rate in this group decreases progressively when compared with the combination of other predictors.

ROBOTIC SURGERY
P6493 | BENCH
Minimally invasive transcatheter ventricular restoration (TCVR)
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Background: Post myocardial infarction left ventricle (LV) remodeling is the key process in worsening the outcome of the patients with ischemic heart disease. This single center study is the first report of transcatheter technique of LV volume reduction (TCVR) for ischemic cardiomyopathy.

Patients and methods: 10 patients (Ø age 63.5 years; 7 M/3W; Ø BSA 1.93); all with LV apical-septal aneurysm, were indicated for TCVR procedure. Hybrid approach is performed in catheterization lab/hybrid room under fluoroscopy. Revisit anchor pllication concept is based on surgical introduction of external anchor placed through left mini-thoracotomy and internal anchor introduced by puncture technique from right internal vein. The primary endpoint of the Revisit study was safety and total reduction of LVESVI.

Results: In 10 patients we carried-out TCVR fully hybrid way. Average time of the procedure was 226 minutes. The procedure was done in all patients successfully and an average 3 anchors per patient were placed. In one month the total reduction of LVESVI was 39% (baseline LVESVI 126 ml/m2, one month LVESVI 78 ml/m²), LV EF increase from Ø 32% at a baseline to 41%, NYHA at baseline 2.5 dropped to 1.5 at one month, 6 minutes walking test increased from baseline 382m to 449 m. Only one patient got significant TIA immediately after the procedure with fast recovery.

Conclusion: 1.our single center results confirmed transcatheter TCVR “exclusion” of LV aneurysm safe and effective; 2. learning curve is reasonable short; 3.the real clinical benefit needs to be confirmed by larger studies.
AORTA, PERIPHERAL ARTERIAL AND VENOUS SURGERY

P6494 | BEDSIDE
Bypass surgery versus endovascular therapy in chronic hemoidealosis patients with critical limb ischemia due to infra-inguinal disease
Background: Lower limb revascularization with surgical or percutaneous procedures remains a treatment challenge for critical limb ischemia (CLI). It remains controversial which procedure should be optimized. On the other hand, CLI is frequently seen in hemodialysis (HD) patients, who are consistently at a highest cardiovascular risk. We investigated long-term clinical outcome after bypass surgery or endovascular therapy (EVT) in HD patients with CLI due to infrainguinal disease.
Methods: We enrolled a total of 566 consecutive HD patients electively undergoing infra-inguinal revascularization. Of them, 234 patients underwent bypass surgery and 332 patients underwent EVT. They were followed up to 10 years. Amputation-free survival (AFS), defined as freedom from major amputation or all-cause death, was primarily evaluated. Incidence of any revascularization was also analyzed. To reduce the selection bias between the procedures, propensity score with all baseline characteristics was incorporated into Cox proportional hazards model as a covariate.
Results: Tissue loss was seen in 69.4% of patients, and 42.6% of them had an infra-inguinal popliteal disease. During follow-up period, 61 major amputation (10.6%) and 171 death (30.2%) occurred. Propensity score-adjusted AFS at 10-year was comparable between bypass surgery group vs. EVT group (94.4% vs. 93.6%, log-rank p=0.74), but the bypass group had lower all-cause mortality (41.8±5.7) mm, p<0.0001). The median follow-up was 72 months and isolated AVR could prevent further dilatation in aortic root structures and analyze the anatomical mechanism of AR, and the results of RT-3D-TEE were compared with the operative findings.
Results: (1) RT-3D-TEE showed three types of the anatomical mechanism of AR in patients with type A aortic dissection (normal aortic valve number and quality): incomplete cusps closure or short coaptation length of cusp due to relevant aortic sinus dilatation or dissection (type I); aortic leaflet prolapse due to cusp commissural fusion tethering in the internal flap (type II); diastolic internal flap prolapse through the aortic valve orifice resulting in incomplete aortic valve closure (type III). (2) The RT-3D-TEE demonstration results of functional anatomic mechanism of AR have a good consistency to those of operative findings (Kappa=0.867). (3) The Youden index of RT-3D-TEE on type I, II and III were 0.93, 0.86 and 0.73 respectively, the misdiagnosis rate were 0.8%, 8.5% and 2% respectively; and none of the missed diagnosis rate were 6.7%, 5% and 25% respectively. (4) Surgical strategies for aortic root predicted by RT-3D-TEE have a good consistency to optimal surgical treatment selections (Kappa=0.919).
Conclusions: RT-3D-TEE could be used to visually and accurately demonstrate the anatomical mechanism of AR in patients with type A dissection, providing necessary and objective imaging support for surgeons to select a personalized aortic root surgical strategies, especially a valve-sparing aortic root replacement.

P6497 | BEDSIDE
Assessment of aortic dissection risk in Marfan syndrome patients by analysis of aortic viscoelastic properties
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Background: Marfan syndrome is an autosomal dominant genetic disorder characterized by an abnormal fibrillin-1 (a structural protein of connective tissue) synthesis. Aortic root dilatation and dissection are the main problems affecting patients progressing in these patients. Their pharmacological prophylaxis with losartan or warfarin is the main drug counteracting the aortic root dilatation, but a close follow-up is required to assess therapeutic response rate and to identify non-responders. Unfortunately genotypes-phenotypes studies do not allow to determine the exact risk profile in these patients and there is no reliable method to accurately predict their risk of aortic dissection.
Purpose: Aim of this study was to evaluate non-invasive markers for identification of Marfan patients at higher risk of aortic complications.
Methods: We studied 187 Marfan patients (identified according to 2010 Revised Ghent Criteria and positive genetic analysis age 32.5±16.5 yrs (mean±SD), 52 patients (27.8%) had undergone surgical aortic valve replacement (David or Bentall procedure). Central pressure curves were recorded by PulsePen tonometer, and the aortic viscoelastic aortic properties were studied by determination of cardiovascular stiffness (C), pulse wave velocity (PWV) and aortic wave velocity through Doppler (AVR). The routine practice to remedy valve dysfunction, can prevent further dilatation in ascending aortic root structures and analyze the anatomical mechanism of AR, and the results of RT-3D-TEE were compared with the operative findings.
Results: (1) RT-3D-TEE showed three types of the anatomical mechanism of AR in patients with type A aortic dissection (normal aortic valve number and quality): incomplete cusps closure or short coaptation length of cusp due to relevant aortic sinus dilatation or dissection (type I); aortic leaflet prolapse due to cusp commissural fusion tethering in the internal flap (type II); diastolic internal flap prolapse through the aortic valve orifice resulting in incomplete aortic valve closure (type III). (2) The RT-3D-TEE demonstration results of functional anatomic mechanism of AR have a good consistency to those of operative findings (Kappa=0.867). (3) The Youden index of RT-3D-TEE on type I, II and III were 0.93, 0.86 and 0.73 respectively, the misdiagnosis rate were 0.8%, 8.5% and 2% respectively; and none of the missed diagnosis rate were 6.7%, 5% and 25% respectively. (4) Surgical strategies for aortic root predicted by RT-3D-TEE have a good consistency to optimal surgical treatment selections (Kappa=0.919).
Conclusions: RT-3D-TEE could be used to visually and accurately demonstrate the anatomical mechanism of AR in patients with type A dissection, providing necessary and objective imaging support for surgeons to select a personalized aortic root surgical strategies, especially a valve-sparing aortic root replacement.
ized (p=0.317, p<0.001) and ascending aorta diameter (standardized β=0.271, p<0.001) as major factors associated with annual ascending aortic dilatation rate in BAV patients after AVR. The incidence of adverse aortic events was significantly higher in BAV-AI group (15.5% vs. 4.5%, p=0.008). Cox regression analysis further revealed aortic insufficiency (HR=3.723, p=0.019) and preoperative ascending aortic diameter >45mm (HR=16.840, p<0.001) as independent risk factors for adverse aortic events.

Conclusions: BAV patients with aortic insufficiency demonstrated higher risk for accelerated ascending aorta dilatation and adverse aortic events after AVR. Prophylactic aortic intervention along with AVR procedure might be warranted among BAVR patients with ascending aorta diameter over 45mm, especially those with aortic insufficiency valve dysfunction.

P6498 | BEDSIDE
Bicuspid aortopathy: does it really exist? An histological study
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Background: Bicuspid aortic valve (BAV) is frequently associated with ascending aortic aneurysms (AA), which has been linked to intrinsic aortic wall fragility ("bicuspid aortopathy"). However, the mechanisms leading to development or progression of AA in BAV disease are poorly understood. Our aim was to analyze media structure in AA of patients with and without BAV to further define the features of bicuspid aortopathy.

Methods: 134 consecutive patients (75% males, mean age 63) undergoing elective aortic surgery were included and classified according to valve morphology (54 BAV patients had BAV). All clinical variables, including aortic dimensions, pattern of dilatation and valve function were prospectively collected. Samples of ascending aortic wall were obtained during surgery and processed for light microscopy at a dorsal aortic level that evaluated each of the sections. Total thickness of the media, depth of penetration of vasa vorumusum within the media and degenerative changes were analyzed (fibrosis, elastic fibers fragmentation, cystic medial necrosis and calcification).

Results: BAV patients were significantly younger (p<0.001) than those having a tricuspid valve (TAV) and presented with less comorbidity. Maximum aortic diameters at the time of surgery were significantly larger in patients with TAV (56 mm vs 52.7 mm, p=0.004), but we found no differences regarding the pattern of dilatation. In patients with BAV the most frequent valve lesion was stenosis (41%), whereas valve regurgitation (61%) was the most common valve dysfunction in patients with TAV (p<0.002). Media thickness was not significantly different in both groups. Patients with TAV showed a more prominent vasa vorumusum network, characterized by a significantly deeper penetration in the media layer (516 micron vs 356 micron, p<0.001). These differences persisted after correcting for total media thickness. No differences were found in the presence or severity of cystic medial necrosis or calcification. However, fibrosis was more extensive and the proportion of patients showing elastic fibers fragmentation was higher among those with a TAV (p=0.002 and p=0.002, respectively).

Conclusion: There were no major differences regarding aortic media structure in these two groups of patients. Some degenerative changes (i.e fibrosis and elastic fibers fragmentation) were even more marked in TAV patients. These patients also had more prominent pattern of vascularization of the media layer. Our data do not support a different surgical attitude in patients with AA and a BAV.

P6499 | BEDSIDE
Thrombogenic state after vascular surgery and perioperative cardiovascular events
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Background: Cardiovascular events (CVE) are the most limiting prognostic factor after vascular surgery. The underlying mechanism is thrombosis in patients with high atherosclerotic burden.

Purpose: To identify baseline coagulation markers related to CVE and to analyze the behavior of those markers after surgery.

Methods: Thrombin generation, assessed as endogenous thrombin potential (ETP) and ETP ratio (with- or without thrombomodulin), and platelet aggregation in response to arachidonic acid (Aggr) were evaluated before and after surgery, for 183 patients under aspirin use. Patients were monitored for CVE detection. A total of 82 patients had similar thrombolysis, stroke, reoperation due to thrombosis and cardiac death. Our ethics committee approved the study and patients provided informed consent.

Results: The only baseline coagulation marker independently related to CVE was Aggr, so that patients in the 4th quartile had a 2.42 fold increased risk (p=0.034). After exclusion of patients without post-operative test and 53 who received heparin derivers, we analyzed the behavior of ETP, ETP-ratio and Aggr for 110 patients. There was a marked increase in ETP: 648 ±54 min / 869 ±67 min in ETP- ratio 0.41±0.25 X 0.61±0.28; p<0.001, as a significant decrease in Aggr: 5.34±2.56 X 3.38±2.53; p<0.001. We calculated the individual variable differences (%) before and after surgery, and then we compared those means between patients with and without CVE. There was no difference in ∆ETP (p=0.87), ∆ ETP-ratio (p=0.61) or ∆platelet count (p=0.57), but patients with CVE had a greater ∆Aggr (−4.27 X−1.37; p=0.04).

Conclusion: There is a pro-thrombotic state triggered by the surgical stress. The apparent contradiction of increase in thrombin generation and decrease in Aggr suggests platelet consumption, which is greater when CVE occurs. Aspirin responsiveness before surgery is more important than net thrombin generation for the occurrence of perioperative CVE.

P6500 | BENCH
Screening for abdominal aortic aneurysm during echocardiographic examination in high risk patients
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Background: The aneurysm of the abdominal aorta (AAA) is one of major devastators cardiovascular pathologies. Its screening in the general population is costly and unrealistic, but examination of the abdominal aorta appears reasonable in high risk cardiological population.

Patients and methods: As the abdominal aorta is easily accessible to standard transthoracic echocardiographic equipment, we tested this hypothesis in 682 consecutively referred patients. 465 (67.19%) men and 227 women (32.80%) by imaging the abdominal aorta at the end of the cardiac examination. The acquisition of the dynamic images was carried out in the transverse plan by a probe 3 S phased array sector with electronic sweeping at variable frequency (8.1–3.5 MHz) and electronic sweeping.

Results: The native infra renal segment most often involved in AAA was visualized in 674 out of 692 patients what corresponds to a feasibility of 97.4%. It takes only a reasonable time of the maximum 5 minutes and does not generate any additional cost.

An AAA was detected among 31 patients (4.6%), the ratio of men to women was 7.11:1. Risk factors associated with AAA were to current and former smoking and age.

We reported some echocardiography specific factors, such as left ventricular hypertrophy and dilation and poor left ventricular ejection. In this study makes it possible to propose a surgical act among 06 patients (0.9% of the population studied) after the discovery of an aneurysm diameter more than 55mm.

Conclusion: Prevalence of dilative alterations of the abdominal aorta is high in cardiological patients. Visualization during transthoracic echocardiography of the most important infra renal segment is nearly always feasible (97.4%). Since detection of life-threatening but asymptomatic AAA may save lives by offering safe elective surgical treatment or stenting, opportunistic examination of the abdominal aorta during routine transesophageal echocardiography, which involves little time and no additional cost, would appear to be highly effective and should be included in routine examinations, at least in patients over 60 years of age.

P6501 | BENCH
Role of matrix metalloproteinase single nucleotide polymorphisms in thoracic aortic aneurysm development
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Objectives: Thoracic aortic aneurysm (TAA) is a dangerous disorder with very strong genetic component, while all involved genes are not known yet. Matrix metalloproteinases plays crucial role in TAA development. Therefore, we investigated whether polymorphisms in MMP genes were associated with TAA.

Methods: The genotypes of MMP1, MMP2, MMP9, MMP13 genes were determined for 287 patients with TAA (mean age 55.4±10.3, m:f ratio 2.8:1, maximum aortic diameter 54.2±11.1 mm) and 227 controls (mean age 56.5±10.3, m:f ratio 2.4:1, maximum aortic diameter 34.4±3.7 mm) using real time PCR. The associations of genotypes with TAA were assessed using logistic regression models adjusted for sex, age and hypertension.

Results: The polymorphism -8202 A/G (rs11697325) of MMP9 was strongly associated with TAA. Carriers of rs11697325 AA genotype were at increased risk of TAA development having the odds ratio (OR) was 2.7 (95% Confidence interval CI) 1.2–6.1. Maximum aortic diameter was significantly higher in carriers with AA variant (58.2±16.4 mm) compared with AG (49.8±11.7 mm) and GG (48.8±11.7 mm) genotypes (p<0.05). There were no any association of MMP1, MMP2, MMP9, MMP13 genes polymorphisms with TAA.

Association of MMP polymorphism with TAA

| Genotype | Case Control OR 95%CI P-Value |
|----------|-----------------|----------|---------------|
| AA       | 201             | 174      | 0.92           | 0.61–1.4 | P=0.7 |
| AG       | 31               | 40       | 2.7            | 1.2–6.1 | P=0.01 |
| GG       | 55               | 43       | Ref            |         |

Conclusion: Among studied MMP genes polymorphisms rs11697325 MMP9 gene variants only had strong association with TAA. Persons with AA variant of rs11697325 are predisposed for greatest dilatation. Investigation of TAA associated SNPs might improve risk assessment in this group and are believed to help in appropriate and timely selection patients for surgical treatment.

Acknowledgement/Funding: Financing of the Russian government
P6502 | BEDSIDE
Influence of the false lumen status on acute type A aortic dissection without urgent surgical repair
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Background: Recently much attention has been focused on partial thrombosis of the false lumen in acute aortic dissection. However, the issue about partial thrombosis of the false lumen has not been clearly elucidated especially in type A aortic dissection.

Purpose: The purpose of this study was to evaluate the influence of status of the false lumen including partial thrombosis in patients with acute type A aortic dissection received initial medical treatment.

Methods: Sixty-two patients (29 males, mean age 73±13 years) with acute type A aortic dissection received initial medical treatment at 4 hospitals were enrolled. Patients were divided into three groups according to the status of the false lumen on enhanced computed tomography image (complete thrombosis, n=26; partial thrombosis, n=28; patent, n=8). Furthermore, patients with partial thrombosis were divided into two groups; thrombus dominant partial thrombosis if more than 50% of the false lumen was thrombosed (n=18), and flow dominant partial thrombosis as for the rest (n=10).

Results: In-hospital mortality rate was significantly higher in patients with patent false lumen (75% in patent, 25% in partial and 19% in complete) (vs partial, p<0.01, vs complete, p<0.01, respectively). In patients with partial thrombosis, flow dominant partial thrombosis had significantly higher in-hospital mortality rate than thrombus dominant partial thrombosis (60% in flow dominant, 5.8% in thrombus dominant; p<0.01).

Conclusion: The patients with partial thrombosis and complete thrombosis of the false lumen might have better in-hospital outcomes compared with patent false lumen acute type A aortic dissection without urgent surgical repair. Furthermore in partial thrombosis, the proportion of thrombus seems to influence short-term mortality.

P6503 | BEDSIDE
Carbon dioxide-aided angiography decreases contrast volume and prevents kidney injury in peripheral vascular interventions
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Background: Chronic kidney disease is a common comorbidity in patients with peripheral artery disease. In this population, the use of iodinated contrast media (ICM) bears an enhanced risk of contrast-induced nephropathy (CIN), a condition associated with significant morbidity and mortality. Lowering ICM volume is an effective strategy to prevent CIN.

Objective: We investigated the safety and efficacy of carbon dioxide gas (CO2) as a supplemental alternative contrast agent to decrease contrast volume during fluoroscopy-guided peripheral vascular procedures in routine daily practice.

Materials and methods: We compared ICM volume, irradiation time, technical success, and kidney function in 191 consecutive peripheral interventions of the lower extremity (n=63 iliac, n=83 femoral, n=24 popliteal, n=36 below-the-knee) in patients with Fontain IIb-IV that were performed with ICM alone (n=154) or with the aided or exclusive use of CO2 (n=37).

Results: In 154 cases we used only ICM, in 33 both ICM and CO2, and in 4 carbon dioxide exclusively. The technical success rate (overall average 97%), total irradiation (23±16 min), and intervention time (80±37 min) were not significantly different between the ICM and CO2 groups and no severe procedure-related complications were noted. The average contrast volume was significantly lower in the CO2 group (34±14 ml [Iliac: 48±53 ml; Iliac: 24±53 ml] as compared to the ICM group [112±76 ml [Fontain Iib: 125±79 ml; IIb: 95±55 ml]], p<0.0001 vs CO2 each). Although creatinine and eGFR were significantly lower in the CO2 groups at baseline (CO2: 2.1±1.3 mg/dl and 22±34 ml/min, ICM: 1.1±0.6 mg/dl and 76±28 ml/min, p<0.0001 each), the rate of CIN was significantly lower in CO2 (5%) as compared to ICM (19%, p<0.04).

Conclusion: Our analysis underscores that CO2 is an alternative contrast agent that can be applied safely, efficiently, and routinely to reduce contrast volume and prevent CIN during peripheral interventions even in patients with disease of the popliteal artery and below-the-knee and critical limb ischemia.

P6504 | BEDSIDE
Increased pulse wave velocity indicates presence of coronary artery disease in patients with abdominal aortic aneurysms
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Background: Pulse wave velocity (PWV) is a valid, clinically feasible, measure of arterial stiffness and a strong predictor of future cardiovascular events and all-cause mortality in patients with CAD. The aim of the present study was to assess aortic elastic properties in patients with abdominal aortic aneurysms (AAA) with and without coexisting coronary artery disease (CAD).

Methods: We enrolled 95 patients with AAA eligible for interventional repair (European Society for Vascular Surgery Guidelines) and 73 patients with CAD. A group of 29 healthy subjects served as controls (HC). PWV was measured in all participants using Compilor method. The presence of CAD was documented by at least one coronary stenosis - 70% at coronary angiography.

Results: Patients with AAA and HC did not differ in anthropometrical characteristics, lipoid profile and blood pressure levels (p<0.05). PWV was found considerably higher in AAA group compared to HC group (11.92±2.69 ms vs. 7.63±2.38 ms, p<0.001). Importantly, among patients with AAA, those patients with concomitant history of CAD (n=41) had PWV 112±76 ms (Fontain IIb: 125±79 ms; III&IV: 95±65 ms), p=0.04). Univariate analysis revealed significant correlations of PWV with systolic blood pressure (beta regression coefficient=0.428, p=0.012), diastolic blood pressure (beta=0.393, p=0.024), the presence of CAD (p=0.05), 5% as compared to ICM (19%, p=0.04).

Conclusion: PWV is higher in patients abdominal aortic aneurysms compared to healthy controls. Increasing PWV values are a valid marker of concomitant CAD in patients with abdominal aortic aneurysms.

P6505 | BEDSIDE
Impact of one-stage systematic endovascular treatment for multilevel (femoropopliteal and below the knee) lesions in patients with critical limb ischemia
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Background: The purpose of this study is to investigate whether one-stage endovascular treatment (EVT): systematic interventions in multilevel (femoropopliteal and below the knee) lesions, is effective to achieve wound healing in patients with critical limb ischemia (CLI).

Methods: We retrospectively analyzed 189 lesions of patients with Rutherford category 5 (168 patients, male 56%; mean age 73±10 years) who underwent EVT in our institute between April 2007 to September 2014. All the lesions were with multilevel overlapped (FP and BTK) lesions. We divided them into two groups; one-stage EVT group (90 limbs; EVT of both FP and BTK at one time) and conventional EVT group (98 limbs; EVT in FP alone). Outcome measures were complete wound healing, amputation-free survival (AFS) and major adverse limb events (MALE) and periprocedural complications including distal embolism, pseudo aneurism, blood transfusion and undergoing hemodialysis.

Results: Mean follow up period was 23±18 months. Wound healing rate at 1 year was significantly higher in one-stage EVT group than in conventional EVT group (47.8% vs. 32.7%, p=0.03). Freedom from MALE was tended to be higher in one-stage EVT group (51.0% vs. 37.8%, p=0.06) whereas there was no significant difference in AFS (49.0% vs. 52.2%, p=0.65) and periprocedural complications (11.1% vs. 8.2% p=0.49). At 3.6 months and 1.5 years after initial EVT, there was significant difference in healing rate between two groups (17.3%, 38.0% and 74.4% vs. 17.3%, 27.4% and 54.1%, p=0.04). After multivariate analysis, one-stage EVT group was an independent predictor of wound healing.

Conclusions: One-stage systematic EVT for FP and BTK lesions may be effective to achieve wound healings in CLI patients without increase of complications.
**P6506 | BEDSIDE**

Central blood pressure correlates with size of abdominal aortic aneurysm

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**Introduction:** Central blood pressure reflects arterial stiffness and vascular resistance better than brachial artery measurement. There are data demonstrating that parameters of central blood pressure predict progression of abdominal and peripheral blood pressure.

**Methods:** We studied 57 patients (18 women, 39 men; mean age: 73±8), diagnosed with AAA. Parameters of central blood pressure were determined non-invasively by applanation tonometry (SphygmoCor). Size and morphology of AAA were evaluated with ultrasound.

**Results:** The AAA diameter ranged from 30 to 55 mm (median: 45 mm). The analysis showed no correlation between the AAA diameter and age, height or weight, but confirmed a negative correlation with parameters of central blood pressure, while there was no significant correlation with brachial measurements.

Table 1. Correlation between central, peripheral blood pressure parameters and the maximum aortic diameter

<table>
<thead>
<tr>
<th>Blood pressure parameter</th>
<th>r</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td>Central</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C_S (systolic pressure)</td>
<td>-0.275</td>
<td>0.05</td>
</tr>
<tr>
<td>C_P1 (first systolic peak pressure)</td>
<td>-0.266</td>
<td>0.05</td>
</tr>
<tr>
<td>C_P2 (second systolic peak pressure)</td>
<td>-0.275</td>
<td>0.05</td>
</tr>
<tr>
<td>Peripheral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P_S (systolic pressure)</td>
<td>-0.256</td>
<td>NS</td>
</tr>
<tr>
<td>P_P1 (first systolic peak pressure)</td>
<td>-0.254</td>
<td>NS</td>
</tr>
<tr>
<td>P_P2 (second systolic peak pressure)</td>
<td>-0.255</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Conclusions:** Our data show that the size of AAA may affect parameters of central blood pressure probably by modification of the backward (reflected) wave.

**CIRCULATORY ASSIST AND OTHER**

**P6507 | BEDSIDE**

Acute proteolysis of Von Willebrand factor at initiation of continuous-flow left ventricular assist devices

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**Background:** A high rate of surgical bleedings is observed after implantation of continuous-flow Left Ventricular Assist Devices (CF-LVAD). Several studies have reported that CF-LVAD therapy induce a constant degradation of von Willebrand factor (VWF) high molecular weight multimers (HMWM), essential for haemostasis. Although HMWM loss has been reported within days after LVAD implantation, the precise time course of VWF degradation is still unknown. Moreover, the mechanism underlying HMWM loss is still debated since both mechanical demolition and shear-induced proteolysis have been reported.

**Aims:** To investigate the time course of VWF degradation at CF-LVAD therapy and its underlying mechanisms.

**Methods:** A time-course of VWF degradation was assessed in-vitro using a HeartMate II- (HM-II) model circulatory system (MCS) and after HM-II implantation in patients in-vivo (n=8). In-vitro, HM-II MCS was perfused with anticoagulated human blood from healthy donors at 9000 rpm (n=10), as in HM-patients, and at 3000, 6000, and 12000 rpm (n=3). Three more runs were performed at 9000 rpm with EDTA, an unspecific inhibitor of enzymatic proteolysis. Samples were collected, both in vitro and in-vivo, before (T0) and after initiation of HM-II support (T5. T30 and T180 minutes) for VWF antigen, propeptide (VWFpp), VWF proteolytic fragments, VWF multiimeric analysis, and PFA-Closure time ADP (PFA-CADP).

**Results:** VWF degradation in-vitro was dependent from HM-II speed (12000>9000>6000 rpm) and almost fully inhibited by EDTA at 9000 rpm. At 6000 rpm) and almost fully inhibited by EDTA at 9000 rpm. At 6000 rpm, VWF degradation was more pronounced in-vitro (p<0.0001) than in-vivo (p<0.01). PFA-CADP was significantly increased 5 min after initiation of LVAD support in-vivo (p<0.01). An acute increase of VWFpp, already significant at 5 min (p<0.01), was observed in in-vivo indicating an acute liberation of VWF by vascular endothelium. A time-dependent increase in VWF proteolytic fragments was observed in HM-II patients.

**Conclusion:** VWF degradation occurs within 5 minutes after CF-LVAD implantation in accordance with the high bleeding rate reported after this surgery. Shear-induced proteolysis seems the main contributor of HMWM loss while mechanical demolition of VWF seems accessory.

**P6508 | BEDSIDE**

Structural and functional echocardiographic responses to left ventricular assist device implantation: focus on the right ventricle

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**Background:** There are limited prospective, serial echocardiographic data on the structural and functional changes of cardiac chambers in response to continuous-flow left ventricular assist device (LVAD) implantation. Data on right ventricular (RV) recovery are particularly limited.

**Methods:** We conducted an interim analysis of serial echocardiograms performed (before) within 7 days and 30 and 90 days after LVAD implantation as part of an ongoing prospective study. In addition to standard parameters, we obtained RV mechanics with speckle tracking.

**Results:** Among the first 22 patients, 20 (91%) survived to 90 days; all survivors (age 53±14 years; 8 women; 8 white, 12 black; 11 HeartMate II, 9 HeartWare: 11 underwent transplant; 9 underwent LVAD implantation completed the protocol. Overall, LV and left atrial size decreased significantly by 30 days without change in LV ejection fraction (Table 1). Right-sided pressures and pulmonary vascular resistance consistently decreased over time. Despite a small decrease in RV systolic size, conventional functional RV parameters depicted conflicting results: one-dimensional measures (TAPSE, RV S') suggested substantial RV function worsening whereas fractional area change and myocardial performance index suggested improvement. However, global longitudinal strain and strain rate suggested no actual change in RV function.

**Conclusions:** Despite a decrease in right-side pressures after LVAD implantation, minimal short-term changes in RV size and mechanics suggest no immediate improvement in RV function. If further confirmed, these findings may have clinical implications for LVAD candidates with poor baseline RV function.

**Acknowledgement/Funding:** American Heart Association.
suffering from mediastinitis due to OAF or CMF (N=2)—inc. a single patient with previous oesophageal stenting who had developed massive mediastinal infection post-interventionally and required stent removal. The 3 remaining OPF pts—without signs of acute mediastinitis—were treated by pericardial drainage and oesophageal stenting.

Results: The respective in-hospital and 1-year mortality rates were 0 and 18.2% (N=2). After a median follow-up (100% complete) of 34.0 months (IQR 8.9–118.7), 8 patients (72.8%) were still alive. Postoperative complications comprised post-cardiomyopathy low cardiac output syndrome (N=1), new stroke (N=2), respiratory insufficiency (N=4), requiring percutaneous transhepatic (N=3) and re-thoracotomy for haemorrhage (N=1) or right pneumoectomy (N=1). No relevant complications were noted in the 3 OPF pts treated by oesophageal stenting.

Conclusions: High-risk patients suffering from oesophageal fistulation into the atrium, pericardium, pleural cavity or intra-aortic balloon counterpulsation RA may be successfully treated by open surgery or oesophageal stenting. However, we feel that oesophageal stenting should be avoided in patients with clinical signs of acute mediastinitis (OAF and CMF) to avoid stent infection with adverse outcome.

P6510 | BEDSIDE

The utility of CHA2DS2-Vasc and HAS-BLED scores as predictor of thromboembolic and bleeding risk after left ventricular assist device implantation

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Purpose: CHA2DS2-VASc score predicts thromboembolic (TE) event risk and HAS-BLED score predicts major bleeding risk in patients on anticoagulation with atrial fibrillation. We aimed to evaluate if these scoring systems would be predictive of TE and major bleeding complications following continuous-flow left ventricular assist device (CF-LVAD) implantation.

Methods: Baseline CHA2DS2-VASC and HAS-BLED scores were retrospectively determined for patients with CF-LVADs. We identified 145 patients who received a HeartMate II (n=31), Heartware (n=113) and ReliantHeart (n=1) LVAD implanted in a single center between 12/2010 and 12/2014. After device implantation, all patients were on warfarin (goal INR 2–3) as well as 300 mg of aspirin daily.

Results: Mean age was 50.7±11.2 years, 85.5% were male and 53.1% had ischaedic cardiomyopathy. Median length of support was 316 days (range 31–1060) with 22 TE (15.2%) and 32 major bleeding (22.1%) events. The mean (±SD) CHA2DS2- VASc score was 2.3±1.4 and 2.5±1.2 (p=0.2) in patients with and without TE event, respectively. The mean (±SD) HAS-BLED score was 1.8±0.8 and 1.42±0.6 (p=0.004) in patients with and without major bleeding, respectively.

Conclusion: Baseline high HAS-BLED score was predictive of major bleeding events following CF-LVAD implantation, while baseline CHA2DS2- VASC score was not predictive of TE events.

P6511 | BEDSIDE

Comparison of radiation exposure between vascular approach sites in diagnostic coronary angiography and interventional procedures in a contemporary time period analysis


Purpose: Recently, more interests are focused on radiation exposure during catheterization. From many observational studies, transfemoral approach has been suspected as a culprit of higher radiation exposure to patients and operators. However, recent several meta-analysis and studies which evaluated large patient population by only experienced operators revealed that transradial approach might be same with transfemoral approach in terms of radiation exposure. We evaluated the radiation exposure between transradial and transfemoral approach during catheterization in a contemporary time period.

Methods: Between February 2014 to July 2014, 544 consecutive diagnostic coronary angiography and percutaneous coronary intervention (PCI) by experienced operators was evaluated in a single catheterization laboratory. We compared the dose area product (DAP) and air kerma (AK) between transradial and transfemoral approach. Right heart catheterization, coronary spasm provocation test, peripheral or aortic procedure, and device procedures were excluded in this study.

Results: Among them, 337 cases (61.9%) were diagnostic coronary angiography and the other 207 cases (28.1%) were PCI cases. Overall transfemoral approach was done in 385 (70.4%) cases [281 (83.4%) cases in diagnostic angiography and 102 (49.3%) cases in PCI, respectively] and transradial approach was done in 383 (70.4%) cases [281 (83.4%) cases in diagnostic angiography and 102 (49.3%) cases in PCI, respectively]. DAP and AK were significantly lower in transradial group compared to transfemoral group (45496±45329.3 vs. 73727±53951.5 mGy·cm² and 798±5398.9 vs. 1272±1098.3 mGy·cm², respectively). However, DAP and AK per number of runs did not differ between the two groups (3,116.9±1,465.4 vs. 3,294.7±1,877.2 mGy·cm² and 51.6±27.8 vs. 53.9±28.7 mGy·cm², respectively). Vascular access site was not associated with radiation exposure dose, considering urgency and diagnosis at the time of procedure, body surface area, age, sex, and accessibility procedures such as intravascular ultrasound examination, fractional flow reserve, optical coherence tomography, and intra-aortic balloon counterpulsation.

Conclusion: CRT-D may not rescue inotrope-dependent patients with advanced HF. LVAD treatment should be considered instead of CRT-D in such too sick patients.

P6512 | BEDSIDE

Cardiac resynchronization therapy can be a rescue therapy for inotrope-dependent patients with advanced heart failure?

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Background: Although the “off-label usage” of cardiac resynchronization therapy with defibrillator (CRT-D) has spread recently in advanced heart failure (HF) patients in the real-world practice, its clinical effect remained uncertain.

Methods: A total of 84 in-hospital -65-year old patients with advanced HF undergoing CRT-D were enrolled, and the predictors of cardiac death <1 year were examined.

Results: Seventeen patients (20%) had been dependent on inotropes at the time of CRT-D implantation, and 17 suffered cardiac death within a year. Both inotrope dependence and elevated plasma levels of B-type natriuretic peptide (BNP) (>30 pg/mL) at the time of CRT-D implantation were independent predictors of cardiac death within a year by Cox regression analyses (p<0.05 for both). These 2 parameters could significantly stratify 1-year ventricular assist device (VAD)-free survival: inotrope-dependent (BNP group low 1) and high BNP (2), or inotrope-dependent (BNP group low 3) or high BNP groups (4) (98, 77, 57, and 17%, respectively, p<0.001) (Fig A). In contrast, there were no significant differences in actual 1-year survival among the four groups (Fig B). Logistic regression analyses demonstrated that baseline left bundle branch block and left atrial diameter ≤47 mm were significant predictors of a good response to CRT-D defined as the improvement of LV ejection fraction >10% during six months (p<0.05 for both).

P6513 | BEDSIDE

Right ventricular function improves through pump speed optimization in patients on long-term left ventricular assist devices


Background: Optimal interaction between left ventricular assist device (LVAD) and right ventricular (RV) function is paramount for survival in patients receiving mechanical assistance as destination therapy (DT). Assessment of adequate LVAD pump speed is recommended before hospital discharge. However, the role of systematic re-assessment of optimal speed setting in ambulatory patients at long-term follow-up is unclear.

Purpose: The aim of the current study was to assess whether echocardiographically guided pump speed optimization is associated with improved clinical and echocardiographic performance at 3 months follow-up.

Methods: Ambulatory HeartWare DT-LVAD patients underwent speed optimization 5 months after implantation. Echocardiographically assessed LVAD pump speed was echocardiographically assessed for incremental speed settings with steps of 100 rotations per minute to determine optimal hemodynamics. Evaluation at 3 months follow-up included laboratory and echocardiographic measurements.

Results: Assessment of optimal pump speed was performed in 14 patients (58±13 years; 11 males; 19 [IQR 10–32] months on LVAD support). In 7 patients (50%) pump speed was adjusted (increase 171±111 RPM; p<0.01). Three months after optimization RV fractional area change (RV FAC) improved (28±6 to 31±11%) without RV diastolic dysfunction (DD) 44±9 to 43±8 mm. Furthermore, pro-brain natriuretic peptide level (pro-BNP) had decreased (3349±1732 to 2658±1386 ng/L), while glomerular filtration rate (GFR) tended to increase (50%) pump speed was adjusted (increase 171±111 RPM; p<0.01).
Effect of LVAD pump speed optimization.

Conclusion: Systematic re-assessment of LVAD speed setting reveals the need for optimization in a substantial proportion of patients on long-term support, resulting in enhancement of RV function, a decline in pro-BNP, and a tendency towards improved GFR.

P6514 | BENCH
A novel right heart assist device - the perkat (percutaneous catheter pump technology)
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Background: Acute right heart dysfunction is a life-threatening condition with a poor prognosis and occurs in the setting of right ventricular infarction, severe pulmonary embolism, post cardiac transplant, and post left ventricular assist device. Temporary mechanical right ventricular support could be a reasonable adjunctive treatment option.

Purpose: Our intention was to develop a novel percutaneously implantable and pulsatile working device for patients with severe right heart failure.

Methods: The PERKAT (PERKutane KATheterpumptechnologie - percutaneous pump technology) device consists of a self-expandable nitinol cage which is covered with layers of membranes. The outer membrane consists of over hundred foil valves. On the proximal side there is a flexible outlet trunk with a pigtail shaped ending. The whole system is folded into an 18 French sheath and is completely percutaneously implantable in seldinger technique and should be placed in the inferior vena cava, with the flexible outlet trunk bypassing right atrium and right ventricle while the pigtail end sitting in the pulmonary trunk. After nitinol cage deployment, the IABP balloon has to be inserted into the cage and connected with a IABP console. After starting the IABP support blood runs into the nitinol cage during balloon deflation through the foil valve concept of the membranes. During balloon inflation blood is guided through the flexible trunk and leaves the device through valves at the pigtail ending.

Results: In an in-vitro setting with a 40 ccl IABP balloon the device was evaluated with increasing pump cycles of 80, 90, 100, and 110/min. In this series, PERKAT generated a flow of 2.5, 2.8, 3.0, and 3.1 l/min, respectively. In-vivo evaluation in a sheep model of acute right heart failure was performed to investigate the implantation procedure and hemodynamic effect. Implantation was feasible with excellent function and right ventricular support resulting in a 60% increase of cardiac output from 1.3 l/min (nativem measurement in cardiac shock) to 2.1 l/min (with PERKAT support). The device was easy to remove into the sheit without difficulties.

Conclusion: The novel PERKAT device offers a circulatory support of more than 3 l/min in an in vitro setting. First in vivo experiments in sheep demonstrated feasibility and hemodynamic effects of the device. Current studies are investigating the hemodynamic effect of the device in an animal model of right heart failure. Based on the first results we believe that the system is a hopefully approach and the hemodynamic effect of the device in an animal model of right heart failure.

P6515 | BEDSIDE
Efficacy of drug eluting balloons for patients with in-stent restenosis: a meta-analysis of 8 randomized controlled trials
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Background: The optimal treatment for in-stent restenosis (ISR) of both baremetal stent (BMS) and drug eluting stent (DES) is currently unclear.

Objective: The aim of this meta-analysis was to assess the role of drug eluting balloon (DEB) as an optimal treatment for ISR.

Methods: We searched PubMed, MEDLINE, EMBASE, BIOS and Web of Science from 2005 through July 2014. Eight Random controlled trials, enrolling 1413 patients, were included in the meta-analysis. Main endpoints of interest were late lumen loss (LLL), minimal lumen diameter (MLD), binary in-segment restenosis (BR), diameter stenosis (DS), major adverse cardiac events (MACE), target lesion revascularization (TLR), death cases, myocardial infarction (MI), stent thrombosis (ST).

Results: Compared with POBA, DEB treatment significantly reduced the risk of MACE[R R 0.37, p < 0.01], decreased the incidence of death [RR 0.44, p=0.04], TLR[RR 0.27, p < 0.01], and associated with better outcomes of LLL [-0.50 (-0.67, -0.35)mm, p < 0.01], MLD[MD 0.53 (0.44,0.63), p < 0.01], DS[-17.06 (-20.49, -13.63), p < 0.01]. However, the differences were not significant between DEB treatment and DES treatment in all primary and secondary endpoints.

Conclusions: Drug-eluting balloon is an optimal treatment in treating ISR when compared with POBA. However, it has similar effects with drug-eluting stent.

P6516 | BEDSIDE
Treatment of drug-eluting stents in-stent restenosis with paclitaxel-coated balloon angioplasty: insights from the French real-world prospective GARO registry
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Background: Data about paclitaxel-eluting balloon (PCB) angioplasty to treat drug-eluting stents (DES) in-stent restenosis (ISR) were mainly collected in selected patient populations in the setting of randomized trials. The main goal of this prospective registry was to confirm the positive findings of these studies in an unsellected population in clinical practice.

Methods: Consecutive patients with DES-ISR treated by PCB angioplasty were recruited in this prospective real-world registry. The primary endpoint was clinically driven target-lesion revascularization (TLR) at 9 months. Secondary endpoints included acute technical success, in-hospital outcomes, 9-month major adverse cardiac events (MACE) a composite of death, myocardial infarction (MI) and TLR and the occurrence of target vessel revascularization.

Results: A total of 206 patients (67±10.2 years, 80.6% male, 41.3% diabetics) with 210 lesions were recruited. Unstable coronary artery disease was present in 55.3% of patients. The time from DES implantation to DES-ISR was 3.0±2.4 years. Quantitative analyses revealed that patterns of treated DES-ISR were focal in 55.7% and diffuse in 44.3%. The reference diameter was 2.76±0.64 mm. The 9-month follow-up rate was 90.8% (187/206). At 9 months, the TLR rate was 7.0% (13/187) whereas the rates for MACE, MI and cardiac death were 10.7% (20/187), 4.8% (9/187) and 2.1% (4/187) respectively. Results were consistent in patients with paclitaxel and non-paclitaxel-eluting stents (PES) ISR.

Conclusion: This large prospective registry demonstrated acceptable rates of TLR and MACE at 9 months after treatment of DES-ISR by PCB angioplasty. PCB angioplasty was equally effective in patients with PES-ISR and non-PES-ISR.

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P6517 | BEDSIDE
Results of percutaneous coronary intervention of stent restenosis lesions with subsequent paclitaxel eluting balloon catheter at a very long-term follow-up
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Introduction: Drug eluting balloons currently constitute one of the therapeutic
tools used in percutaneous coronary intervention (PCI) of in-stent restenosis lesions. Nowadays, their results at a very long-term follow up are unclear.

**Purpose:** The main objective of this study was to evaluate the efficacy and safety of second-generation Sequent Please® paclitaxel eluting balloon (PEB) over in-stent restenosis at 6 years.

**Methods:** We prospectively included 121 consecutive patients (67±13 years, 79.3% male) with 121 restenotic lesions treated with PEB between March 2009 and March 2014. We evaluated the presence of major cardiac events (MACE) after a prolonged clinical follow-up (median 43 months): death, nonfatal myocardial infarction, target lesion revascularization (TLR) and thrombosis.

**Results:** 47.1% of patients had stable coronary artery disease and 52.9% acute coronary syndromes (47.9% Non-ST-STEMI and 5% STEMI). 53.7% of patients were diabetic. 10.7% of lesions were bifurcations. 36.4% were focal restenosis (type IA or IC of Mehran classification) and 63.6% were diffuse restenosis (type II or IV). 31.4% were drug-eluting stent (DES) restenosis and 68.6% bare metal stent (BMS) restenosis. Predilation at high atmospheres was performed in 93.4% of patients with a balloon/stent diameter ratio of 1–1.5. PEB inflation, at a mean pressure of 18.2±1.6 atm, had a duration of at least 45 seconds. There were no significant differences regarding baseline characteristics of these two groups neither in the MACE rate after a long-term follow-up (p=0.6). During follow-up, 8.3% of patients experienced adverse events: 7 patients died (2 cardiovascular and 5 non-cardiovascular deaths), TLR rate was 5% and there was one case of non-fatal myocardial infarction (0.8%). No cases of thrombosis were observed, immediately after the procedure nor during follow-up. 24.8% of patients had an angiographic follow-up.

**Conclusions:** Despite the presence of both clinical (53.7% diabetic patients) and angiographic (diffuse restenosis 63.6%) unfavorable risk factors, treatment with Sequent Please® PEB over BMS or DES in-stent restenotic lesions, provide a very good results at a very long-term follow up.

**P6518 | BENCH**

Efficacy of a novel paclitaxel-eluting balloon in reducing in-stent restenosis in a porcine model

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**Background:** Drug eluting balloon (DEB) is an attractive alternative to drug-eluting stents because they provide short duration of drug exposure, while potentially reducing restenosis.

**Purpose:** The purpose of this study was to evaluate the effectiveness of a novel paclitaxel-eluting balloon (PEB) in reducing in-stent restenosis in the porcine model.

**Methods:** We implanted 18 metallic stents in 7 domestic swines, inserting 1 stent per major coronary artery. Stent postdilation was performed with the paclitaxel-eluting balloon (n=6), polymer-coating balloon (n=6) and control balloon (n=6). Microscopic evaluation of stented coronary arteries was done at 28±2 days post treatment. The restenosis rate and the vascular healing parameters (endothelialization rate, neointima fibrin and vascular injury) were analyzed.

**Results:** The restenosis rate of PEB group was significant lower compared with the polymer-coating balloon group and control group (19.3%±7.8% vs. 29.4%±13.7% vs. 37.6%±18.1%) by QCA. The vascular injury and inflammation scores were very low and similar among three groups. The marked increase in neointima fibrin (1.7±0.6 vs. 0.4±0.3 vs. 0.3±0.3) and lower endothelial rate (3±0.6 vs. 4.0±0 vs. 4.0±0.0) in the PEB group compared to the polymer and control groups indicated the effective drug deposition. DEB treatment also produced generally mild to moderate hypocellularity in both the neointima (1.7±0.5 vs. 0.1±0.3 vs. 0.1±0.3) and in the media (2.0±0.7 vs. 0.0 vs. 0.0), which suggested the efficacy of drug transfer.

**Histopathology and histomorphometry analysis at 28-day follow-up**

**Conclusion:** In this preclinical trial, treatment of stented coronary artery with PEB resulted in a significant reduction of stenosis rate. The marked increase of neointima fibrin and moderate hypocellularity in the PEB group indicated a drug deposition response.

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**P6519 | BEDSIDE**

The incidence and risk factors of late catch up phenomenon after second generation DES deployment

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**Background:** The previous studies showed clinical restenosis within 1 year after PCI had been remarkably reduced with the appearance of second generation drug-eluting stents (DES). However, the late catch up (LCU) phenomenon remains one of the issues even in the DES era. The aim of this study is to investigate the incidence and risk factors of LCU after second generation DES deployment.

**Methods:** We performed PCI for the novo 2456 lesions in 1955 patients that were treated with second generation DES (zotarolimus-eluting stent: ZES, everolimus-eluting stent: EES, and biolimus-eluting stent: BES) in a single center from April 2009 to December 2012. Of that, 1752 lesions (71.3%) were clinically followed up more than 1 year and performed 6–12 month follow up angiography. We divided into LCU group and non-LCU group and assessed the incidence, outcomes, and predictive factors of the LCU phenomenon, defined as secondary revascularization 1 year after index stenting.

**Results:** The mean clinical follow up period was 745±265 days. Of all lesions, the LCU was found in the 98 lesions (3.9%). There were no significant differences in terms of patient background and lesion characteristics except HD, DM, and diabetes. However, the late catch up phenomenon at 1 year after second generation DES deployment occurs in 3.9% and the predictive factors are HD, SF, tortuosity, and MLD. Of that, SF is the highest risk for LCU phenomenon.

**Conclusion:** The LCU phenomenon after second generation DES deployment occurs in 3.9% and the predictive factors are HD, SF, tortuosity, and MLD. Of that, SF is the highest risk for LCU phenomenon.
**P6521 | BEDSIDE**

Three-year clinical outcomes after treatment of drug-eluting Stent restenosis with paclitaxel-eluting balloon vs. everolimus-eluting stent

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**Background:** Drug-eluting stent (DES) implantation is a very effective treatment for bare-metal stent restenosis (BMS-ISR). The optimal treatment for DES-ISR remains undefined. There are promising but limited clinical follow-up data concerning drug eluting balloons (DEB) in the treatment of DES-ISR. This study compared three-year clinical outcomes after use of drug-eluting balloon (DEB) to second generation everolimus-eluting stent (EES) for treatment of DES-ISR.

**Methods:** This observational study included 86 patients with 86 DES-ISR. 40 patients were treated by repeat PCI using an EES. 46 patients were treated by repeat PCI using a DEB. Follow-up periods were 36 months. The primary end-point of the study was survival free of major adverse cardiac events (MACE) at three year follow-up. Secondary endpoints were survival free of need for revascularization of the target lesion and definite stent thrombosis (ST).

**Results:** Baseline clinical parameters were comparable between the two groups. The two groups were comparable with regards to lesion length, reference vessel diameter, and minimal lesion diameter. There were no differences between the two groups with regards to restenosis length, length of the previously implanted restenotic stents, length of study device (EES 20.5±12.9 mm, DEB 21.2±5.6 mm, p=0.745), stent diameter. Clinical follow-up during the total follow-up period was obtained in 99% of patients. Freedom from major adverse cardiac events at three year follow-up were 42.5% and 32.6% (p=0.3779) for the EES and DEB groups, respectively. Target lesion revascularization rates, rates of myocardial infarction and death for the EES and DEB group at three year follow-up were 25% versus 13%, p=0.1756, 7.5% versus 8.6%, p=1.0000, and 15% versus 17.3%, p=1.0000, respectively. Clinical ST occurred in none of the patients of the DEB group and in one patient of the EES group (1 day after the index procedure) (0% vs. 2.5%, respectively, p=0.4681).

**Conclusion:** Efficacy of DEB for treatment of DES ISR is comparable to second generation EES at three year follow-up. Although use of a DEB for treatment of DES ISR is a common treatment strategy, the use of a DEB should be considered in the treatment of DES ISR.

**P6522 | BEDSIDE**

Incidence and distribution of thin high signals detected by optical coherence tomography in patients treated with paclitaxel-coated balloon

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**Introduction:** The effectiveness of paclitaxel-coated balloon (PCB) catheter in patients with in-stent restenosis has been established. In addition, a recent report has demonstrated that frequency-domain optical coherence tomography (FDOCT) presents thin high signals on in-stent restenotic tissue after PCB angioplasty.

**Purpose:** We aimed to investigate the incidence and distribution of thin high signals after PCB angioplasty for in-stent restenosis.

**Methods:** FDOCT images were obtained after PCB angioplasty from 14 lesions in 13 patients with in-stent restenosis, electively treated by single PCB catheter. For these lesions, the extent of thin high signals was assessed by the agreement of two observers who were blinded to the PCB length. For evaluating the distribution of thin high signals, the sum of the arc was visually estimated at the frame showing minimal lumen area of each lesion.

**Results:** The representative case is shown in the figure below. Thin high signals were detected in all 14 lesions. The length of thin high signals showed agreement with PCB length (19.4±6.4 mm vs. 18.4±4.4 mm, p=0.56), although the correlation was poor (R=0.29; p=0.32). The sum of the arc with thin high signals was different depending on the lesion; maximum: 165 degrees, minimum: 30 degrees, mean ± standard deviation: 71.8±39.1 degrees.

**Conclusions:** This study demonstrated that the thin high signals observed by FDOCT are indicative of paclitaxel coverage on in-stent restenotic tissue. Distribution of drug following PCB angioplasty may be different depending on the lesion. Further investigations may be warranted to explore whether the distribution of paclitaxel impacts on clinical outcomes after PCB angioplasty.

**P6523 | BEDSIDE**

Estimation value of prediction plasma osteopontin levels in patients undergoing percutaneous coronary intervention


Coronary stents are commonly used for treatment of coronary artery disease nowadays. However there are promising improvements in stent technology, new problems have been encountered with their increasing use. Main problem is the inability to predict patients who will develop stent restenosis. Osteopontin (OPN), a calcium-binding, phosphorylated glycoprotein and a macrophage chemotactic protein, is originally identified as a mediator associated with bone remodeling, chronic inflammatory and autoimmune diseases and subsequently demonstrated to play an important role in cardiovascular disease development. Clinically, a significant association between plasma OPN levels and atherosclerotic plaque formation has been demonstrated, independent of traditional risk factors. The aim of our study is to evaluate predictive value of serum osteopontin levels for stent restenosis.

Our study group consists of the 91 patients with previous stent implantation history and has an indication for coronary angiography, 60 of them are in free of restenosis group and 31 of them are in restenosis group and 80 patients with normal coronary angiogram for control group. In study group mean age was 60.8±9.7 years, and 83 (94.9%) of patients were male, mean time passed to control coronary angiography was 36.7±35.1 months. Serum OPN levels were measured by eLSA method.

We found statistically significant difference of OPN levels between groups (p=0.001). The difference is statistically significant between restenosis group and control group (p=0.002). The difference between restenosis group and free of restenosis group is also statistically significant (p=0.011) but there is no significant difference between control group and free of restenosis group (p=0.312). In conclusion, OPN levels are significantly higher in patients with coronary artery disease (p=0.008). In multiple regression analysis with every 100 pg/ml increase in osteopontin level was found to be associated with 2.9-fold increase in development of restenosis.

In conclusion, OPN levels can be used as a marker of stent restenosis but further studies with large patient populations are required to examine predict if value of OPN and factors that affect OPN levels.

**P6524 | BEDSIDE**

Long-term results of treatment of in-stent restenosis in aortocoronary saphenous vein grafts with paclitaxel-eluting balloon and paclitaxel eluting stent

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**Background:** Although percutaneous coronary intervention (PCI) for native vessel stenoses and in stent restenosis (ISR) have been established and enhanced with drug-eluting stents, conduit lesion interventions have been more controversial. The procedural characteristics and long-term outcomes of patients with SVG-ISR have not been reported.

This study compared 12 months clinical outcome after use of paclitaxel-eluting balloon (PEB) to first generation paclitaxel-eluting stents (PES) for the treatment of SVG-ISR.

**Methods:** This was a retrospective single center study which included 41 consecutive patients with 41 SVG-ISR treated with either PES or PEB. 31 patients were treated by repeat PCI using a PEB. 10 patients were treated by repeat PCI using a PES. All procedures were technically successful. The primary endpoint of the study was survival free of 1 degree adverse cardiac events (MACE) defined as death from any cause, MI or need for target lesion revascularization (TLR) at 12 months follow-up. Secondary endpoints were survival free of need for TLR and definite stent thrombosis (ST). Need for TLR was determined based on significant narrowing of the lumen within the stent or the lesion including 5-mm distal or proximal to the stent (≥50% angiographic diameter stenosis) in the presence of symptoms or objective signs of ischemia.

**Results:** Baseline clinical and angiographic parameters were comparable between the two groups. Clinical follow-up during the total follow-up period was obtained in all of patients. Freedom from major adverse cardiac events at long term follow-up were 20% and 6.4% (p=0.2454) for the PES and DEB groups, respectively. Target lesion revascularization rates, rates of myocardial infarction

**Conclusion:** OPN levels can be used as a marker of stent restenosis but further studies with large patient populations are required to examine predict if value of OPN and factors that affect OPN levels.

**Conclusion:** Efficacy of DEB for treatment of DES ISR is comparable to second generation EES at three year follow-up. Although use of a DEB for treatment of DES ISR is a common treatment strategy, the use of a DEB should be considered in the treatment of DES ISR.
and death for the PES and DEB group at one year follow-up were 10% versus 6.4%, p=1.0000, 10% versus 3.2%, p=1.0000, and 10% versus 0%, p=0.2439, respectively. There was no definite ST observed in both groups at 12 months.

Methods: From April 2007 to October 2012, 408 consecutive patients undergoing de novo lesion PCI with reference vessel diameter greater than or equal to 3.5 mm were prospectively enrolled into this study. All enrolled patients were divided into DES group (n=308) and BMS group (n=100). We obtained 24-month clinical outcome including death, myocardial infarction (MI), thrombosis, target lesion revascularization (TLR), target vessel revascularization (TVR), and adverse cardiac events (the composite of death, MI, and TVR). We used Cox’s proportional-hazards models to assess relative risks of all the outcome measures after propensity matching.

Results: After propensity match, 100 DES-treated patients were matched to 100 BMS-treated patients. The patients treated with BMS were associated with higher risk of TLR (HR=2.24, 95% CI: 1.41–3.57, P=0.0007), TVR (HR=1.80, 95% CI: 1.21–2.68, P=0.004) and MACE (HR=1.47, 95% CI: 1.05–2.07, P=0.024).

Conclusion: In patients requiring stenting of large coronary arteries use of DES was associated with significant reductions in the risks of TLR, TVR and MACE at long-term follow-up.

P6525 | BEDSIDE
Percutaneous coronary intervention for restenosis with stent fracture after drug-eluting stent implantation for de novo vs. in-stent restenosis lesions

Background: Stent fracture (SF) is related to restenosis after drug-eluting stent (DES) implantation. As percutaneous coronary intervention (PCI) cases for complex lesions increased, those for restenosis with SF also increased; however, their results remain unclear.

Purpose: To compare the results of PCI for restenosis with SF after DES implantation between de novo and in-stent restenosis (ISR) lesions.

Methods: From November 2002 to December 2013, 10437 patients with 17798 lesions underwent DES implantation successfully. Of these, 14412 lesions were angiographically followed up after 6 to 8 months (midterm f/u) and 10999 lesions were followed up 12 months after midterm f/u. If myocardial ischemia was suspected, coronary angiography was performed at any time. Restenosis with SF was defined as a restenosis lesion within 5 mm from a SF site. SF occurred in 602 (4.2%) of the 14412 lesions, and restenosis with SF occurred in 214 lesions, in which PCI was performed on 199 lesions. The 199 lesions consisted of 146 de novo lesions and 53 ISR lesions at the time before DES implantation causing restenosis with SF.

Results: As shown in the figure, the cumulative incidence of re-restenosis in ISR lesions increased over a long period of time and was much higher than that in de novo lesions.

Conclusion: The results of PCI for restenosis with SF after DES implantation in ISR lesions were more undesirable. DES implantation for ISR lesions with possibility of SF requires reconsideration.

P6526 | BEDSIDE
Clinical outcome after successful implantation of drug eluting and bare metal stents in large coronary arteries
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Objective: Randomized trials have demonstrated that drug-eluting stents (DES) reduce the risk of target vessel revascularization (TVR) compared to bare-metal stents (BMS). This benefit is less pronounced as artery diameter increases. Whether DES is superior to BMS for larger coronary arteries in the setting of routine clinical practice is unknown. This study sought to evaluate the safety and effectiveness of DES compared to BMS for patients with large coronary vessels.

Conclusions: The results of PCI for restenosis with SF after DES implantation in ISR lesions were more undesirable. DES implantation for ISR lesions with possibility of SF requires reconsideration.

P6527 | BEDSIDE
Morphological and circulatory markers of the in-stent restenosis: matching and relevance
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AIM: Evaluation of the correlation between morphological markers assessed in tissue pattern of in-stent restenosis (ISR) and circulatory markers in patients with ISR.

Materials and methods: Using the techniques of confocal and immunofluorescence microscopy and electron microscopy, expression and quantity of extracellular RNA (eRNA), reactive oxygen species (ROS), IL-1β, TNF-α, MMP-2, TIMP-2, fibrillar collagen type I and its markers of synthesis (PICP) and degradation (CITP) have been determined in tissue pattern of ISR and normal coronary artery (control) taken from 19 died patients. In 73 patients with ISR the serum levels of 36 markers of systemic inflammation, oxidative stress as well as RNA-ase, MMP-2 and CITP have been measured and compared with control markers referred to 27 healthy persons.

Results: The ISR evolution is associated with eRNA expression raising in stented coronary artery wall. Its quantity increased proportionally to ISR degree achieving in muscular media of moderate-severe restenosis a 3–4 times increment compared to control. Likewise the ROS, IL-1β and TNF-α expression increased correlated to ISR degree. More than that, between these markers and eRNA has been established a robust positive correlation. Extracellular matrix reorganization is a hallmark sign of ISR exhibited mostly by excessive fibrillar collagen type I degradation, CITP being elevated up to 5 times in media of severe ISR, and denaturized collagen I molecules accumulated in neointima. On the other hand, PICP has fallen of 4-fold, MMP-2 expression markedly (in a range of 3–5 times) elevated in RIS while TIMP-2 in a similar ratio decreased, suggesting thus a real cause of boosted collagen degradation.

Remarkably, close changes have been found in the blood. The used multi-marker panel showed a notable activation of inflammation and oxidative stress as well as RNA-ase, MMP-2 and CITP have been measured and compared with control markers referred to 27 healthy persons.

Conclusions: 1. The conspicuous matching between morphological and circulatory markers offer a strong support concerning the role of inflammation and oxidative stress in ISR pathogenesis, and eRNA appears as a putative triggering factor. 2. Assaying of the underlined circulatory specific markers can be an important and reliable step in ISR diagnosis and prognosis.

P6528 | BEDSIDE
The level of plasma myeloperoxidase predicts rate of drug-eluting stent restenosis
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Background: Restenosis is one of the main problems after percutaneous coronary intervention (PCI) even with drug-eluting stents (DES) implantation. Few data on the role of neutrophil activation in developing restenosis after DES implantation is available.

Purpose: To evaluate the prognostic value of the level of myeloperoxidase (MPO) in predicting the development of restenosis after PCI with DES implantation.

Methods: The study included 55 patients (41 males) aged from 57 to 71 years (mean age 62 years), with coronary artery disease, who undergoing coronary intervention with DES. The patients treated with BMS were associated with higher risk of TLR (HR=2.24, 95% CI: 1.41–3.57, P=0.0007), TVR (HR=1.80, 95% CI: 1.21–2.68, P=0.004) and MACE (HR=1.47, 95% CI: 1.05–2.07, P=0.024).

Conclusion: In patients requiring stenting of large coronary arteries use of DES was associated with significant reductions in the risks of TLR, TVR and MACE at long-term follow-up.
groups did not differ in age, sex, relationship smokers and nonsmokers, the presence of hyperlipidemia. Mean MPO level in group with restenosis was 122.9 pmol/l (78.5–238.5 pmol/l), and in the group without restenosis 67 pmol/l (75.4–135 pmol/l). By the level of MPO patients were divided into two groups: those with MPO levels below the median (<99.0 pmol/l, n=31) and above the median (>99.0 pmol/l, n=24). In the group with MPO below the median of distribution restenosis rate was lower (4 patients, 14%) than in the group with MPO levels above the median of the distribution (9 patients, 60%), p<0.05. Conclusion: In the patients undergoing PCI with DES implantation and with higher levels of plasma MPO the occurrence of restenosis was more frequent than in the patients with lower levels of MPO, which allows to suggest a link between increased activity of MPO and restenosis.

P6529 | BEDSIDE
Incidence of in-stent restenosis over 13 years - a study based on a national registry
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Background: In-stent restenosis (ISR) is one drawback of coronary angioplasty with stent implantation. Purpose: We investigated the incidence of ISR, its clinical presentation and treatment after PCI for proximal LAD artery disease.

Methods: From all patients (pts) undergoing percutaneous coronary intervention (PCI) from 2002 to 2014, we selected those who had previously history of PCI (n=15326). ISR was defined as diameter stenosis >50% in stent segment, being seen on angiography in which, at least, 1 stent lesion was treated up until 2015. They were divided in 3 temporal groups: 2002–2003 (group 1, n=179, 5.8%) – bare metal stent era; 2004–2008 (group 2, n=816, 26.6%) – 1st generation stent era; 2009–2014 (group 3, n=3074, 67.8%) – 2nd generation stent era. For each group we compared clinical features and treatment.

Results: Over time, it has been observed a reduction in ISR incidence (24.8 vs 23.5 vs 16.6%; p for trend <0.001). Pts from group 3 were older (p=0.01), had higher prevalence of hypertension (63.7 vs 75.6 vs 78.4%; p<0.001), dyslipidemia (81.5 vs 68.5 vs 73.9%; p<0.001) and diabetes (31.3 vs 33.5 vs 38.5%; p=0.012). They also had more frequently history of previous myocardial infarction (p<0.001). Although admissions were more frequently due to stable angina (41% of total) or post non-ST segment myocardial infarction (16.3% of total), it was noticed, over time, an increasing admission due to ST segment elevation myocardial infarction (1.1 vs 7.4 vs 11.4%; p<0.001) and unstable angina (1.1 vs 1.8 vs 3.7%; p<0.001). Most of pts presented with good systolic ventricular function, but an increase of pts with moderate (2.6 vs 9.0 vs 11.2%; p<0.001) and severe (1.3 vs 4.5 vs 4.7%; p<0.001) systolic dysfunction was observed. From 3069 PCI performed, a total of 3461 IRS lesions were treated. It was observed, at most, 3 IRS lesions for PCI. Over time, the most frequent presentation was 1 lesion for PCI (88.4% of total), being noticed a decreasing in number of multiple IRS lesions (15.1 vs 11.3 vs 9.6%; p<0.035). Incidence of ISR has increased in left descending coronary artery (34.5 vs 39.8% p<0.001 and treatment was more frequently performed in more complex lesions (p<0.001). It was noticed a reduction in treatment with stent (72.7 vs 74.4 vs 52.8%; p<0.001) and an increasing use of only PCI balloon (39.3 vs 57.8 vs 45.8%; p=0.002) and trombolysis (0.6% vs 2.2% vs 0.0%).

Conclusion: In spite of increasing in risk profile of pts over time, it was observed a reduction of incidence of ISR and multiple IRS lesions. It also was observed an increasing number of interventions avoiding second stent implantation.

P6530 | BEDSIDE
Bifurcation angle between left main trunk and left anterior descending artery is independently related to restenosis after stent implantation for proximal left anterior descending artery disease
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Background: Restenosis after percutaneous coronary intervention (PCI) for proximal left anterior descending (LAD) artery disease is still a significant clinical problem. Although many risk factors for restenosis after PCI have been identified so far, coronary anatomical characteristics for restenosis have not been fully studied.

Purpose: The aim of this study is to investigate the relationship between LAD bifurcation angle and restenosis after PCI for proximal LAD artery disease.

Methods: We analyzed the data of consecutive 177 patients undergoing PCI for native LAD artery, followed by coronary angiography (CAG) from 2008 to 2013. The bifurcation angles between left main trunk and LAD artery (LMT-LAD angles) were measured using left or right anterior oblique (LAO or RAO) caudal view in CAG.

Results: Stent restenoses were found in 33 out of 177 patients. 12 patients had an in-stent restenosis and 21 patients had an in-segment restenosis. The mean LMT-LAD angle was measured as 34.1°±18.5° among all the patients. The average LMT-LAD angle measured in patients with no-restenosis and in-stent restenosis was 32.0°±18.1° and 52.2°±14.5°, respectively, in LAO caudal view with significant difference between these two groups (P<0.001). We also observed that the average LMT-LAD angle in patients with no-restenosis and in-segment restenosis was 17.5°±10.1° and 27.3°±14.3°, respectively, in RAO caudal view (P<0.001). Multivariate analysis showed that indicators for in-stent restenosis were final minimum diameter, lesion length and LMT-LAD angle (OR, 0.12; P=0.036, OR, 10.13; P=0.016 and OR, 7.63; P=0.035, respectively) and indicators for in-segment restenosis were LMT-LAD angle and distance between the ostial LAD artery and proximal edge of stent (OR, 3.83; P=0.024 and OR, 6.37; P=0.006, respectively).

Conclusion: This study suggests that larger LMT-LAD angle is associated with restenosis after stent implantation for proximal LAD artery disease.
Conclusions: New generation DES could be a preferable treatment modality for ISR at the RCA ostial lesion.

P6534 | BEDSIDE
Is bare-metal stent still useful for improving outcomes of percutaneous coronary intervention? From the FU-Registry
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Background: It is not clear the role bare-metal stent (BMS) plays in the field of percutaneous coronary intervention (PCI) in the current drug-eluting stent (DES) era.

Purpose: To identify whether the clinical and angiographic outcomes of BMS implantation are equivalent to those of DES in large vessels.

Methods: Among 2197 patients (2653 lesions) in the FU-Registry, a follow-up coronary angiogram was available for 859 patients (1032 lesions) of which 344 patients (405 lesions) were treated with BMS and 515 patients (627 lesions) with DES. In those patients, the cut-off value of lesion reference (LR) regarding ISR was 0.9% in the BMS group and 0% in the DES group (P=0.09). The incidence of definite stent thrombosis was similar between the two groups (0.9% in BMS, 0% in DES; P=0.31). At 9 months follow-up, death or myocardial infarction occurred 2.9% in the BMS group, vs. 1.1% in the DES group. Mean LR and lesion length in BMS was 3.08mm in BMS and 2.72mm in DES. The clinical and angiographic outcomes with LR larger than 3.08 was compared between the BMS and the DES groups.

Results: Baseline patient characteristics were similar between the two groups except the lower incidence of prior PCI in the BMS group. Mean LR and lesion length in BMS and DES were 3.5±0.3 mm vs. 3.3±0.3 mm (P=0.001) and 14.2±6.2 mm vs. 19.1±12.6 mm (P<0.001), respectively. At 9 months follow-up, death or myocardial infarction occurred 2.9% in BMS patients vs. 39.4±43.7% in DES patients (P<0.001), respectively.

Conclusions: New generation DES could be a preferable treatment modality for ISR at the RCA ostial lesion.

P6535 | BEDSIDE
In-stent neoatherosclerosis can be a possible mechanism of the impaired flow after re-percutaneous coronary intervention for the in-stent restenosis
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Background: Although in-stent restenosis generally have stable process with an early peak in neointimal proliferation, impaired coronary flow [TIMI 0, 1, 2] is sometimes experienced after re-percutaneous coronary intervention (re-PCI) for the in-stent restenotic sites (ISRs), and its etiology is not clear. On one hand, in-stent neoatherosclerosis (ISNA) have been reported by pathological findings or optical coherence tomographic (OCT) studies, which has been reported as a cause of late stent complications.

Purpose: The aim of this study was to investigate the incidence of impaired flow after re-PCI for ISRs and to evaluate the relationship between impaired flow after re-PCI and in-stent neoatherosclerosis.

Methods: From April 2004 to August 2014, we had performed PCI to consecutive 1751 ISRs. ISRs were defined more than 75% diameter stenosis with ischemia. Post re-PCI coronary flow was angiographically evaluated in retrospective manner. Impaired coronary flow was judged by two skilled interventionists. 233 ISRs were examined by OCT during re-PCI to ISRs.

Results: Impaired flow after re-PCI to ISRs had developed in 48 ISRs (2.7%). ISRs defined by OCT was found in 29 lesions (11.2%) in 38 limbs at mean duration from initial PCI to re-PCI [71.7±53.4 vs. 39.4±43.7, P=0.01]. In multivariate analysis, the impaired flow had significantly correlated to ISRs with ISNA [odds ratio:8.29, 95% confidence interval:1.29 to 52.2, P=0.05]..

Conclusions: Impaired flow was seen in 2.7% of the lesions after PCI to ISRs. Impaired flow occurred significantly higher in the lesions with in-stent neatherosclerosis.

PROGNOSIS I

P6536 | BEDSIDE
Usefulness of geriatric nutritional risk index for assessing the nutritional status and its prognostic impact in elderly patients with acute heart failure
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Background: Malnutrition was reported to be an important determinant of worse clinical outcomes in elderly patients with heart failure (HF). However, the appropriate tools for evaluating the nutritional status in HF patients remain unclear. Recent studies showed that geriatric nutritional risk index (GNRI) was a useful tool for assessing the nutritional status in elderly patients.

Purpose: To evaluate the prognostic significance of GNRI in HF patients.

Methods: We examined 477 consecutive patients with acute HF (AHF) in our prospective registry. Those with under 65 years of age, acute coronary syndrome and without accessible GNRI data on admission were excluded. Finally, 364 patients were obtained and divided into two groups according to the GNRI; lower
To investigate the prognostic value of TTKG in patients with ADHF.

**Results:** During a mean period of 218 days, adverse events occurred in 96 patients (26%). Lower GNRI group had higher age ($P<0.01$), lower systolic blood pressure (SBP) ($P=0.01$), and higher plasma brain natriuretic peptide (BNP) level ($P=0.01$) than higher GNRI group. There were no significant differences in terms of sex, serum creatinine, sodium levels, and left ventricular ejection fraction (LVEF) between two groups. The incidence of adverse events was significantly higher in lower GNRI group than higher GNRI group (Figure). In multivariate analysis, lower GNRI was an independent determinant of adverse events (HR 0.97, 95% CI 0.94–0.99, $P<0.005$) among variables including age, SBP, BNP level, and LVEF.

**Conclusions:** Lower GNRI was independently associated with worse clinical outcomes in elderly patients with AHF, and GNRI may be a useful tool for evaluation of nutritional status and identifying high-risk patients.

**P6537 | BEDSIDE**

The prognostic value of the transtubular potassium gradient in patients with acute decompensated heart failure

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**Background:** The renin-angiotensin-aldosterone system (RAAS) is involved in the pathophysiology of acute decompensated heart failure (ADHF). The transtubular potassium gradient (TTKG) has been reported to reflect renal aldosterone bioactivity, and may be a novel prognostic indicator of RAAS activity than plasma aldosterone concentration.

**Purpose:** To investigate the prognostic value of TTKG in patients with ADHF.

**Methods:** We analysed 100 ADHF patients and 30 control subjects. Prior ADHF hospitalisations within the last 12 months were identified in each patient. We measured morning TTKG values at discharge in ADHF patients, as well as the following possible prognostic factors of chronic heart failure: plasma brain natriuretic peptide, serum sodium, creatinine, urea nitrogen concentration, and left ventricular ejection fraction (LVEF) using echocardiography. TTKG was also measured in the control subjects. The clinical outcomes were 100-day cardiac mortality and ADHF readmissions. Cox regression analyses were used to determine the independent predictors of the outcomes. ADHF patients were divided into tertiles based on TTKG values, and the cumulative survival estimates of each group were calculated using the Kaplan-Meier method.

**Results:** TTKG was significantly higher in ADHF patients than in control subjects (4.8±1.9 vs 3.6±1.3; $p<0.001$). The results identified TTKG (hazard ratio: 1.37; 95% confidence interval: 1.16–1.62, $p<0.001$), LVEF, and prior ADHF hospitalisations to be independent predictors of the outcomes. Kaplan-Meier analysis confirmed a stepwise decrease in event-free survival as TTKG values increased (Figure).

**Conclusion:** Our findings showed that TTKG at discharge is a novel prognostic marker in ADHF patients, and may be a useful guide in their clinical management.

**P6538 | BEDSIDE**

Left ventricular global longitudinal displacement assessed by tissue Doppler imaging is the strongest echocardiographic predictor of all-cause mortality in patients with heart failure

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**Introduction:** Tissue tracking (TT), obtained by tissue Doppler imaging (TDI), can be utilized to assess the mitral annular longitudinal displacement (LD) during systole.

**Purpose:** In this study, we wanted to investigate the prognostic value of LD in a large cohort of Heart failure patients and compare LD to the conventional and novel echocardiographic measurements.

**Methods:** Transthoracic echocardiographic examinations of 1061 patients were retrieved from our hospital heart failure clinic’s database. The exams were performed from 2005 to 2013. The echocardiographic images were subsequently analyzed obtaining data by conventional echocardiographic measurements, and in-occidental strain and TDI from the parasternal and apical projections. Global LD was calculated as a mean from the three apical projections with sampling at six mitral annular sites in total.

**Results:** During a median follow-up of 40 months 177 (16.7%) patients died. Mean global LD in this group was 5.01±2.41 cm. A remaining 884 (83.3%) of patients were alive at follow-up with a mean global LD of 6.70±2.53 cm. The risk of dying increased with decreasing tertile of LD, being approximately 5 times higher for patients in the lowest tertile compared to the highest tertile (1. tertile vs. 3. tertile: HR: 4.78, 95% CI: 3.04–7.24, $p$-value=0.001) (see figure).

**Conclusion:** In patients with severe heart failure, global LD is an independent predictor of all-cause mortality. Furthermore, global LD proved to be a superior prognostic indicator when compared to conventional echocardiographic parameters and GLS.
left ventricular ejection fraction >40% (from 17 to 38%). In contrast, the prevalence of dilated cardiomyopathy was decreased from 26% to 14%. The 3-year mortality rate was significantly improved from 24% to 14% (P<0.01), where the difference in the mortality rate between ischemic and non-ischemic CHF noted in the CHART-1 (29 vs. 22%, P<0.01) disappeared in the CHART-2 (15 vs. 14%, P=0.40) (Figure).

Conclusions: These results indicate that the prevalence of ischemic CHF, especially that of preserved LVFLE, has markedly increased in Japan and that the progression of CHF patients has been improved along with implementation of evidence-based medications, particularly in those with ischemic CHF.

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P6540 | BEDSIDE
Quantification of fibrosis in left ventricular endomycocardial biopsy can be a valuable tool to estimate prognosis and individualize therapy in heart failure patients
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Introduction: Endomyocardial biopsy (EMB) contributes important information to the diagnosis and etiology of cardiomyopathies. Myocardial fibrosis, defined by a substantial increase in the collagen volume fraction (CVF) of myocardium, has been shown to be one common histopathological feature in dilated idiopathic cardiomyopathy (DCM), which leads to diastolic dysfunction and possibly worsens systolic function. However, large, longitudinal studies investigating the correlation between histopathological characteristics of EMB and clinical course and prognosis of patients with DCM are still missing.

Purpose: In this study we investigated the prognostic value of fibrosis as a common histopathological finding in a large DCM cohort with a follow up period of up to 10 years.

Methods: We included a total number of 643 patients who had undergone left ventricular EMB (LV-EMB) due to suspected DCM. Using automated image processing and analysis softwares, we developed algorithms based on Bayesian classification to automatically evaluate high-resolution automated scans of LV-EMB for fibrosis. Univariate as well as multivariate analyses between histopathological and clinical findings of these patients have been carried out.

Results: Using machine learning techniques, we established an automated method for quantification of fibrosis in patients’ LV-EMB. Classification of myocardial fibrosis based on Trichrome (Tr) and Elastic van Gieson’s stainings (EVG) showed very good agreement. We could also show that LV-EMB is a safe procedure with a total complication rate of 2.3% in 100 patients in our center with no case of death. Further data analyses showed that the extent of fibrosis significantly correlates with cardiac biomarkers such as hsTnT (P=0.01) and NT-proBNP (P=0.048) as well as with cardiac imaging such as LV-EF (P=0.02), LV-ESD (P=0.01), LV-EDD (P=0.01), LV-ESV index (P=0.02), and LV-EDV index (P=0.02) measured with cardiac MRI. Kaplan Meier survival curves showed that percentage extent of fibrosis was a significant predictor of all-cause mortality (P=0.02) and cardiovascular mortality, heart transplantation or cardiopulmonary resuscitation (P=0.001).

Conclusions: Our results suggest that EMB is a reliable and precise tool to characterize DCM. These data may help improve risk stratification of patients with DCM by using fibrosis in clinical decision making.

P6542 | BEDSIDE
Association of compromised right ventricular function with reduced exercise tolerance predicts survival in patients with chronic heart failure
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Background: Although right ventricular (RV) ejection fraction (EF) is an important determinant of effort tolerance, little is known about the role of RV function and exercise performance in outcome prediction of patients with chronic heart failure (HF).

Aim: We sought to evaluate the impact of RV function and 6-minute walking test (6-MWT) in risk stratification of patients with chronic stable HF.

Methods and results: 628 ambulatory patients (mean age: 70±12 yrs; 32% female) with chronic HF and left ventricular (LV) dysfunction underwent a complete exercise performance in outcome prediction of patients with chronic heart failure (HF).

Exercise performance in outcome prediction of patients with chronic heart failure (HF).

Conclusions: Malnutrition assessed with CONUT was an independent determinant of post-discharge death in AHF patients. Simple addition to the existing prognostic model significantly improved the predictive accuracy. CONUT might be the best nutritional assessment tool for risk stratification in HF.

P6544 | BEDSIDE
Association of compromised right ventricular function with reduced exercise tolerance predicts survival in patients with chronic heart failure
C. Cucco1, A.B. Scardovi2, G.G. Galeotti3, A. Simonioiu3, M.C. Scali1, S. Ghio3, A. Rossi1, P.L. Temporelli4, M. Marzilli5, F. L. Dini6 on behalf of Network Labs Ultrasound (NEBULA) in Heart Failure Study Group. 1Azienda Ospedaliero - Universitaria Pisana, Pisa, Italy; 2Ospedale Santo Spirito, Roma, Italy; 3Division of Cardiology, Fondazione IRCCS Polidocena S. Matteo, Pavia, Italy; 4Department of Biomedical and Surgical Sciences, Verona, Italy; 5Fondazione Maugeri, Veruno, Italy

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Methods and results: 628 ambulatory patients (mean age: 70±12 yrs; 32% female) with chronic HF and left ventricular (LV) dysfunction underwent a complete exercise performance in outcome prediction of patients with chronic heart failure (HF).

Exercise performance in outcome prediction of patients with chronic heart failure (HF).

Conclusions: Malnutrition assessed with CONUT was an independent determinant of post-discharge death in AHF patients. Simple addition to the existing prognostic model significantly improved the predictive accuracy. CONUT might be the best nutritional assessment tool for risk stratification in HF.

P6544 | BEDSIDE
Association of compromised right ventricular function with reduced exercise tolerance predicts survival in patients with chronic heart failure
C. Cucco1, A.B. Scardovi2, G.G. Galeotti3, A. Simonioiu3, M.C. Scali1, S. Ghio3, A. Rossi1, P.L. Temporelli4, M. Marzilli5, F. L. Dini6 on behalf of Network Labs Ultrasound (NEBULA) in Heart Failure Study Group. 1Azienda Ospedaliero - Universitaria Pisana, Pisa, Italy; 2Ospedale Santo Spirito, Roma, Italy; 3Division of Cardiology, Fondazione IRCCS Polidocena S. Matteo, Pavia, Italy; 4Department of Biomedical and Surgical Sciences, Verona, Italy; 5Fondazione Maugeri, Veruno, Italy

Background: Although right ventricular (RV) ejection fraction (EF) is an important determinant of effort tolerance, little is known about the role of RV function and exercise performance in outcome prediction of patients with chronic heart failure (HF).

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Conclusions: Malnutrition assessed with CONUT was an independent determinant of post-discharge death in AHF patients. Simple addition to the existing prognostic model significantly improved the predictive accuracy. CONUT might be the best nutritional assessment tool for risk stratification in HF.
Methods: We retrospectively identified all patients who underwent cLVAD placement and survived to discharge at our centre between 2007 and 2013 (n=114). Analysis was performed on demographic, clinical, and procedural data. Multivariable analysis was used to assess for predictors of mortality. The primary outcomes of interest were time to mortality and first hospitalization after LVAD.

Results: Age ≥70 was associated with increased mortality and time to readmission (figure 1). Using Cox analysis, after controlling for age, gender, and race, baseline creatinine ≥1.5 was the only independent predictor of mortality (HR 1.9 [CI 1.1–3.3], p=0.028). No significant predictors for readmission were identified.

Conclusions: Our data support the notion of advanced age as a risk for death with LVAD support, even with a highly selected population felt to be at acceptable risk. Similar to previous analysis, the cause of death in the advanced age group is not well established and may reflect co-morbidities associated as much as LVAD problems or renal dysfunction. Unique in our analysis is demonstration of higher readmission rates in the advanced age group, suggesting higher morbidity in this cohort. LVAD support should be considered cautiously with advanced age, and renal insufficiency may be a marker of increased mortality in this cohort.

P6544 | BENCH Determinants and prognostic significance of delirium in patients with acute heart failure

Background: Delirium is a common and serious, but potentially preventable syndrome in critically ill condition, such as acute heart failure (AHF). It is important to identify patients at risk for delirium who may benefit from earlier preventive strategies. However, determinants of delirium and its prognostic significance in AHF patients remain unknown.

Methods: We examined 477 consecutive AHF patients who admitted to our institution between January 2013 and December 2014 from prospective registry. Patients with acute coronary syndrome were excluded. Finally, 454 patients were included in this study. Delirium was diagnosed based on the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU).

Results: Delirium was observed in 111 patients (24%) during hospitalization. Patients with delirium were older (80 vs. 74 years, P < 0.01) and had higher prevalence of cerebrovascular disease (CVD) (38% vs. 20%, P < 0.01) and malignant tumor (21% vs. 13%, P < 0.02), higher serum glucose (167 vs. 140 mg/dL, P < 0.01) and CRP (2.3 vs. 1.4 mg/dL, P < 0.02) levels, lower serum albumin (3.6 vs 3.8 g/dL, P=0.01) and free T3 (2.1 vs. 2.4 pg/mL, P=0.03) levels on admission than those without. Patients with delirium had longer hospital stay (23 vs. 20 days, P=0.03), higher utilization of nursing care after discharge (59% vs. 5%, P < 0.01) and higher rate of 90-day adverse events defined as composite of all cause death, worsening heart failure (23% vs. 8%, P < 0.01) than those without. In multivariate logistic regression analysis, the development of delirium (OR 3.30, 95% CI 1.78–6.10, P < 0.01), as well as lower systolic blood pressure (−135mmHg) (OR 2.28, 95% CI 1.19–4.52, P=0.01) and NYHA functional class IV (OR 2.14, 95% CI 1.14–4.08, P=0.02), was an independent determinant for 90-day adverse events. Furthermore, multivariate logistic regression analysis indicated that higher age (> 80 years) (OR 2.69, 95% CI 1.66–4.41, P < 0.01), history of CVD (OR 2.59, 95% CI 1.55–4.35, P < 0.01) and hypalbuminemia (serum albumin <3.5mg/dL) (OR 1.99, 95% CI 1.15–3.44, P=0.01) were independent determinants of the development of delirium.

Conclusions: AHF patients with development of delirium have unfavorable outcomes, particularly higher adverse events, longer hospitalizations, and a greater degree of dependence on nursing care after discharge. These findings suggest that early recognition and prevention of delirium may be important to improve clinical outcomes in AHF patients.
**P6547 | BEDSIDE**

**Apolipoprotein J but not high-density lipoprotein is an independent predictor of mortality in patients with advanced heart failure**

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**Background:** ApoJ, inflammation and atherogenesis are implicated in the multifactorial pathophysiology of heart failure (HF). The high density apolipoprotein J, also known as clusterin, is associated with high-density lipoprotein (HDL) and exerts multiple anti-apoptotic, anti-atherogenic, cell-protective and anti-inflammatory properties.

**Purpose:** To assess the predictive value of apolipoprotein J and HDL in advanced HF patients.

**Methods:** Apolipoprotein J plasma levels and HDL serum levels were determined in 346 patients with advanced systolic HF (median age 75 years, 66% male).

**Results:** During a median follow-up of 4.9 years (IQR: 4.6–5.2), 55.9% of patients died. Apolipoprotein J (median 277 ug/ml [IQR: 216–344 ug/ml]) was a significant inverse predictor of all-cause mortality with a hazard ratio (HR) per 1-standard deviation (SD) of 0.79 (95% confidence interval [CI]: 0.69–0.92, P=0.002). This association remained significant after multivariable adjustment for demographic, clinical predictive variables and N-terminal pro-B-type natriuretic Peptide (HR per 1-SD 0.84, 95% CI: 0.72–0.98, P=0.03). The predictive value of apolipoprotein J did not significantly differ between patients with ischemic and non-ischemic HF (P=0.401).

Conclusions: Circulating apolipoprotein J with its cytoprotective and anti-inflammatory effects is an independent inverse predictor of mortality in advanced HF patients. Our data indicate an implication of apolipoprotein J in HF progression.

**PROGNOSIS II**

**P6548 | BEDSIDE**

**Pericardial effusion is a marker of increased mortality in thalassemia major patients**

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**Introduction:** In different types of not-hematological diseases the presence of a small pericardial effusion (PE) was associated with worse survival even after adjustment for patient characteristics, suggesting that it is a marker of underlying disease. In thalassemia major (TM) pericardial effusion was shown to be one of the manifestations of heart disease but its potential prognostic importance has never been investigated in the modern era. Cardiovascular Magnetic Resonance (CMR) by cine SSFP sequences was demonstrated to be extremely sensitive to even a small amount of PE.

**Purpose:** This is the first prospective study evaluating if the presence of pericardial effusion is associated with increased mortality in TM.

**Methods:** 1259 patients (648 females, 31.02±8.64 years) enrolled in the Myocardial Iron Overload in Thalassemia (MIOT) were prospectively followed from their first CMR scan. CMR was used to quantify myocardial iron (MIO) overload by a multislice multiecho T2* approach and to assess biventricular function parameters and to detect PE by cine SSFP sequences.

**Results:** PE was present in 25 (2.0%) patients. Patients with and without PE were comparable for age and ratio of men/women. At the baseline, the percentage of patients with MIO (global heart T2*<20 ms) was comparable between patients with and without PE (12.0% vs 28.7%; P=0.074) and left ventricular and right ventricular ejection fraction were not significantly different between the two groups.

Mean follow-up (FU) time was 44.5±20.35 months and there were 15 deaths. Mortality was greater for patients with PE compared to those without PE (8.0% vs 1.1%, P=0.034).

Conclusions: PE is quite rare in TM patients and it is not related to MIO. An important role in the development of PE could be played by the iron-induced pericardial siderosis but, due to the limitations of the current non-invasive CMR techniques, we were not able to address this issue.

**P6549 | BEDSIDE**

**Outcomes in patients with probable cardiac sarcoidosis in comparison with definite cardiac sarcoidosis**

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**Background:** Although early diagnosis of cardiac sarcoidosis (CS) is important to initiate steroid treatment before pathological lesions are irreversible, it is difficult to confirm the diagnosis even in patients who have signs compatible with CS. In a clinical setting, patients with probable CS who satisfy only clinical cardiac findings for CS are not uncommon. However, patients with probable CS are not treated with steroids because their prognosis is unknown.

**Aim:** To aim to compare outcomes in patients with probable CS to those in patients with definite CS treated with steroids.

**Methods:** The study population consisted of 101 consecutive patients who satisfied clinical cardiac findings for CS. Patients with definite CS were defined as having histological or clinical confirmation of CS according to the Japanese Ministry of Health and Welfare guidelines revised by Japanese Society of Sarcoidosis and Other Granulomatous Disorders, and were treated with steroids. Patients with probable CS were defined as having only the CS diagnostic guidelines’ clinical cardiac findings but not definite CS because of no histological or extracardiac sarcoidosis, and were not treated with steroids. The endpoint was major adverse cardiac events (MACE), including cardiac death, ventricular fibration, sustained ventricular tachycardia, or hospitalization due to heart failure.

**Results:** Forty-seven patients had definite CS and the other 54 had probable CS. Except for serum angiotensin-converting enzyme levels and left ventricular dysfunction, clinical characteristics were similar between the two groups. Over a median follow-up of 15 months (range, 1–149 months), MACE occurred more frequently in patients with probable CS than in those with definite CS (74% vs. 53%, p=0.029). Kaplan-Meier analysis showed that the event-free survival rate was worse in patients with probable CS than in those with definite CS (log-rank test, p=0.006). Cox proportional hazard analysis showed that MACE were independently associated with probable CS, New York Heart Association functional class III or IV, and history of sustained ventricular tachycardia or ventricular fibrillation.

**Conclusion:** Outcomes are worse in patients with probable CS than in those with definite CS treated with steroids. Our finding suggest that the initiation of steroid treatment can be considered for patients who satisfy only clinical cardiac findings for CS. Further investigation is needed to assess therapeutic strategies for patients with probable CS and to determine how the diagnostic approach is modified.

**P6550 | BEDSIDE**

**Prevalence and impact of coronary artery disease in patients with Takotsubo cardiomyopathy**

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**Background:** Takotsubo cardiomyopathy (TTC) is suggested to occur in the absence of coronary artery disease (CAD). However recent studies show, that CAD may be present in patients with TTC. Therefore, the role of CAD in TTC has been underestimated, and data on the prevalence and its impact on prognosis are still limited.
Purpose: We sought to investigate the prevalence of CAD and its impact on prognosis in patients with TTC.

Methods: 1639 patients with TTC were enrolled in our study. Out of these 1517 patients with complete information on the coronary artery status were included in the final analysis.

Results: Coexistent obstructive CAD was present in 15.3% (n=233) of all TTC patients. Out of these, 21.9% were diagnosed with multi-vessel disease (MVD; n=51) while 78.1% (n=182) presented with only single-vessel disease (SVD). 65.2% (n=152) of the patients had mid-grade stenosis of 50–69% and 34.8% had high-grade stenosis of ≥70% (n=84). The mortality (13.3% vs. 7.8%, p=0.004) and MACCE rate (20.0% vs. 13.6%, p=0.003) of TTC patients with CAD was substantially higher in patients without significant stenosis after 5 years of follow up. Patients with TTC and MVD had even higher mortality (25.5% vs. 10.4%, p=0.002) and MACCE rates (33.3% vs. 17.0%, p=0.001) compared to those with SVD. In a multivariate analysis, MVD emerged as an independent predictor of death and MACCE (HR 3.10, 95% CI 1.14–8.40, p=0.027; HR 2.80, 95% CI 1.17–6.67, p=0.021; respectively).

Conclusions: Our study highlights that the prevalence of CAD is higher than previously thought. Furthermore, co-existence of CAD might lead to a worse outcome including increased death and MACCE rates. MVD is probably associated with an unfavorable prognosis in patients with TTC.

P6551 | BENCH

YKL-40 in chronic heart failure: Analysis from the controlled rosuvastatin multinational trial in heart failure (CORONA)

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Background: The inflammatory biomarker YKL-40 is associated with the presence and severity of coronary artery disease and may predict adverse outcome. We hypothesized that circulating YKL-40 can give prognostic information in patients with ischemic heart failure (HF) and identify a subgroup of patients who may benefit from statin therapy.

Methods: The association between serum levels of YKL-40 and the primary end point (cardiovascular [CV] death, nonfatal myocardial infarction, nonfatal stroke), all-cause mortality, CV death, the composite of all-cause mortality/hospitalization for worsening of HF or the coronary end point was evaluated in 1344 patients aged >60 years with ischemic HF in a subset of patients from the Controlled Rosuvastatin Multinational Trial in HF (CORONA) population (n=5011), randomly assigned to rosuvastatin 10 mg or placebo.

Results: Serum levels of YKL-40 were associated with outcome in univariate analysis, but added no predictive information after full multivariable adjustment including hs-CRP and NT-proBNP. Statin treatment moderately reduced YKL-40 levels, whereas an increase was observed with placebo (difference in change between the groups p=0.002). A significant interaction between baseline YKL-40 and rosuvastatin on the primary endpoint (p=0.008) and CV death (p=0.027) was observed. Thus, whereas rosuvastatin had no effect on those with intermediate or high YKL-40 levels, patients with low YKL-40 had significantly reduced CV death by rosuvastatin in tertile 1 also after full adjustment (primary outcome, HR 0.50 [0.30–0.82], p=0.006; CV death, HR 0.54 [0.30–0.97], p=0.040).

Conclusions: Circulating levels of YKL-40 were of limited predictive value in patients with chronic ischemic systolic HF. However, a beneficial modification of outcome was observed with statin therapy in patients with low YKL-40 levels.

P6552 | BEDSIDE

Clinical utility of combined platelet count and neutrophil-to-lymphocyte ratio in predicting cardiovascular outcome in patients with chronic heart failure

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Background: Neurohumoral and inflammatory activation is thought to play a key role in the pathophysiology of Chronic Heart Failure (CHF) and inflammatory cytokines such as interleukin-6 (IL-6) have been associated with the disease progression, mediating adverse cardiac remodelling. Neutrophil-to-Lymphocyte ratio (NLR) and reactive thrombocytosis are cellular components of systemic inflammation, which are modulated by cytokines especially IL-6. Here we investigated the prognostic impact of a combination of platelet count and NLR (collectively named the CPNR) in predicting cardiovascular outcome in CHF patients.

Methods: We reviewed 1557 CHF patients (mean age 75±11 y, 66% males) from the BIOSTAT-CHF Scotland cohort. Blood were drawn and routine laboratory measurements including full blood count was performed at baseline from which NLR and platelet count was determined. Patients with both an elevated platelet count (>275) and an elevated NLR (>3) were allocated a score of 2, and patients showing two or neither were allocated a score of 0 or 1, respectively. Multivariable Cox proportional hazard models were used to evaluate the prognostic impact of CPNR.

Results: Mortality rates (95% CI) were higher in CPNR 2 (CHF: 129, & CVD: 116 deaths per 1000 person years) as compared to CPNR 1 (CHF: 86, & CVD: 99 deaths per 1000 person years) and CPNR 0 (CHF: 28 & CVD: 42 deaths per 1000 person years) and a multivariable Cox proportional hazard model showed that CPNR was a significant risk factor for cardiovascular outcome (CHF, HR=1.65 CI: 1.3–2.2; CVD, HR=1.5 CI: 1.2–1.9) and CHF hospitalization (HR=1.3 CI: 1.1–1.5).

Conclusion: An elevated CPNR is significantly associated with worse outcome in CHF patients. The CPNR is an inexpensive, easy to perform test and can be used in risk stratification of CHF patients.

P6553 | BEDSIDE

Incidence and predictors of new-onset heart failure in patients with atrial fibrillation: the fushimi af registry

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Background: Heart failure (HF) is the important comorbidity associated with atrial fibrillation (AF) and related to poor prognosis. Despite that pre-existent HF or organic heart disease is a strong predictor for development of HF, it is suggested that AF per se may precipitate HF. However, the incidence and predictors of new-onset HF in AF patients without prior HF or organic heart disease were not clearly understood.

Methods: The Fushimi AF Registry, a community-based prospective survey, was designed to enroll all of the AF patients who visited the participating medical institutions in Japan. Follow-up data were available in 1,279 patients (3.4 ± 1.3 follow-up periods, 777 days). At baseline, 2,070 patients had neither prior HF (history of HF hospitalization, HF symptoms, or left ventricular (LV) dysfunction (EF < 40%)) nor any organic heart disease (valvular heart disease, cardiomyopathy, previous myocardial infarction). We investigated the incidence and predictors of new-onset HF in these patients.

Results: During the follow-up period, 64 (3.1%) patients experienced hospitalization for HF (incidence rate of 1.4 per 100 person-years). The incidence of HF was much less than that in the patients with prior HF or heart disease (7.8 per 100 person-years; p < 0.0001). Patients developing new-onset HF were older than those without HF development, and had more comorbidities including previous stroke, anemia, chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), and mild LV dysfunction (EF<60%); the prevalences of hypertension and coronary artery disease were comparable between the groups. In the univariate analysis, age, type of AF (permanent or persistent), previous stroke, anemia, CKD, COPD, prescription of loop diuretics, and mild LV dysfunction were associated with new-onset HF. Multivariable Cox proportional hazard analysis showed that female gender (hazard ratio (HR) 2.1, 95% confidence interval (CI) 1.1–4.1), anemia (HR 3.1, 95% CI 1.5–6.1), COPD (HR 4.8, 95% CI 1.7–11.6), and mild LV dysfunction (HR 3.2, 95% CI 1.6–6.4) were independent predictors for new-onset HF. In the Kaplan-Meier analysis, new-onset HF was associated with higher mortality during the follow-up period (34.8% vs 11.7%, p < 0.006).

Conclusion: Among AF patients, those without prior HF or organic heart disease are less likely to develop new-onset HF, and it was associated with poor prognostic value factors for short-term mortality of patients with acute heart failure have been reported, their prognostic predictive abilities, mostly evaluated at admission, are not satisfactory. We examined whether sequential organ failure assessment (SOFA) score obtained during treatment had further impact in addition to traditional prognostic factors.

Methods: We investigated consecutive 432 acute heart failure patients hospitalized in cardiac care unit from January,2009 to December, 2013 (mean age:75.7±15.2y.o., female:46.7%, mean LVEF:42.8±16.5%, ischemic etiology:30.8%). An elevated SOFA score on admission were significantly associated with worse outcome (30-day mortality). We made prognostic risk score of 30-day mortality from traditional risk factors at admission (age, systolic blood pressure, blood level of hemoglobin, blood urea nitrogen and sodium) and evaluated prognostic value of maximal SOFA score during treatment (with exception of neurological criterion) by multivariable logistic regression analysis.

Results: Thirty-day mortality was 6.3% (27 cases). In addition to risk score at admission (Table), maximal SOFA score after admission was identified as an independent prognostic factor of 30-day mortality (Odds Ratio [95% confidence Interval]: 1.45 [1.27–1.70], p<0.0001; 0.0001, 0.0037, respectively), and showed more detailed risk stratification (Figure).

Conclusion: Sequential organ failure assessment during treatment might have remarkable impact on mortality in acute heart failure. We might be able to predict
30-day mortality of acute heart failure

Results: After a 1-year follow-up, 197 deaths were identified. Those who presented with CTP class B or C had a markedly increased risk of death in comparison to patients with CTP class A, with an adjusted hazard ratio of 2.0 (95% confidence interval, 1.5 to 2.8; P<0.001). After combining with renal function based on estimated glomerular filtration rate (eGFR) of either ≥60 mL/min/1.73m², the highest risk was observed when CTP class B or C and eGFR <60 mL/min/1.73m². When only one of their functions was abnormal, patients with CTP class B or C have more risk of death compared with patients with eGFR ≥60 mL/min/1.73m².

Conclusions: CTP scores significantly associated with death in patients with ADHF, and may be a stronger predictor for death than eGFR.

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P6558 | BEDSIDE
Prognostic impact of fat volume in men versus women with acute decompensated heart failure

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Background: Obesity paradox is well recognized in patients with heart failure, which is traditionally based on body mass index (BMI). Although fat distribution varies by gender, the prognostic impact of body composition (fat mass) has not been fully elucidated in patients admitted with acute decompensated heart failure (ADHF), relating to gender.

Methods and results: We studied 301 patients admitted with ADHF (men, n=170 and women, n=131) who were consecutively followed up with 6 months. Simple body mass index (BMI) was calculated as weight divided by height squared (kg/m²). The percentage of fat mass (%FM) was calculated by the following estimated formula: body weight (kg) – (7.38×0.02908+urinary creatinine[mg/day]). We used percentage of fat mass (%FM) normalized by their body weight. During a follow-up period of 4.2±3.2 yrs, 95 patients died. At multivariate Cox analysis, %FM but not BMI was significantly associated with the mortality independently of age, systolic blood pressure, estimated glomerular filtration rate and serum sodium level in not only men but also women. Patients with lower %FM (below the median value) had a higher risk of mortality than those with

P6559 | BEDSIDE
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higher %FM in men (%FM -15.2%; adjusted hazard ratio: 2.1 95% CI [1.2–3.8], 49% vs 22%, p = 0.0001) and women (%FM-20.8%; adjusted hazard ratio:2.4 95% CI [1.1–5.2], 36% vs 17%, p = 0.0056).

Conclusion: Lower percent body fat was associated with the long-term poor outcome in both gender with ADHF, which suggested that adipose tissue is cardioprotective in the context of ADHF.

P6559 | BEDSIDE
Worsening heart failure in acute decompensated heart failure admissions: In-hospital and post discharge impact on prognosis
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Worsening heart failure (WHF) identifies patient subset with poor prognosis in acute decompensated heart failure (ADHF) admissions. However, its real impact on outcome is not fully understood.

Aims: To describe the prevalence and impact of WHF on hospital, post discharge and 180-day prognosis in patients (P) admitted for NYHA class III/IV ADHF.

Methods: A total of 693 consecutive P admitted for ADHF between March 2011 and December 2014 were analyzed. WHF was defined as worsening signs or symptoms of ADHF requiring rescue IV therapy. Demographic, clinical and biochemical data were compared. In-hospital, post discharge and 180-day outcomes were reported.

Results: WHF was present in 127 P (18.3%). Although both groups did not differ in terms of gender, comorbidities and previous treatment, WHF P were younger (65 vs 71 years old; p < 0.001) and had more frequently clinical evidences of hypoperfusion (35 vs 7.8%; p < 0.001) admission. P with WHF had lower blood pressure (113/70 vs 137/79 mmHg; p < 0.001), left ventricular ejection fraction (34±17 vs 41±16%; p < 0.001), low T3 serum level (80 vs 69%; p = 0.03), higher right ventricular systolic pressure (54±23 vs 46±15 mmHg; p < 0.001) and Uraemia (66±38 vs 58±32 mg/dl; p = 0.02), as more frequently hypotraenemia (61 vs 47%; p < 0.001), and Cholestasis (91 vs 80%; p = 0.001) admission.

In-hospital mortality (27.6 vs 5.7%; p < 0.001; OR 6.3; CI95% 3–10) and early readmission (45.8 vs 19.4%; p = 0.001) were higher in WHF P, but follow-up mortalit-y and readmission rates were similar at 180-d (p=NS).

Length of stay (LOS) was longer in WHF P (15 vs 7 days; p < 0.001), as prolonged LOS (>7 days) (76 vs 34%; p < 0.001). In-hospital complications were more frequently observed in P with WHF, including Diuretic resistance (24 vs 5%; p < 0.001) and inotropic use (59 vs 14%; p < 0.001).

Whereas the combination of low T3 levels, cholestasis and hyponatraemia at admission was highly prevalent in WHF P (36 vs 0%; OR 1.6; CI95% 1.3–1.9; p < 0.001), hypotraenemia at admission (HR 3.4; CI95% 1.8–6; p < 0.001) and worsening renal function (HR 2.5; CI95% 1.5–4; p = 0.001) were identified as independent predictors of WHF development.

We found low T3 at admission (HR 4.6; CI95% 1.3–15; p = 0.001), WHF (HR 3.7; CI95% 1.8–8; p < 0.001) and Diuretic resistance (HR 3.6; CI95% 1.8–8; p = 0.002) as independent predictors of in-hospital mortality.

Conclusions: WHF was prevalent in P admitted for ADHF. It was associated with more complications during hospitalization for ADHF, including in-hospital mortality and early readmission. WHF risk prediction at admission might aid in decision making in ADHF setting.

P6560 | BEDSIDE
Prognosis and predictive factors for normalization of left ventricular ejection fraction in dilated cardiomyopathy
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Introduction and purpose: Our aim is to know what factors are related to restoration of the left ventricular ejection fraction (LVEF) in order to early identify this subgroup of patients with a better prognosis.

Methods: A cohort of 387 consecutive outpatients with dilated cardiomyopathy was analyzed. We considered that LVEF was normalized when it was over 55% at the end of follow-up.

Results: Mean age 64.5±12.1 years, female gender 25.6%. Mean follow-up was 64.5±12.1 months. Normalization of the LVEF occurred in 20.9% (81 p) of patients.

Regarding long-term prognosis, overall mortality or heart transplantation (HTx) was 5.1% (4p) in patients with normalization of LVEF vs 30.1% (93p) in patients with impaired LVEF (p < 0.001). Combined event (death, HTx or heart failure hospitalization) was 9.0% (7 p) in patients with normal LVEF vs 45% (139 p) in patients depressed LVEF.

Factors independently related to normalization of the LVEF were female gender (OR 2.22; 95% CI 1.15–4.35; p = 0.018), New York Heart Association–Functional Class (NYHA–FC) at the end of the follow-up (OR 0.47; 95% CI 0.30–0.74; p < 0.001), presence of atrial fibrillation (OR 0.53; 95% CI 0.28–0.99; p = 0.05), number of coronary arteries with severe stenosis (OR 0.41, 95% CI 0.27–0.65; p < 0.001), degree of mitral regurgitation at the end of the follow-up (OR 0.29, 95% CI 0.10–0.8; p = 0.01) and time until first event –death, HTx or hospitalization for heart failure (OR 1.02, 95% CI 1.01–1.03; p = 0.020).

Conclusions: LVEF was normalized in a fifth of the population which had a significantly better prognosis.

The profile of the patient who normalized LVEF was a woman with mild NYHA–FC, without atrial fibrillation, absence of severe stenosis in coronary arteries, lack of significant mitral regurgitation and no early cardiac events.

P6561 | BEDSIDE
Age, clinical characteristics and outcomes for patients hospitalized with acute heart failure: insights from the Gulf acute heart failure registry (Gulf CARE)
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Background: Acute Heart failure (HF) is a leading cause of hospitalization for adults and associated with worse outcomes worldwide.

Purpose: To evaluate age differences in clinical characteristics and outcomes among patients hospitalized with acute HF in the Middle East.

Methods: Data were collected from the Gulf acute heart failure registry (Gulf CARE) which is a retrospective multicenter study from seven adjacent Gulf countries. Patients were divided into 3 groups: <65 years, 65–74 years and ≥75 years and their clinical characteristics and hospital outcomes were analyzed. Mortality and re-hospitalization rates were assessed at 3 and 12 month follow up.

Results: Among 5,005 consecutive acute HF patients. The overall mean age was 59±15 years, 60% were <65 years, 25% were 65–74 years and 15% were ≥75 years old. Increasing age was associated with higher rates of diastolic HF and Co-morbid chronic diseases. Among elderly, ischemic and hypertensive heart diseases were the most prevalent cause of acute HF (P < 0.001). Elderly patients were more likely to have higher systolic blood pressure, higher troponin, first BNP or NT-Pro BNP, first mean urea and creatinine levels, and lower heart rate (P < 0.001 for all). Moreover, they are more likely to have worse in-hospital course: Atrial fibrillation, stroke (P < 0.04), major bleeding and systemic infection (P < 0.05). The 3- and 12 months mortality and re-hospitalization rates were higher in elderly (P < 0.001 for all) (Table 1). Old age was independent predictors for 3-month (age 65–74: OR 1.55; 95% CI 1.15–2.08, and age ≥75: OR 2.90; 95% CI 1.54–5.40) and 12-month mortalities (age 65–74: OR 1.68; 95% CI 1.39–2.04, and age ≥75: OR 2.22; 95% CI 1.15–4.35; p = 0.018). The 3- and 12 months mortality and re-hospitalization rates were higher in elderly (P < 0.001 for all) (Table 1).

Conclusion: Age, clinical characteristics and outcomes for patients hospitalized with acute heart failure: insights from the Gulf acute heart failure registry (Gulf CARE)
Conclusions: Elderly patients hospitalized with acute HF had differential characteristics and unfavorable short- and long-term outcomes. Evidently there is need for substantial research to improve outcome of acute HF among elderly patients.

Acknowledgement/Funding: Gulf CARE is an investigator-initiated study conducted under the auspices of the Gulf Heart Association and funded by Servier, Paris, France.

P6562 | BEDSIDE
Troponin I by new ultrasensitive single molecule array technology: the determinants and prognostic role in chronic systolic heart failure

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Introduction: Even small elevations of cardiac troponin I (cTnI) may have clinical significance.

Purpose: We examined determinants and prognostic value of cTnI measured by novel ultra-sensitive assay in a heart failure (HF) cohort.

Methods: Stable advanced HF patients referred for ICD/CRT or pre-transplant (Tx) work-up, underwent in-hospital assessment and were prospectively followed (combined endpoint of death/urgent Tx/LVAD). cTnI was measured by an automated digital immunoassay based on single molecule array (SIMOA) technology (LoD: 0.01 ng/L).

Results: 362 patients (84% males, NYHA 2.7±0.6, 54% coronary disease-CAD) were examined. cTnI was detected in 100% (median: 15.3 ng/mL, IQR: 7.6–35.7, range: 0.4–1770, left-skewed distribution). Log-cTnI was significantly higher in males (+30%), diabetics (+24%), in patients with CAD (+24%), atrial fibrillation (+48%) and/or without ACEi/ARB therapy (+142%). Log cTnI correlated with age (+0.17), LV mass (+0.17), eGFR (+0.15), fasting glucose level (+0.20) and HgbA1C (+0.15). After 1086±724 days, 55% patients reached the endpoint. Log-cTnI was associated with worse outcome by K-M (figure A) and Cox analyses (HR 1.45, 1.2–1.8, p=0.0008). The association was considerably stronger in the lower range (<200 ng/L) of cTnI distribution (figure B). In the untransformed data, cTnI was associated with outcome only after removal of 2.5% of outlying values (< 400 ng/L) that likely reflect silent IM or myocarditis.

Conclusions: cTnI predicts long-term outcomes in stable HF patients, particularly in the low-range of values, most likely reflecting pathological processes distinct from high-range elevations. Low-range cTnI elevations are associated with aging, CAD, gender, diabetes, renal dysfunction, atrial fibrillation and lack of ACEi/ARB therapy.

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P6564 | BENCH
Characteristics and outcome of patients admitted to hospital with heart failure according to the severity of peripheral oedema in the national (England & Wales) heart failure audit

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Introduction: The main presentations of heart failure requiring admission to hospital are breathlessness and peripheral oedema; many patients present with a mixed picture. Most studies of “acute” heart failure focus on breathlessness but peripheral oedema might be the more important presentation. We have here tested the hypothesis that severity of oedema is associated with in-hospital mortality during index admission and after discharge.

Methods: Data was collected from April 2007 to March 2013 in more than 90% of hospitals in England & Wales for patients with a primary death or discharge diagnosis of heart failure. For this analysis, patients were grouped into “no”, “mild”, “moderate” and “severe” peripheral oedema. Patients’ characteristics and mortality during the index hospital admission for up to three years after discharge were reported.

Results: Of 136,790 patients with a confirmed diagnosis of heart failure, peripheral oedema on admission was absent in 24%, mild in 25%, moderate in 32% and severe in 18%. Patients without oedema were younger (median age 77 years) as compared to mild, moderate and severe oedema (80, 80, and 79 years respectively (P <0.001). Patients who had no oedema were more likely to have LVSD (68%) as compared to other groups (60%, 56% and 54% respectively) (P <0.001) and had shorter length of stay during the index admission (6 (IQR 3–13) days compared to 7 (IQR 3–14), 9 (IQR 5–17) and 12 (6–21) days respectively (P <0.001). Index admission mortality was 7%, 8%, 10% and 16% (P<0.001) respectively and at final censorship 39%, 46%, 52% and 59% (median follow-up 344 (IQR 94–766) days). The hazard ratio of death was 1.79 in patients with severe (P <0.001). 1.49 with moderate (P <0.001) and 1.23 (P <0.001) with mild oedema when compared with those patients who did not have oedema.

Conclusion: Fewer patients with severe peripheral oedema had LVSD compared to those presenting with mild, moderate or no oedema. Mortality during index admission and after discharge increased with severity of peripheral oedema.

P6565 | BEDSIDE
Determinants of shock and mortality in Takotsubo cardiomyopathy: a cohort study

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Introduction: Takotsubo cardiomyopathy (TTC) is a form of catecholamine-induced myocardial inflammation. Once considered a rarity, TTC is now recognized as accounting for up to 10% of “heart attacks” in women, with associated in-hospital mortality of approximately 3%, largely through development of cardiogenic shock with preceding hypotension. We have shown that hypotension in TTC is multifactorial, encompassing vasodilatation as well as negative inotropy. We have now sought to identify both clinical and physiological determinants of (1) shock, and (2) in-hospital death associated with shock among TTC patients.

Methods: We evaluated 208 consecutive TTC patients (94% female; median age of 67 years old). Of these, 29 (13.9%) developed shock and died subsequently died. Apart from demographics, we considered extent of endogenous catechol release, inflammatory activation (CRP, NT-proBNP) and haemodynamics as possible modulators of outcomes utilizing univariate followed by multivariate analyses.
Results: (A) Determinants of shock: On univariate analyses, both CRP and NT-proBNP release were significantly higher in patients developed shock (Figure 1) with CRP remained a significant (p<0.05) multivariate correlate. (B) Determinants of mortality: Patients who died were significantly older than those who survived shock (76±14 vs 63±17, p<0.05) and were more likely to have received treatment with intravenous catechol (73% vs 45%, p<0.00): the latter was a multivariate determinant of mortality (p<0.05).

Conclusion: These data suggest that clinical measures of extensive inflammatory activation in TCC predicts shock, and emphasize that further administration of catechol in such patients may be counter-productive.

P6568 | BEDSIDE Atrial fibrillation in acute heart failure: A secondary analysis of the ALARM-HF registry

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Background: Atrial fibrillation (AFib) has been associated with worse outcome in heart failure patients, but hitherto evidence remains inconclusive. We assessed the clinical characteristics and short-term outcome in AHF patients presented with AFib in 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 clinical characteristics and in-hospital mortality between patients with AFib at presentation and those in sinus rhythm (SR).

Results: Baseline AFib was present in 2184 patients (44%), including 982 with paroxysmal AFib and 1044 with permanent AFib. Compared to patients in SR, those with AFib were significantly older, more frequently female and had more frequently NYHA class III or IV symptoms (all p<0.001) along with higher prevalence of non-cardiovascular comorbidities including lung disease, chronic renal disease, anemia and depression (all p<0.001; for anemia, p=0.030). In-hospital mortality was higher in AFib patients [crude HR: 0.79, 95% CI: (0.67, 0.95), Figure]. This difference was eliminated after adjustment for several baseline variables [adjusted HR: 0.87, 95% CI: (0.57, 1.32), Figure]. Similarly, subgroup analyses by baseline characteristics showed no significant differences in mortality after adjustment.

Conclusions: Hospitalized AHF patients with AFib at presentation represent a high-risk group with increased in-hospital mortality. This worst short-term outcome seems to be related to their constellation of risk factors and comorbidities and not to the arrhythmia itself.

P6567 | BEDSIDE Echo and natriuretic peptide guided therapy in chronic systolic heart failure: a propensity score analysis from an observational study of 1,137 patients

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Background: Natriuretic peptides (NPs) and echo-Doppler are not only useful tools in acute heart failure (HF), their role may be also valuable in the manage- ment of stable patients during long-term follow-up, since they can actually con- tribute to a more complete understanding of the pathophysiology of the disease. Therefore, we believe that NPs and Doppler echocardiography, when utilized se- rial in an integrative and personalized manner, can be useful in monitoring ambu- latory patients that are high risk for exacerbation with a significant benefit to the clinical outcome. The complimentary of methodologies can overweight their intrinsic limitations, with crucial benefits for the patient.

Aim: The purpose of our study was to investigate the role of Doppler echocar- diography and NPs assessment during follow-up visits in ambulatory patients with chronic HF.

Materials and methods: This was a multicenter, retrospective, observational study that involved 1,137 consecutive outpatients (total cohort) previously hospi- talized for HF. Group A (Echo-NP-guided group) consisted of 570 patients (mean EF%: 0.30±0.08), whose management was guided according to the presence of echo-Doppler signs of elevated left ventricular filling pressure and NPs serum lev- els; whereas group B (clinically-guided group) consisted of 567 pts (mean EF%: 0.33±0.09), whose management was based on clinical judgment, and echocardiog- raphy was repeated only if symptoms changed. Propensity score matching was used to match pairs based on treatment strategy (matched cohort).

Results: The median follow-up duration was 40 months. During follow-up, after propensity matching, worsening of renal function (>0.3 mg/dL increase in serum creatinine) was observed in 12% of group A and in 23% of group B (p<0.001). The dose of loop diuretics did not change in Group A, while it increased by 13% in group B (p<0.0001). Survival analyses showed a lower incidence of death (HR 0.59, 95% CI: 0.37–0.95, p=0.031), and death or worsening renal function (HR 0.68, 95% CI: 0.48–0.98, p=0.036) in group A compared to group B.

Conclusion: The results of this observational study suggest that patient’s man- agement can be effectively guided on the basis of Doppler echocardiography and NPs. The improvement in clinical outcome of stable patients with systolic HF who underwent follow-up evaluations that included echocardiography and assessment NPs can be attributed to prevention of clinically overt pulmonary congestion, re- fractoriness to loop diuretics and a better titration of cardiovascular drugs.

PROGNOSIS V

P6568 | BEDSIDE Outcomes prediction in heart failure by measures of heart rate variability dynamics

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Purpose: Chronic Heart Failure (CHF) patients in New York Heart Association (NYHA) Class 1 or 2 for symptoms with a left ventricular ejection fraction of 35% or less and electrocardiogram evidence of asynchronous contraction of the heart may now receive treatment with Cardiac Resynchronisation Therapy (CRT) with a defibrillator (CRT-D) in order to improve quality of life, prognosis and symptoms. Until recently, only patients in NYHA Class 3 or 4 received this treat- ment. CRT-D has higher device-related mortality than CRT alone, has a finite benefit scope with only a subset of patients truly yielding benefit, and is more costly. With the use of CRT-D set to increase, identification of patients with a low risk of sudden cardiac death (SCD) is important but remains a challenge. Heart rate variability (HRV) is an independent predictor of mortality in CHF pa- tients. The authors investigated applying a novel mathematical algorithm to CHF patients whose long-term follow up data and HRV are known.

Methods: The R-R intervals extracted from 24 hour ambulatory ECGs recorded as part of the UK-HEART trial were reanalysed. For each subject the differential entropy H (calculated over 24 hour HRV sequences) and D coefficient (derived from the relationship between the short (u)1 and medium term (u)2 fractal dimen- sions determined by detrended fluctuation analysis) were recorded to investigate two novel metrics of HRV. The impact of H & D on survival was evaluated by fitting a Cox model. The data set comprised 397 CHF patients in NYHA Class 1 to 3 for symptoms.

Results: Both H and D have strong association with survival (p<0.0001). Spear- man’s test of rank correlation showed a significant negative correlation between the two quantities, suggesting they are measuring different aspects of HRV dy- namics. The bootstrap estimate of the area under the receiver operating charac- teristic curve (a measure of discrimination accuracy) was 0.69. A prognostic index was created which allowed patient stratification into high and low risk groups.

Conclusions: The parameters derived from differential entropy and fractal anal- ysis of HRV are strongly associated with survival in CHF patients. Previously, only HRV characterised by variance and low frequency spectral power exhibited a weak association. This novel approach allows a low-risk subgroup of patients with CHF to be identified with high specificity, providing better predictions of death compared to currently available methods, allowing expensive and risk-inducing in- vasive device therapies to be targeted more appropriately.
P6569 | BENCH
Increase in ultra-sensitive troponin I is associated with poor prognosis in patients with acute heart failure
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Background: Novei ultra-sensitive assays for cardiac troponins (TnI) allow to reliably detect very low cardiac Tn concentrations in the blood reflect of minor myocardial damage. We evaluated whether such tests may provide practically useful information for the management of patients with acute heart failure (AHF).

Methods: For this study, we prospectively recruited patients hospitalized with AHF who on admission had cardiac TnI level assessed in our hospital laboratory below 3-times of the upper reference limit (URL, ie <0.21 ng/mL). Ultra-sensitive cardiac TnI (us-TnI) analysis was based on new diagnostic platform - immunoassay-besides enzyme immunoassay (Singulex, Alameda, CA). The blood samples were taken on admission, after 24, 48 hours and on discharge. A significant rise in us-TnI was defined as at least one subsequent us-TnI value 20% higher than baseline.

Results: We analyzed 136 patients with AHF (age: 65±13 years, 78% men, 22% AHF de novo). The median us-TnI levels with the percentage above the usTnI URL (ie < 10.19ng/mL) were: on admission: 13.13ng/mL (59%), 24-h: 13,16ng/mL (60%), 48-h: 13,27ng/mL (55%), on discharge: 1:02ng/mL (51%). Among 96 patients who presented on admission with negative TnI measured with standard methodology in our laboratory 42% had usTnI above URL. These patients had higher creatine level, more often coronary artery disease, chronic kidney disease and diabetes mellitus (p<0.01 in all comparisons). During hospital stay, significant rise in us-TnI was detected in 40% of patients. These patients had all-cause mortality (26.3% vs 4.9%, p=0.002) and more often had diabetes mellitus (p<0.001), in all comparisons). During 1-year follow-up there were 36 (26%) cardiovascular deaths. Baseline level of usTnI did not predict survival (log-rank test p=0.7), however, 1-year cardiovascular mortality was significantly higher in those who developed us-TnI rise (39% vs 16%, p=0.024). Interestingly, in the multivariable models us-TnI rise either at 24 or 48 hours (HR: 2.7 [1.1–6.8], p=0.04) and at 24 or 48 or on discharge (HR: 3.1 [1.0–9.5], p=0.05) was associated with higher mortality.

Conclusion: In AHF patients, assessment of cardiac troponin I with the ultra-sensitive, provides important clinical message including prognostic information. This test may be useful to identify high risk patients whom might be appropriate for more aggressive management.

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P6570 | BESIDE
Sleep-disordered breathing are associated with impaired cardiac sympathetic innervation and incrementally predict prognosis in heart failure patients
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Background: Unfavorable effects of sleep-disordered breathing (SDB) in heart failure patients are well established. Aim of the present study was to assess the relationship between SDB, cardiac sympathetic innervation and prognosis in HF patients.

Methods: Ninety-four patients (66±18 years) with systolic HF (median left ventricular ejection fraction 32.1%) underwent nocturnal cardiorespiratory monitoring to assess presence and type of SDB by Apnea/Hypopnea Index (AHI), and sympathetic innervation and incrementally predict prognosis in heart failure patients. We considered 342 TI patients enrolled in the Myocardial Iron Overload (ICM) and chronic heart failure (CHF). To investigate the relationship between gene variants in endogenous hydrogen sulfide synthesis enzymes gene variants in the 5-year prognosis of patients with ischemic cardiomyopathy related chronic heart failure in Chinese Han population
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Backround: Endogenous hydrogen sulfide (H2S) is considered as the third gaseous transmitter and exert cardio-protective actions in ischemic cardiomyopathy (ICM) and chronic heart failure (CHF).

Results: Endogenous hydrogen sulfide synthesis enzymes gene variants in the 5-year prognosis of patients with ischemic cardiomyopathy related chronic heart failure in Chinese Han population

P6571 | BESIDE
Multi-parametric cardiac magnetic resonance for prediction of cardiac complications in thalassemia intermedia: a prospective multicenter study
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Background: Cardiovascular Magnetic Resonance (CMR) has an established role in managing and predicting prognosis of patients with Thalassemia Major (TM), Thalassemia Intermediare (TI), a milder variant of beta-thalassemia seen in a different clinical and prognostic profile; pulmonary hypertension (PH) is a more common complication in TI patients. We prospectively determined the predictive value of CMR parameters, including measurement of right ventricular mass by CMR, in patients with TI.

Methods: We considered 342 TI patients enrolled in the Myocardial Iron Overload Network in Thalassemia network; about half of them (178/302, 59.9%) were transfusion-dependent. Myocardial and liver iron overload were measured by T2* multi echo technique. Atrial dimensions, left and right ventricular mass and systolic function were quantified by cine images. Late gadolinium enhancement (LGE) images were acquired to detect myocardial fibrosis.

Results: Twenty-three patients were excluded because a cardiac complication was present at the time of first CMR, so we prospectively followed 319 patients. All 319 patients were white, with a mean age at time of their first scan of 38.02±11.69 years and 165 (51.7%) of them were females. Mean follow-up time was 52.2±24.87 months (median 54.64 months).

Cardiac events were recorded in 22 patients (6.9%); heart failure (HF) in 1 patient, arrhythmias in 12 patients, pulmonary hypertension (PH) in 7 patients and myocardial infarction (MI) in 2 patients. Due to the low number of events, only arrhythmias, PH and cardiac complications globally considered were taken as cardiac outcomes for univariate and multivariate analysis.

In the multivariate analysis RV hypertrophy was the only independent predictive factor for arrhythmias (HR=33.83, 95% CI: 6.07–188.74, P<0.0001) and PH (HR=73.33, 95% CI: 10.00–537.57, P<0.0001). When cardiac complications were considered all together, RV hypertrophy (HR=14.12, 95% CI: 11.42–14.12, P<0.0001) and myocardial fibrosis by LGE (HR=6.59, 95% CI: 1.33–32.67, P<0.021) were independent prognostic factors in the multivariate analysis.

Conclusions: For the first time we studied the prognostic value of right ventricular mass by CMR imaging in TI patients. We found that RV hypertrophy identified patients at high risk for arrhythmias and PH. Both RV hypertrophy and fibrosis detected by LGE were independent predictive factor for cardiac complications. Measurement of RV mass should be part of the multi-parametric CMR study of patient with thalassemia intermedia.
P6573 | BEDSIDE

The role of GDF-15, a marker of fibrosis, in cardiogenic shock
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Purpose: To investigate circulating levels of Growth-differentiation factor 15 (GDF-15) in cardiogenic shock (CS) and their associations with etiology, markers of myocardial injury and all-cause mortality.

Methods: GDF-15, TnT and NT-proBNP was determined at baseline in 178 patients with CS of various etiologies in the prospective European multi-center CardiShock study. Differences in GDF-15 levels between groups of CS etiology (acute coronary syndrome (ACS) (n=143) and non-ACS (n=35)) were assessed and the influence of GDF-15 on 90-day mortality.

Results: Mean age was 67 years, 26% were women and 42% of the patients died. Median levels of GDF-15 in the study population was 9577 pg/ml (interquartile range (IQR) 4502 - 19115), with no significant difference between ACS and non-ACS groups (8647 pg/ml [IQR 4497–18232] vs. 9171 pg/ml [IQR 4617–29825]; p=1.0). The correlation of GDF-15 with hsTnT (rs 0.137, p=0.07) or NT-proBNP (rs 0.37, p<0.001) was moderate at most.

Mortality at 90 days was higher in patients with GDF-15 levels above median (all p<0.05). ACS group 59% vs. 31%, p<0.001; non-ACS group 41% vs. 17%, p=0.11). In univariate analysis GDF-15 above median was significantly associated with 90-day mortality (OR 3.0; 95% CI 1.6–5.7; p=0.001). On a multivariable analysis GDF-15 above median still seemed to be associated with a doubling of 90-day mortality risk (OR 2.4; 95% CI 0.9–6.3; p=0.07).

Conclusions: GDF-15 levels are markedly elevated on admission in CS of both ACS and non-ACS etiology. There is no relevant correlation between levels of GDF-15 and TnT, a measure of myocardial injury. GDF-15 levels above median are associated with increased mortality in CS, but the clinical utility of GDF-15 in this population with very high overall mortality remains to be determined.

P6574 | BEDSIDE

The use of different methods for the selection of patients with non-ischemic cardiomyopathy for cardiac resynchronization therapy
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Aim: The aim of the study was to use various methods of selection of patients for cardiac resynchronization therapy (CRT) and to evaluate prospects of methods implementation in clinical practice to increase treatment efficacy.

Materials and methods: The study comprised a total of 180 patients aged 32 to 75 years (55±12 years) with dilated cardiomyopathy (DCM), NYHA functional class III heart failure, left ventricular (LV) ejection fraction (EF) of 30.13±8.6%, 6-min walk test distance of 290.5±64.3 m, end diastolic volume (EDV) of 220.7±50.9 mL, intraventricular and interventricular dysynchrony of >120 ms. At the selection stage, patients were divided into three groups: group 1 (n=50) that received assessment of myocardial metabolism defect (MMD) by radionuclide methods, group 2 (n=70) that received assessment of tricuspid annular systolic velocity (TASV), and control group.

Results: One-year follow-up study showed that 141 patients (78.3%) clinically responded to CRT; 39 patients (21.7%) did not respond to CRT. Evaluation of the selected methods demonstrated that 6 (12%) 127.24±3%, 20 (33.3%) patients did not respond to CRT in group 1, 2, and 3, respectively. Group 1 included 44 responders (88%) whose MMD was >15% prior to CRT; if initial MMD was >15%, patients did not respond to CRT. Group 2 included 53 responders (75.7%) whose TASV was >10 cm/s (12.5±2.1 cm/s) (p=0.0001).

Conclusions: (1) Preserved myocardial metabolism (LV MMD <15%) is a predictor of efficacious CRT in DCM patients. (2) Tricuspid annular systolic velocity is an independent predictor of response to CRT; TASV enables to identify CRT responders with sensitivity of 85% and specificity of 83% at the selection stage. (3) For selection of patients for CRT, the administration of all presented methods is rational in order to increase treatment efficacy.

P6575 | BEDSIDE

Prognostic predictors in a population-based cohort study of outpatients across different heart failure phenotypes
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Background: Although heart failure (HF) is a syndrome characterized by important variability in clinical manifestations and response to treatment, there is paucity of information on the different predictive factors and their prognostic impact across HF phenotypes.

Purpose: To evaluate and compare the predictive power of prognostic factors in a population-based cohort study of outpatients with different HF phenotypes (LVEF<40% - HfEF; LVEF 41–49% - HFrEF; LVEF ≥50% - HfPEF).

Methods: From November 2009 to October 2013, we retrospectively considered all consecutive HF outpatients, with available LVEF, enrolled in the Cardiovascular Observatory. Clinical variables of study population were derived from the E-data chart for Outpatient Clinic collected in a regional Data Warehouse.

Results: A total of 2424 patients (57% males; mean age 78±8; NYHA 3–4 20%) were considered. Of these, 1457 (60%) had HfEF, 358 (15%) HFrEF, 609 (25%) HfPEF. At a follow-up of 28±14 months, 502 patient were dead (21%), 168 (28%) among HfEF cases, 60 (17%) among HFrEF and 273 (19%) among HfPEF. The overall high mean age and frequent non cardiac comorbidities (median number 2) ran similarly across different HF phenotypes. In the overall population, the multivariable model included age (HR 2.41; p=0.003), male sex (HR 1.63; p<0.001), NYHA class III-IV (HR 1.52; p=0.009), systolic blood pressure (SBP) <110 mmHg (HR 2.05; p<0.001), hypernatremia (HR 1.68; p=0.028), anemia (HR 1.43; p=0.011), diabetes mellitus (HR 1.46; p=0.019), chronic obstructive pulmonary disease (HR 1.41; p=0.028), moderate-to-severe aortic valve disease (HR 1.45; p=0.048) and ACE/ARBs (HR 0.68; p=0.014) significant only in HfPEF. Among predictors, SBP <110 mmHg (HR 2.45; p=0.05) and betablockers (HR 0.67; p=0.036) were significant only in HfEF, whereas anemia (HR 1.42; p=0.027), betablockers (HR 1.41; p=0.046) and ACE/ARBs (HR 0.68; p=0.014) were significant only in HfPEF.

Conclusions: In our cohort study of outpatients characterized by advanced age and frequent non cardiac comorbidities, covariates generally included in available risk HF models showed distinctly different predictive power according to HF phenotypes. These data suggest that HF risk models could be effectively applied in real world patients across different HF phenotypes.

P6576 | BEDSIDE

Severe hyponatremia and in-hospital deterioration of sodium is associated with increased mortality in patients admitted with acute heart failure

Introduction: Hyponatremia predicts poor prognosis in patients with acute heart failure (AHF). However, the association of severity of hyponatremia and changes of sodium (Na) level with long-term outcome has not been delineated.

Methods: Patients hospitalized for AHF composed this registry. Data of biochemically and echocardiographic parameters were collected. Hyponatremia was defined as serum Na level <135 mEq/L. Linking to National Death Registry identified the clinical outcomes of all-cause mortality and cardiac death, with a follow-up duration of up to 4 years.

Results: Among 2556 patients, 360 patients (78.0±12.4±year-old, 63.6% men) had on-admission hyponatremia. The hyponatremic subjects were older, with more co-morbidities of diabetes and stroke. Among the hospitalization, 1051 subjects had decreases of Na level at discharge. The on-admission Na levels were...
In Kaplan-Meier analysis, patients with high SYNTAX scores (≥) confidence interval: 1.04 to 1.11; P<0.0001) After accounting for age, sex, medications, hematocrit, and renal function, subjects with hyponatremia at admission and decreasing Na level during hospitalization have an increased risk of death (HR 2.222, 95% CI 1.292–3.283) with reference to those with normonatremia at admission and on-treatment non-dropping Na level.

**Conclusion:** The on-admission hyponatremia is an independent predictor of in-hospital, short-term, and long-term mortality in hospitalized patients of AHF. Combined the on-admission hyponatremia with the changes of Na level during hospitalization further improved the risk classification of AHF.

**P6579 | BEDSIDE**

**Comparison of usefulness of coronary SYNTAX score in patients with prior heart failure with preserved ejection fraction versus with reduced ejection fraction: a sub-analysis of shinano registry**

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**Background:** Coronary artery disease (CAD) is common in patients with heart failure (HF), but little is known about the prognostic significance of coronary lesion complexity in patients with HF with preserved ejection fraction (HFpEF) versus those with reduced ejection fraction (HFrEF).

**Purpose:** To investigate whether coronary SYNTAX score, which is a coronary lesion complexity scoring system, could improve risk stratification in HF patients with CAD, and to compare the usefulness of SYNTAX score in patients with HFpEF vs. HFrEF.

**Methods:** We enrolled 200 patients (age, 73±11 years) with prior HF who underwent percutaneous coronary intervention. Patients were tracked prospectively for 12 months. The study endpoint was the composite of major adverse cardiovascular events (MACE) including all-cause death, myocardial infarction, and stroke.

**Results:** Adverse events were observed in 33 patients (16.5%). Ninety-nine patients were HFpEF (EF ≥50%) and 101 patients were HFrEF (EF <50%). In Kaplan-Meier analysis, patients with high SYNTAX scores (≥12.5) showed worse prognoses than those with low SYNTAX scores (<12.5) (27.2% vs. 7.4%, P<0.0001). Multivariate Cox proportional hazards analyses revealed that SYNTAX scores were inversely associated with in-hospital, short-term, and long-term mortality in patients with AHF.

**Conclusions:** In prior HF patients with CAD, high SYNTAX scores predicted a high incidence of MACE. SYNTAX score might be a more useful parameter to improve risk stratification in patients with HFpEF than those with HFrEF.

**Prognostic value of NT-proBNP in heart failure with preserved versus reduced ejection fraction (From the Korean Heart Failure [KoHF] registry)**

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**Introduction:** Although plasma level of NT-proBNP is a reliable prognostic factor in patients with heart failure (HF), it is still unclear how differently it predicts adverse outcomes in HF with preserved ejection fraction (HFpEF) versus versus reduced ejection fraction (HFrEF).

**Purpose:** To identify the prognostic value of N-terminal–pro-brain natriuretic peptide (NT-proBNP) in HFpEF versus HFrEF.

**Methods:** From the Korean Heart Failure (KoHF) registry, a prospective multicenter cohort for consecutive patients who were hospitalized for acute HF syndrome, those with valid NT-proBNP and left ventricular ejection fraction (LVEF) measurements were extracted. Patients with LVEF >40% were categorized as the HFpEF (N=467), and those with ≤40% as the HFrEF groups (N=1,018).

**Results:** Patients with HFrEF had significantly lower NT-proBNP level than those with HFpEF. NT-proBNP levels and clinical outcomes

**Conclusion:** The on-admission hyponatremia is an independent predictor of in-hospital, short-term, and long-term mortality in hospitalized patients of AHF. Combined the on-admission hyponatremia with the changes of Na level during hospitalization further improved the risk classification of AHF.
with HF–EF (3.312 pg/mL vs. 5.644 pg/mL, p < 0.001). Event-free survival did not differ between the two groups either in terms of death from any cause (88.3% vs. 86.4%, p = 0.151) or the composite of death or HF readmission at 1 year (72.6% vs. 71.2%, p = 0.375). Increasing levels of NT-proBNP was significantly associated with poor outcomes. However, the relationship was not different among the HF–EF and HF–PE groups (interaction p = 0.987 for all-cause death; p = 0.349 for the composite of all-cause death or HF hospitalization).

Conclusion: Plasma level of NT-proBNP is the most powerful prognostic factor in both HF–EF and HF–PE. Although patients with HF–PE have lower NT-proBNP levels, the prognosis of a patient with HF–PE referred from a given NT-proBNP level is similar with his/her counterpart with HF–EF.

**P6580 | BEDSIDE**

Which patient with left ventricular ejection fraction ≤40% and when during 3 years after discharge home from acute myocardial infarction - analysis of joined PL-ACS and AMI-PL registries

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Patients with left ventricular ejection fraction (LVEF) ≤40% require close monitoring after discharge from AMI. Therefore we assessed which patient with LVEF ≤40% and when during the 3 years after discharge from AMI had the worst survival function and when die during 3 years after discharge home from acute myocardial infarction - analysis of joined PL-ACS and AMI-PL registries.

Methods: PL-ACS is a clinical registry, however it does not cover all hospitals. AMI-PL is a nationwide database of AMI, derived from the only public, obligatory, health insurer in Poland, and provide data on hospitalizations, procedures, and deaths. We combined PL-ACS and AMI-PL data for 4461 survivors from AMI discharged home in 2009 with LVEF ≤40%.

Results: Patients with LVEF ≤40% comprised 26% of all discharged patients. Of them 87% were treated invasively. 3-year mortality after discharge was 30% and one-third of deaths were during first 6 months following AMI (figure). Predictors of 3-year mortality are presented in the table.

**Table 1**

<table>
<thead>
<tr>
<th>Relative risk (95% CI)</th>
<th>Relative risk (95% CI)</th>
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<tbody>
<tr>
<td>Age (per 5 years more)</td>
<td>1.25 (1.21–1.29)</td>
</tr>
<tr>
<td>LVEF (per 5% less)</td>
<td>1.23 (1.18–1.28)</td>
</tr>
<tr>
<td>Invasive treatment</td>
<td>0.68 (0.58–0.8)</td>
</tr>
<tr>
<td>History of renal failure</td>
<td>1.23 (1.18–1.28)</td>
</tr>
<tr>
<td>History of follow-up</td>
<td>1.43 (1.22–1.69)</td>
</tr>
<tr>
<td>NYHA class (per 1 more)</td>
<td>0.98 (0.97–1.01)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.12 (1.08–1.16)</td>
</tr>
<tr>
<td>Current smoking</td>
<td>0.9 (0.8–1.0)</td>
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**Conclusion:** Patients discharged home after AMI with reduced LVEF ≤40% are at high risk of death especially during first 6 months.

**P6581 | BEDSIDE**

Right ventricle deformation, systolic function and pressure overload which one the key prognosticator in outpatients with systolic heart failure

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Background: Right ventricle (RV) geometry and function, along with the pulmonary pressure are major predictors of the outcome in outpatients with systolic heart failure (SHF).

Aim: To evaluate which one the key prognosticator in outpatients with SHF: the RV deformation, systolic function or pressure overload.

Population and methods: 143 outpatients with SHF followed-up in a Heart failure unit, age 68.0±12.6 years old, NYHA class III (34.3%) and median NT-proBNP 1871 pg/mL. RV systolic function was characterized by the TAPSE and RV systolic dysfunction or pressure overload.

Results: 1) 3-year death rate was 36.4%. 2) Death was significantly associated with greater sPAP (p=0.009), lower TAPSE (p=0.007) and STr (p=0.001) and worst RVGS (p=0.001). 3) The ROC curve for death was associated with sPAP (AUC=0.63 p=0.027), TAPSE (AUC=0.65 p=0.003), STr (AUC=0.7 p=0.002) and RVGS (AUC=0.73 p=0.001). (3) The survival curve and greater risk of death was associated with the worst quartile of all parameters. However the TAPSE –16.8 (HR=5.8, 95% CI 1.7–19.9; p=0.005) was the independent predictor of survival.

**Conclusion:** RV systolic function, deformation and pressure overload were strong predictors of the 3-year survival of outpatients with SHF. Nevertheless, TAPSE which is an easy to perform measure was the independent predictor of death.

**P6582 | BEDSIDE**

KIM-1 and NAG: new predictors for long-term progression of chronic kidney disease in patients with heart failure

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Background: Patients with chronic heart failure (CHF) are often characterized by the cardiorenal syndrome (CRS). The aim of the present study was to assess which novel markers of kidney dysfunction in patients with CHF are able to predict progression of chronic kidney disease (CKD) in patients with CHF.

Methods: New renal biomarkers, kidney injury molecule-1 (KIM-1), N-acetyl-B-D-glucosaminidase (NAG) and Neutrophil Gelatinase-Associated Lipocitin (NGAL), were assessed from urine samples of 191 patients included in the AMI-PL registry. During a 5-year-follow-up, renal function was assessed by creatinine and eGFR (MDRD) and was available for 135 patients (the other 14 patients died). Further, data regarding all-cause mortality was obtained.

Results: 35 patients (26%) developed a progression of chronic kidney disease during the follow-up period, as defined by a reduction of at least one CKD stage. No difference regarding age, sex, BMI, hypertension, diabetes or EF was present between patients with and without progressive renal disease (each p > 0.5). In baseline, creatinine concentrations and eGFR were significantly different between both groups (sCr: 1.21±0.72 vs. 1.05±0.41, p=0.049; eGFR: 64.2±20.7 vs. 78.1±25.8 ml/min/1.73m², p=0.001). In a Kaplan-Meier-analysis, KIM-1 and NAG were predictors of progressive renal disease (both p < 0.01). In a Cox regression analysis, initial eGFR (OR 0.98, 95% CI 0.96–0.99, the p=0.002) and KIM-1–median (OR 2.5, 95% CI 1.22; 5.2; p=0.012) as well as NAG > median (OR 2.6, 95% CI 1.24; 5.45; p=0.012) were independent predictors of progressive renal disease. A ROC-analysis yielded satisfying predictive values for KIM-1 (AUC 0.65) and NAG (AUC 0.63) for progression of CKD. NGAL showed no association with progression of CKD. Further, KIM-1 and NAG were also independent predictors of a combined endpoint of progressive CKD and all-cause mortality by Cox regression analysis (each p < 0.05).

Conclusions: The present study demonstrates a significant progression of renal disease in patients with chronic heart failure during long-term follow-up. Furthermore, it shows a strong association of the new renal biomarkers KIM-1 and NAG with progressive kidney disease in these patients and suggests their usefulness as biomarkers of the cardiorenal syndrome.

Acknowledgement/Funding: none

**P6583 | BEDSIDE**

Impact of diabetes mellitus on acute heart failure

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Background and aim: The prevalence of heart failure among diabetic patients is reported as 20%. Conversely, several heart failure registry data reported high prevalence of diabetes mellitus reaching 40%. Although, the outcomes in heart failure patients combined with diabetes mellitus (DM-HF) have been suggested worse than those without diabetes mellitus (non-DM-HF), the effect of glycemic control has not been reported yet. We aimed to investigate the impact of diabetes mellitus in short term outcomes of acute heart failure patients.

Methods: We analyzed data from the Korean Acute Heart Failure Registry (KoAHF, n=5627) which is a registry of patients hospitalized for acute heart failure syndrome in a regionally-representative tertiary university hospitals in Korea.

Results: 1) 40% had diabetes mellitus. DM-HF patients were older (70.1±11.6 vs 67.4±10.6, p=0.001), more men (55% vs 52%, p=0.017), had more hypertension (72% vs 50%, p<0.001), chronic renal disease (21.6% vs 9.5%, p<0.001), whereas had less atrial fibrillation (25.2% vs 29.1%, p<0.001) than non-DM-HF. 2) Ischemia was both the leading cause (52.7%) and the most frequent aggravating factor (36.1%) in DM-HF patients, which were far more than in non-DM-HF patients (27.5% and 19.8% respectively). Hospital mortality among DM-HF patients was 60% higher than non-DM-HF patients (6.1% vs 3.9%, p<0.001). The difference remained significant after adjusting gender, age, history of hypertension, ischemic heart disease, functional status and serum creatinine.
4) Among DM-HF patients, the status of hyperglycemic control in the range of HbA1C 6–8% did not have any impact either on in-hospital mortality or short-term follow up during 6 months. However, surprisingly, DM-HF patients managed on insulin (DM-HF-Insulin, 49.7% of DM-HF patients) had far worse in-hospital mortality of 9.2% compared with DM-HF patients managed on oral hypoglycemic agents (DM-HF-OHA) (1.5%, p=0.001). In-hospital mortality difference remained significant after adjusting gender, age, history of hypertension, ischemic heart disease, functional status, Hba1C and serum creatinine. If DM-HF-OHA were confined, in-hospital mortality and short-term results were not significantly different compared with non-DM-HF patients.

Conclusions: DM-HF patients had worse prognosis than non-DM-HF patients. Hyperglycemic control status might have little impact either on in-hospital mortality or short-term follow up. Although DM-HF-OHA patients did not have worse outcomes compared, DM-HF-I insulin patients have three folds higher in-hospital mortality, which warrants long-term study.

Acknowledgement/Funding: Research of Korea Centers for Disease Control and Prevention

P6584 | BEDSIDE
Heart failure epidemiology: a population-based analysis of 88,195 patients
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Methods: Population based study that included all the patients with diagnosis of HF in the health areas of the Catalan Health Service. Patients were divided in 3 groups: HF diagnosis made at the primary care setting, patients with a remote (< 1 year) and with a recent (≤ 1 year) HF admission. We analysed 1-year (2013) readmissions, survival and costs.

Results: A total of 88,195 cases were analyzed, of which 14% were HF diagnosis at primary care setting, 71% with a remote HF admission and 15% with a recent HF hospitalization. Mean age was 77.4 years, 55% were women. Comorbidities were frequent, with a median of 6 comorbidities per patient. The most frequent were hypertension, ischemic heart disease, atrial fibrillation, anemia, diabetes, chronic obstructive pulmonary disease, chronic kidney disease, depression and cancer. One-year mortality rate in the whole cohort was 14%, but was higher in patients with a recent hospitalization (24%) than in patients with remote HF hospitalization (13%) and primary care diagnosis (11%). All-cause readmission and the combination of death/HF readmission was also higher in the recent HF hospitalization group compared to the other 2 groups (48% vs 29% vs 21% and 55% vs 34% vs 26%, respectively). In multivariable regression analysis, age, gender, HF group, number of hospital admissions and emergency room visits the previous year were found to be independently associated with the combination of death/HF readmission. Mean healthcare cost associated with heart failure was 6,571 € and was mainly driven by hospitalization (36% of expenditure), pharmacy (22%) and house calls (14%). Health-care costs were higher in patients with a recent hospitalization (9,892 €/year) and 26% of this group had an expenditure higher than percentile 85. The same data were 6,402 € and 14% for patients with a remote HF hospitalization and 4,323 € and 8% for primary care HF diagnosis.

Conclusions: HF patients with a recent hospitalization due to HF are at high risk of subsequent hospitalization or death at 1 year and account for the highest healthcare cost. Although this risk and cost decreases, it is still high in patients with a remote HF admission or primary care HF diagnosis.

P6585 | BEDSIDE
Left atrial emptying function predicts long-term outcome in HFpEF patients
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Background and aim: Although many prognostic variables have been reported, the risk stratification of patients with heart failure and preserved ejection fraction (HFpEF) is still controversial. We investigated the prognostic value of various conventional Doppler echocardiographic parameters on the clinical outcomes of a sample of such patients.

Methods: This study included 139 consecutive patients (62±10 years) with con- current 18-month outcomes with echocardiographic parameters (CE) and the need for hospitalization) due to acute HF signs and/or symptoms. LV end-diastolic and end-systolic dimensions, ejection fraction (EF), mitral and tricuspid annulus peak systolic excursion (MAPSE and TAPSE), myocardial velocities (s’, e’ and a’), left atrial (LAs) dimensions, LA volume and LA emptying fraction were all measured. Mean follow-up was 20.5±5 years.

Results: During the follow-up period, 53 patients (38%) had CE. The hemoglobin level was lower (P<0.02), LV mass index was higher (P<0.002), LA was larger (P<0.002), LV EDD (0.003) and LV ESV (P<0.02) were greater, E/e’ lower (P<0.01), LA emptying fraction was lower (P<0.001), in patients who had cardiac events compared to those who did not. Multivariate analysis identified age (OR=0.982, 95% CI 0.869–0.992; P=0.027) and LA emptying fraction (OR=0.931, 95% CI 0.869–0.997; P=0.041) as independent predictors of CE. A LA emptying fraction <60% was 70% sensitive and 65% specific (AUC 0.74, P<0.001) in predicting CE.

Conclusions: In medically treated patients with chronic HFpEF, left atrial function, but not LA diameter, was associated with increased risk of cardiac events. This study highlights the need for routine LA function monitoring for better optimization of medical therapy in HFpEF patients.
rehabilitations due to heart failure and mortality during 3 years following dis-
charge (table). In multivariat analyses adjusted for baseline characteristics and
parameters from the acute phase of AMI, both LVFE and NYHA class were sig-
nificant predictors of rehabilitations due to heart failure (LVFE HR=1.58, 95% 
CI: 1.50–1.66, p<0.0001; NYHA class HR=1.29, 95% CI: 1.19–1.40, p<0.0001) and
3-year mortality (LVFE HR=1.49, 95% CI: 1.42–1.56, p<0.0001; NYHA class 
HR=1.25, 95% CI: 1.16–1.34, p<0.0001).

<table>
<thead>
<tr>
<th>Rehabilitation due to heart failure</th>
<th>Mortality</th>
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<tbody>
<tr>
<td>NYHA I vs NYHA II or IV</td>
<td>LVFE ≥45%</td>
</tr>
<tr>
<td>NYHA I vs NYHA II or IV</td>
<td>LVFE 36–44%</td>
</tr>
<tr>
<td>NYHA I vs NYHA II or IV</td>
<td>LVFE 26–35%</td>
</tr>
<tr>
<td>NYHA I vs NYHA II or IV</td>
<td>LVFE ≤29%</td>
</tr>
<tr>
<td>NYHA I vs NYHA II or IV</td>
<td>NYHA I vs NYHA II or IV</td>
</tr>
<tr>
<td>NYHA I vs NYHA II or IV</td>
<td>NYHA I vs NYHA II or IV</td>
</tr>
</tbody>
</table>

Conclusion: Functional status at discharge home from AMI has an important
additional effect to left ventricular ejection fraction for long term outcomes.

TREATMENT OF HYPERTENSION II

P6589 | BEDSIDE
Nine-year target systolic blood pressure less than 120 mmHg for more than 65 aged hypertension patients with chronic renal disease

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Background: Many studies demonstrate that systolic blood pressure (SBP) ≥
120 mmHg can provide renal protection in renal disease with hypertension,
but SBP ≤120 mmHg may be able to slow progress of renal disease. How-
ever, target SBP ≤150 mmHg in elderly hypertension patients was recommended in Chinese hypertension guideline in 2005.The long-term safety and efficacy of SBP≤120 mmHg in elderly hypertension patients with chronic renal disease is hardly reported.

Methods: In a prospective, controlled open-label studies, the authors have eval-
uated the safety and efficacy of nine-year treatment on progress of renal dis-
ease and risk of development of cardiovascular disease in 122 -65 aged hy-
pertension patients with chronic renal disease III to IV stage and macroprote-
uria. Before randomization, all patients have already been treated for one-year
with angiotensin converting enzyme inhibitors (ACEI) or angiotensin AT1 receptor
blockade (ARBs) and other antihypertensive drugs, but their SBP are above 140
mmHg. Before randomization, all patients have already been treated for one-year
with or no medications.

Results: By the end of nine year,medication possession ratio between two
groups was similar (94% vs 94%), mean blood pressure in treatment group was
118/68±5/3 mmHg and in control =149±14/13±9 mmHg, Clr clearance increased from
0.6 to 0.8±0.2/m/l/min (p<0.01)in the group of strict control of SBPby contrast, Clr clearance decreased significantly from 52±1.9 to 30±2.8
m/l/min (P<0.01)in the controls. During this time, urine protein excretion decreased
from 1.4±0.5 to 0.2±0.9±24 hours (P<0.0001) in the treatment group, but increased
dramatically in the control group. (3) For patients whose hypertension duration was shorter than 5 years, IVSD decreases were greater than 5 years, IVSD decreases were greater than
0.9±5.2 vs. −0.1±5.8, P=0.033). However, there was no significant difference
between D group vs. D+Ex group.

Conclusion: SBP≤120 mmHg is safe and was more apparently in decreasing proteinuria, slowing the progress of renal disease and reducing the risk of de-
velopment of cardiovascular events in elderly hypertension patients with chronic renal disease and proteinuria.

P6589 | BEDSIDE
Effect of metformin on ventricular remodeling in patients with type 2 diabetes mellitus

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Objective: To explore the effects of metformin on left ventricular remodeling in patients with primary hypertension and type 2 diabetes mellitus as well as the effect of hypertension duration and duration of drug usage.

Methods: We retrospectively analyzed the clinical and echocardiographic data of 176 patients with primary hypertension and type 2 diabetes mellitus admitted to our hospital from January to December 2012. The follow-up period was 6 months to 2 years. The patients were classified into two groups according to the usage of metformin (M1=84) and control group (M2=92). Echocardiographic findings were evaluated both at baseline and follow-up. Sub-
group analyses were used to assess the effect of hypertension duration and duration of drug usage.

Results: (1) At baseline, there was no significant difference in interventricular septum depth (IVSD), left ventricular posterior wall depth (LVPWD), and left ventricular mass index (LVMI) between the two groups. At the follow-up period, IVSD (P=0.001), LVPWD (P=0.04) and LVMI (P=0.01) were lower in metformin group compared with control group. Multiple linear regression indicated that metformin had an important influence of LVMI (β=−0.69, standard error=−0.30, t=−2.31, P=0.02, 95% confidence interval –1.8 to −0.10) and LVMI (β=−6.38, standard error=2.79, t=−2.14, P=0.04, 95% confidence interval –13.7 to −0.71). At the follow-up period, LVMI was lower in both metformin groups compared with control group. For patients whose hypertension duration was shorter than 5 years, LVMI was the lowest in the group of which the patients took met-
formin for more than one year. It was significant lower than that in control group (P=0.04). (2) For patients whose hypertension duration was shorter than 5 years, at the follow-up period, LVMI (P=0.04) was lower in metformin group compared with control group. For patients whose hypertension duration was longer than 5 years, at the follow-up period, IVSD (P=0.01) and LVMI (P=0.02) were lower in metformin group compared with control group.

Conclusions: Metformin may attenuate left ventricular hypertrophy of patients with primary hypertension and type 2 diabetes mellitus. In patients with longer hypertension duration and longer duration of metformin use, metformin may show more effects on the attenuation of left ventricular hypertrophy of patients with primary hypertension and type 2 diabetes mellitus.

Acknowledgement/Funding: Supported by National Natural Science Founda-
tion of China (81030001,81300007)

P6590 | BEDSIDE
Randomized study to determine the effect of unmonitored diet and exercise education on blood pressure (the LSM study)

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Background: Life style modification, such as exercise therapy and Dietary Ap-
proaches to Stop Hypertension (DASH) diet, has been shown to be effective for peripheral arterial hypertension. However, most of the clinical studies regarding life style modification have been done in a monitored setting when in the real word setting, unmonitored diet and exercise are recommended to the patients.

Purpose: To evaluate how unmonitored recommendation of Korean DASH diet and exercise education affects blood pressure in patients with prehypertension or mild hypertension. Subjects with mild hypertension were defined as patients with office blood pressure between 140-160/90–100mmHg who were taking either no or 1 or medications.

Methods: A total of 76 patients, who were aged over 20 and diagnosed as either
prehypertension or mild hypertension, were randomly assign to the control (C) group (n=26), the diet education (D) group (n=25), and the diet and exercise education (D+Ex) group (n=26). The D group and the D+Ex group both received DASH diet education, and the D+Ex group received exercise education. The inter-
vention lasted for 8 weeks, and office BP, central BP, and 24-hour ambulatory
BP were examined before and after the study period. The trial was registered at ClinicalTrials.org (NCT01637909).

Results: Although office BP showed tendency to be reduced in the D+Ex group and the D group compared to the C group, it was not statistically significant. The D+Ex group showed significantly decreased 24 hour average ambulatory BP (systolic BP, −5.8±7.2 vs. −4.9±5.8 ±0.011; diastolic BP, −2.9±5.0 vs. −0.9±5.1 ±0.067) and daytime average SBP/DBP (systolic BP, −5.8±7.2 vs. −3.7±4.9 ±0.033; diastolic BP, −4.4±6.9 vs. −0.5±5.2 ±0.033). However, there was no significant difference in nocturnal ambulatory BP (systolic BP, −4.0±9.9 vs. −3.8±12.6 ±0.5±12.6 ±0.5±12.6
mmHg, P=0.322; diastolic BP, −1.3±7.2 vs. −0.5±7.8 ±0.652). Central aortic pressure showed a tendency to being reduced in the D+Ex group and the D group but without statistical significance.

Conclusion: Unmonitored life style modification through diet and exercise, but not diet alone, was effective for lowering blood pressure. Life style modification had emphasizing both dietary modification and exercise should be accentuated.

Acknowledgement/Funding: This study was supported by an industrial re-
search grant from Sanofi Aventis.

P6591 | BEDSIDE
Influence of fixed-dose combination perindopril/amlodipin on target organ damage in patients with arterial hypertension


To evaluate the antihypertensive effectiveness and changes of target organ dam-
age in patients with arterial hypertension (AH) on fixed dose combination (FDC) (perindopril) (A) and (amlodipin) (P) treatment.

There were included 30 patients (age≥30 yrs, untreated hypertenives with BP>160/100 and ≥200/120 mmHg or who were on monotherapy (except P), but their office BP =140/90 and <200/120 mmHg), whom were evaluated for blood pressure (BP), heart rate (HR), ankle-brachial index (ABI), biochemical blood analysis. Follow-up period was12
months. After wash-out period P/A administered in dose 5/5 mg with up-titration to 10/10mg every 2 weeks. Indapamide was added as the third drug. Primary end-points were BP lowering (office, systolic, central), significant (≥ SD) dynamic of target organ damage signs, tolerance of FDC. Baseline FDC were administered to 34 pts, but 4 were excluded due to intolerance (n=31) or the personal reasons. Office SBP/DBP decrease from 156.4±3.8/96.3±2.2 to 136.1±2.6/76.3±1.1 mmHg (p<0.0001/0.001), 24-hSBP/DBP from 140.2±1.9/86.6±2.2 to 117.8±1.4/74.2±1.1 mmHg (p<0.0001/0.001), cSBP from 142.8±2.5 to 118.3±2.7 mmHg (p<0.001). Target BP was achieved in all patients. Effective BP control followed by positive target organ changes (table). The changes of E/E' and a-albuminuria did not correlate with office BP lowering, but with aorta PWV and Aix75 decreasing. We did not note any significant changes of biochemical patterns.

**Patterns**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aorta PWV, m/s</td>
<td>11.9±0.7</td>
</tr>
<tr>
<td>All</td>
<td>1.00±0.5</td>
</tr>
<tr>
<td>Alburninuria, mg/24h</td>
<td>53.3±15.5</td>
</tr>
<tr>
<td>IMT, mm</td>
<td>1.1±0.03</td>
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<tr>
<td>LVMi, g/m²</td>
<td>108.6±5.5</td>
</tr>
</tbody>
</table>

**P<0.05.**

The treatment based on FDC (P/A) was effective not only in decreasing of office and ambulatory BP, but central SBP too. It led to decreasing of target organ damage. Diastolic left ventricular function and renal damage improving were con-

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**P6592 | BEDSIDE**

**Prevalence, treatment and control of hypertension in middle-aged Mexican adults**

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**Method:** Mexican cohort of 150,000 adults aged ≥35 years when recruited in 1998–2004.

**Purpose:** To analyze the relation between serum uric acid levels, and development of hypertension in a large adult population using the data from Belarusian and Mexican cohorts.

**Results:** There were 2170 persons with normal blood pressure and 1257 persons with hypertension in the studied population. Men and women were similar of mean age. In 5 years 285 new cases of hypertension developed. There was revealed a higher prevalence of hypertension in the studied population. Men and women were similar of mean age. In 5 years 285 new cases of hypertension developed. There was revealed a higher prevalence of hypertension in the studied population.

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**P6594 | BEDSIDE**

**Evaluation of β-thalassemia minor on metabolic profile in patients with newly diagnosed hypertension**

K.M. Lamproupiou1, A. Triantafyllou1, E. Triantafyllou1, P. Karkalousos2, G. Vyssylos1, E. Kapranoy2, K. Kappos1, Evangelismos General Hospital of Athens, Athens, Greece; 2Hippokration General Hospital, Athens, Greece

**Objective:** To analyze the relation between serum uric acid levels, and development of hypertension in a large adult population using the data from Belarusian and Mexican cohorts.

**Methods:** We evaluated metabolic parameters and risk-prediction equations in 23,680 consecutive subjects, that is, 11,192 women and 12,488 men, with newly diagnosed hypertension according to the presence or absence of Tm. Results: Two groups did not differ in gender distribution, age, body mass index or systolic or DBP, but Tm patients had a higher pulse pressure (p<0.01).

**Conclusions:** The study did not find a difference in gender distribution, age, body mass index or systolic or DBP, but Tm patients had a higher pulse pressure (p<0.01). In contrast, hypertensive patients with Tm had a better lipidic profile with significantly lower low-density lipoprotein (LDL, p<0.009), total cholesterol and triglycerides, and higher high-density lipoprotein levels (p<0.001), as well as lower waist-to-hip and waist-to-stature ratios (all p<0.001) compared with hypertensive patients without Tm. There was also a tendency for a lower prevalence of diabetes mellitus in Tm patients. As a result, Tm patients had a lower overall prevalence of metabolic syndrome (26% vs 39%; p<0.001).

**Conclusion:** Tm is a favorable cardiovascular and metabolic profile, beyond the well-known differences in serum lipids. Moreover, although gender differences do exist, women with Tm seem to be equally, if not more, protected as men.

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**P6595 | SPOTLIGHT**

**Serum uric acid and the risk of development of hypertension in the urban population**

O. Podpalova. Vitebsk State Medical University, Vitebsk, Belarus

**Objective:** To analyze the relation between serum uric acid levels, and development of hypertension in a large adult population using the data from Belarusian national representative survey.

**Method and design:** We conducted a 5-year prospective analysis of 3500 individuals living in a district of Vitebsk in 2007/2008 (coverage of the survey was 97.9%). 2010/2011 (coverage of the survey was 77.8%) and 2012/2013 (coverage of the survey was 84%). The initial survey was 84% complete, 2440 (84%) were evaluated according to the WHOISH (1999). The survey included standard questionnaires for detection of cardiovascular risks factors, measures of blood pressure, electrocardiography, serum C-reactive protein, uric acid and cholesterol data.

**Results:** There were 2170 persons with normal blood pressure and 1257 persons with hypertension in the studied population. Men and women were similar of mean age. In 5 years 285 new cases of hypertension developed. There was revealed a significant positive association between IV quartile of serum uric acid level (339–370 mmol/l) and the frequency of newly diagnosed cases of hypertension adjusted for age and sex (df=1; χ² Wald=5.1; p<0.05). According to multivariable regression analysis high uric acid level (>338 mmol/l) (p<0.001) the same as systolic blood level (>120 mmHg) and high body mass index level (>25.7 kg/m²) (p<0.001) are the
most significant factors affecting the frequency of new cases of hypertension in the studied population.

**Conclusions:** The results of our study showed that serum uric acid level is a risk factor of developing hypertension in Belarusian urban population.

**P6596 | BEDSIDE**

Association of urinary sodium excretion with blood pressure and cardiovascular clinical events in South America: The PURE study

P.L. Lamelas1, A. Mente1, M. O’Donnell1, S. Rangarajan1, R. Diaz2, F. Lanas3, P. Lopez Jaramillo1, A. Aveuzum4, K. Teo1, S. Yusuf1 on behalf of PURE investigators.

**Background:** Sodium intake is reported to be a modifiable determinant of hypertension, a principal risk factor for cardiovascular disease and mortality. Information on the relationship of sodium intake with blood pressure and clinical events in populations outside North America and Europe is limited, despite variation in sodium intake across geographic regions.

**Purpose:** Our aim is to assess the association of sodium intake with blood pressure, cardiovascular events and mortality in a cohort from four South American countries.

**Methods:** We studied 17,033 individuals, aged 35 to 70 years, from four South American countries (Argentina, Brazil, Chile and Colombia) participating in a large international prospective cohort. Measures of urinary sodium excretion (SE) were estimated from a morning fasting urine and were used as a surrogate for intake. We assessed the association of SE with blood pressure and the composite outcome of death and major cardiovascular events.

**Results:** Mean SE was 4.76±1.45 g/day per 2.8% of participants had a SE of less than 2.3 g per day, and 0.5% below 1.5 g per day. For each gram of estimated SE there was an increment of 1.52 mm Hg in systolic blood pressure (P<0.001) and an increment of 0.58 mm Hg in diastolic blood pressure (P<0.001). This positive association was nonuniform with steeper slope at a higher SE level (more than 5 g/day) compared to the slope at moderate (3 to 5 g/day) and low (less than 3 g/day) SE, for both systolic and diastolic blood pressure (p<0.002 and p<0.001 for interaction, respectively). With a median follow-up of 4.7 years, the primary composite outcome occurred in 568 participants (3.4%). Compared with SE of 5 to 6 g/day (the reference category), SE of greater than 7 g/day was associated with increased risks of the primary composite outcome (OR 1.73; 95% CI 1.24 - 2.40; P<0.001), death from any cause (OR 1.87; 95% CI 1.23 - 2.83; P=0.003), and major CV disease (OR 1.77; 95% CI 1.12 to 2.71; P=0.014) on multivariable analyses. SE of less than 3 g/day was associated with a nonsignificant increased risk of the primary composite outcome (OR 1.20; 95% CI 0.86 - 1.65; p=0.26), death from any cause (OR 1.25; 95% CI 0.81 to 1.93; p=0.29), and a significant increase in major CV disease (OR=1.50; 95% CI: 1.01 to 2.24; p=0.048), compared with SE of 5 to 6 g/day.

**Conclusions:** Our results support a positive, nonuniform association between estimated urinary SE and blood pressure, and a J-shaped pattern of association between SE and clinical outcomes in this South American cohort.

**Acknowledgement/Funding:** Heart and Stroke Foundation of Ontario, the PHRI, the CIHR, unrestricted grants from several pharmaceutical companies.

**P6597 | BEDSIDE**

The association between urinary sodium to potassium ratio and blood pressure by salt consumption level: the Takahata study

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**Background:** Previous epidemiological studies revealed that urinary Na-K ratio (UNa/K) would correlate to blood pressure (BP), however salt consumption levels in general Japanese population.

**Purpose:** We recruited 3519 participants in 2004–6 at Takahata town, Yamagata, Japan. We aimed to investigate the effects of UNa/K on BP by their salt consumption level in general Japanese population.

**Methods:** We recruited 3519 participants in 2004–6 at Takahata town, Yamagata, Japan. We assessed the association of UNa/K on BP level in this East Asian cohort, this association was attenuated in subjects with low sodium diet.

**Results:** Testosterone deficiency (TD) was defined when TT levels were below 3.4 ng/ml. The presence of carotid plaque and IMT were evaluated by ultrasonography.

**Methods:** Total testosterone (TT) levels were measured in 287 non-diabetic hypertensive men (mean age 55.17 years) with no evidence of clinical atherosclerosis. Testosterone deficiency (TD) was defined when TT levels were below 3.4 ng/ml. The presence of carotid plaque and IMT were evaluated by ultrasonography.

**Results:** 86 (30%) hypertensive patients had TD. Analysis with and without adjustment for age and blood pressure level showed that carotid IMT was inversely and significantly correlated with TT. This association depended on LDL levels (P for interaction <0.05). Subjects were categorized according to LDL levels ([Group 1: (<100 mg/dl); Group 2: (100–129 mg/dl); Group 3: (130–159 mg/dl) and Group 4: (>160 mg/dl)]. Among hypertensive patients with LDL 130–159 mg/dl and >160 mg/dl, patients with TD had significantly higher mean IMT compared to subjects with TT concentration above the cut off level for biochemical definition of TD (1.02 vs 0.94 mm, P<0.005 and 1.17 vs 0.97 mm, P<0.01, respectively, figure). The differences remained significant after adjustment for age and mean blood pressure (all P<0.05). By contrast, among men with either LDL<100 mg/dl or 100–129 mg/dl, mean IMT was similar in both groups (P=NS).

**Conclusions:** In hypertensive men, TD is associated with increased carotid IMT only in those with LDL levels greater than 130 mg/dl.
BP and periodontitis and CD8CD28null Tc

ships remained significant in multivariate analysis accounting for major clinical factors and treatments. Periodontitis severity was not associated with changes in classical, naive, effector or memory T cells or with CD14+CD16+/- monocytes. However, periodontal pocket depth was significantly related to prevalence of immunosenescent CD8+ T cells (CD8+CD28nullCD57+ p < 0.01), which had been linked to hypertension. There was a significant positive correlation between prevalence of these cells and blood pressure (Figure, R = 0.4, p < 0.01) and an inverse correlation with endothelial function (FMD, R = −0.5, p < 0.01). These relationships remained significant in multivariate analysis accounting for age, sex and clinical factors.

Conclusions: Severity of periodontitis affects hypertension control and vascular dysfunction. Increased peripheral blood immunosenescent CD8+ T cells may provide link between these pathologies.

Acknowledgement/Funding: The Wellcome Trust, National Science Centre of Poland, British Heart Foundatlon, Excellence Centre;